IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	42	6.3	2.2	-68.9	7.79	-59.2	(-78.6, -39.9)	9.78	<0.001***
		UPA 15 MG QD	37	6.4	2.9	-48.0	8.08	-38.3	(-58.3, -18.4)	10.08	<0.001***
		UPA 7.5 MG QD	40	6.8	3.9	-39.6	8.04	-29.9	(-49.4, -10.3)	9.90	0.003**
		PLACEBO	37	6.5	5.7	-9.7	8.30				
	US/PR/CANADA										
		UPA 30 MG QD	29	6.3	2.2	-70.0	8.20	-63.0	(-86.4, -39.6)	11.82	<0.001***
		UPA 15 MG QD	25	6.6	2.6	-54.3	8.81	-47.3	(-71.6, -23.1)	12.23	<0.001***
		UPA 7.5 MG QD	28	6.8	4.1	-34.7	8.33	-27.7	(-51.3, -4.2)	11.88	0.021*
		PLACEBO	27	6.7	6.0	-7.0	8.48				
	EU/AUS										
		UPA 30 MG QD	10	6.3	2.2	-68.4	13.69	-62.2	(-104.4, -20.0)	20.71	0.005**
		UPA 15 MG QD	9	6.2	3.2	-43.7	14.43	-37.4	(-80.5, 5.7)	21.18	0.087
		UPA 7.5 MG QD	10	6.8	3.3	-53.5	13.88	-47.3	(-90.3, -4.3)	21.11	0.032*
		PLACEBO	8	5.6	5.1	-6.3	15.53				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.4	-56.0	13.37	-12.8	(-66.0, 40.4)	20.70	0.563
		UPA 15 MG QD	3	5.2	4.4	-23.3	14.89	19.9	(-40.4, 80.2)	23.47	0.436
		UPA 7.5 MG QD	2	6.3	3.1	-43.6	16.20	-0.4	(-58.7, 57.9)	22.68	0.986
		PLACEBO	2	6.4	3.0	-43.2	16.49				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.398

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 1											
	ALL										
		UPA 30 MG QD	42	6.3	3.9	-36.2	4.17	-36.9	(-47.3, -26.6)	5.23	<0.001***
		UPA 15 MG QD	37	6.4	4.5	-28.3	4.32	-29.0	(-39.7, -18.4)	5.39	<0.001***
		UPA 7.5 MG QD	39	6.7	5.4	-19.0	4.33	-19.7	(-30.3, -9.2)	5.33	<0.001***
		PLACEBO	37	6.5	6.2	0.8	4.44				
	US/PR/CANADA										
		UPA 30 MG QD	29	6.3	3.9	-38.0	4.58	-39.0	(-52.1, -25.9)	6.61	<0.001***
		UPA 15 MG QD	25	6.6	4.4	-34.4	4.92	-35.4	(-48.9, -21.8)	6.84	<0.001***
		UPA 7.5 MG QD	27	6.7	5.2	-24.2	4.74	-25.2	(-38.5, -11.9)	6.70	<0.001***
		PLACEBO	27	6.7	6.5	1.0	4.74				
	EU/AUS										
		UPA 30 MG QD	10	6.3	3.9	-39.3	6.66	-34.1	(-54.6, -13.5)	10.07	0.002**
		UPA 15 MG QD	9	6.2	4.8	-20.5	7.02	-15.3	(-36.2, 5.7)	10.30	0.148
		UPA 7.5 MG QD	10	6.8	5.8	-13.8	6.75	-8.6	(-29.5, 12.3)	10.27	0.409
		PLACEBO	8	5.6	5.3	-5.2	7.55				
	JAPAN										
		UPA 30 MG QD	3	6.3	4.2	-33.6	1.91	-16.5	(-24.1, -8.9)	2.95	0.003**
		UPA 15 MG QD	3	5.2	4.1	-19.4	2.13	-2.3	(-10.9, 6.3)	3.35	0.520
		UPA 7.5 MG QD	2	6.3	5.8	-8.4	2.31	8.7	(0.3, 17.0)	3.24	0.044*
		PLACEBO	2	6.4	5.4	-17.1	2.35				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.540

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 2											
	ALL										
		UPA 30 MG QD	41	6.3	2.6	-58.3	5.20	-61.9	(-74.9, -48.9)	6.57	<0.001***
		UPA 15 MG QD	36	6.3	3.2	-46.7	5.40	-50.3	(-63.7, -36.9)	6.78	<0.001***
		UPA 7.5 MG QD	39	6.7	4.7	-28.9	5.37	-32.5	(-45.6, -19.3)	6.65	<0.001***
		PLACEBO	36	6.5	6.3	3.6	5.58				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.3	2.5	-61.5	5.35	-66.6	(-81.8, -51.4)	7.65	<0.001***
		UPA 15 MG QD	24	6.5	3.2	-53.0	5.77	-58.1	(-73.8, -42.4)	7.93	<0.001***
		UPA 7.5 MG QD	27	6.7	4.5	-33.2	5.44	-38.3	(-53.5, -23.0)	7.69	<0.001***
		PLACEBO	27	6.7	6.7	5.1	5.44				
	EU/AUS										
		UPA 30 MG QD	10	6.3	2.4	-64.8	10.24	-57.3	(-90.1, -24.6)	16.05	0.001**
		UPA 15 MG QD	9	6.2	3.5	-41.2	10.80	-33.6	(-67.1, -0.2)	16.39	0.049*
		UPA 7.5 MG QD	10	6.8	5.0	-28.0	10.36	-20.5	(-53.7, 12.8)	16.31	0.219
		PLACEBO	7	5.7	5.1	-7.5	12.37				
	JAPAN										
		UPA 30 MG QD	3	6.3	3.9	-39.7	10.77	-19.1	(-62.0, 23.7)	16.68	0.303
		UPA 15 MG QD	3	5.2	3.3	-34.0	12.00	-13.5	(-62.1, 35.1)	18.91	0.507
		UPA 7.5 MG QD	2	6.3	4.9	-24.0	13.06	-3.5	(-50.5, 43.5)	18.28	0.857
		PLACEBO	2	6.4	5.4	-20.5	13.29				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.499

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 3											
	ALL										
		UPA 30 MG QD	41	6.3	2.1	-64.7	5.45	-68.3	(-82.2, -54.3)	7.05	<0.001***
		UPA 15 MG QD	37	6.4	2.9	-50.7	5.61	-54.2	(-68.5, -40.0)	7.21	<0.001***
		UPA 7.5 MG QD	40	6.8	4.4	-32.6	5.59	-36.2	(-50.2, -22.2)	7.09	<0.001***
		PLACEBO	33	6.5	6.2	3.6	6.02				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.3	2.1	-67.8	5.70	-65.4	(-81.9, -49.0)	8.31	<0.001***
		UPA 15 MG QD	25	6.6	2.6	-60.2	6.01	-57.9	(-74.8, -41.0)	8.51	<0.001***
		UPA 7.5 MG QD	28	6.8	4.2	-38.2	5.69	-35.8	(-52.3, -19.4)	8.27	<0.001***
		PLACEBO	25	6.8	6.2	-2.3	6.02				
	EU/AUS										
		UPA 30 MG QD	10	6.3	1.7	-76.1	9.97	-95.3	(-128.9, -61.7)	16.46	<0.001***
		UPA 15 MG QD	9	6.2	3.5	-40.7	10.51	-59.9	(-94.2, -25.7)	16.77	0.001**
		UPA 7.5 MG QD	10	6.8	4.8	-34.2	10.10	-53.4	(-87.7, -19.2)	16.78	0.003**
		PLACEBO	6	5.4	6.4	19.2	13.10				
	JAPAN										
		UPA 30 MG QD	3	6.3	3.4	-46.1	8.12	-21.2	(-53.5, 11.2)	12.57	0.153
		UPA 15 MG QD	3	5.2	3.1	-38.4	9.05	-13.4	(-50.0, 23.3)	14.26	0.391
		UPA 7.5 MG QD	2	6.3	4.7	-25.6	9.84	-0.6	(-36.0, 34.8)	13.78	0.967
		PLACEBO	2	6.4	5.0	-25.0	10.02				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.306

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	6.3	2.0	-67.6	5.83	-69.5	(-84.5, -54.6)	7.54	<0.001***
		UPA 15 MG QD	36	6.3	2.8	-52.0	6.12	-54.0	(-69.4, -38.5)	7.81	<0.001***
		UPA 7.5 MG QD	40	6.8	4.3	-35.6	6.01	-37.5	(-52.6, -22.4)	7.63	<0.001***
		PLACEBO	33	6.5	6.2	1.9	6.49				
	US/PR/CANADA										
		UPA 30 MG QD	29	6.3	2.2	-67.0	5.86	-62.6	(-79.7, -45.5)	8.61	<0.001***
		UPA 15 MG QD	25	6.6	2.5	-61.6	6.29	-57.2	(-74.9, -39.6)	8.90	<0.001***
		UPA 7.5 MG QD	28	6.8	4.2	-37.9	5.95	-33.5	(-50.7, -16.4)	8.65	<0.001***
		PLACEBO	25	6.8	6.2	-4.4	6.29				
	EU/AUS										
		UPA 30 MG QD	10	6.3	1.3	-80.5	11.78	-102.5	(-142.3, -62.7)	19.46	<0.001***
		UPA 15 MG QD	8	6.1	3.5	-33.7	13.18	-55.7	(-97.1, -14.4)	20.23	0.010**
		UPA 7.5 MG QD	10	6.8	4.5	-37.5	11.96	-59.5	(-100.1, -18.9)	19.84	0.006**
		PLACEBO	6	5.4	6.6	22.1	15.46				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.7	-58.0	6.59	-38.8	(-65.0, -12.5)	10.21	0.013*
		UPA 15 MG QD	3	5.2	2.9	-42.3	7.34	-23.1	(-52.9, 6.6)	11.57	0.102
		UPA 7.5 MG QD	2	6.3	4.1	-35.8	7.99	-16.6	(-45.3, 12.2)	11.19	0.198
		PLACEBO	2	6.4	5.3	-19.2	8.13				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.193

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 5											
	ALL										
		UPA 30 MG QD	40	6.2	1.9	-71.1	6.23	-64.0	(-80.4, -47.6)	8.29	<0.001***
		UPA 15 MG QD	34	6.4	2.6	-54.2	6.56	-47.1	(-64.0, -30.1)	8.58	<0.001***
		UPA 7.5 MG QD	36	6.7	4.0	-37.4	6.59	-30.3	(-47.0, -13.5)	8.46	<0.001***
		PLACEBO	29	6.5	5.6	-7.1	7.19				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.2	1.9	-72.1	6.22	-63.1	(-81.4, -44.7)	9.25	<0.001***
		UPA 15 MG QD	24	6.6	2.4	-62.7	6.68	-53.7	(-72.6, -34.7)	9.55	<0.001***
		UPA 7.5 MG QD	27	6.8	4.3	-36.0	6.31	-26.9	(-45.4, -8.5)	9.28	0.005**
		PLACEBO	23	6.8	5.8	-9.1	6.83				
	EU/AUS										
		UPA 30 MG QD	9	6.1	1.5	-76.8	13.86	-76.8	(-129.2, -24.4)	25.26	0.006**
		UPA 15 MG QD	7	5.9	3.0	-34.7	15.69	-34.7	(-89.1, 19.7)	26.22	0.199
		UPA 7.5 MG QD	7	6.2	3.1	-51.5	15.74	-51.5	(-106.2, 3.3)	26.40	0.064
		PLACEBO	4	5.2	5.2	-0.0	21.02				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.6	-58.2	9.13	-31.1	(-67.5, 5.2)	14.14	0.079
		UPA 15 MG QD	3	5.2	2.9	-44.0	10.17	-16.9	(-58.1, 24.3)	16.03	0.340
		UPA 7.5 MG QD	2	6.3	4.2	-33.6	11.07	-6.6	(-46.4, 33.3)	15.49	0.689
		PLACEBO	2	6.4	4.7	-27.1	11.27				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.361

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 6											
	ALL										
		UPA 30 MG QD	39	6.2	1.8	-69.6	6.39	-61.1	(-77.9, -44.3)	8.50	<0.001***
		UPA 15 MG QD	34	6.4	2.8	-46.8	6.69	-38.3	(-55.6, -21.0)	8.74	<0.001***
		UPA 7.5 MG QD	36	6.6	3.8	-37.8	6.72	-29.3	(-46.3, -12.2)	8.62	<0.001***
		PLACEBO	29	6.5	5.4	-8.5	7.32				
	US/PR/CANADA										
		UPA 30 MG QD	27	6.2	1.8	-73.7	6.56	-57.4	(-76.6, -38.2)	9.68	<0.001***
		UPA 15 MG QD	24	6.6	2.5	-61.0	6.93	-44.7	(-64.4, -25.1)	9.90	<0.001***
		UPA 7.5 MG QD	27	6.8	4.0	-40.6	6.54	-24.3	(-43.4, -5.2)	9.63	0.013*
		PLACEBO	23	6.8	5.4	-16.3	7.08				
	EU/AUS										
		UPA 30 MG QD	9	6.1	1.3	-81.1	13.20	-77.9	(-127.8, -28.0)	24.06	0.004**
		UPA 15 MG QD	7	5.9	3.8	-24.5	14.95	-21.4	(-73.1, 30.4)	24.97	0.402
		UPA 7.5 MG QD	7	6.2	3.1	-53.2	14.99	-50.1	(-102.2, 2.1)	25.14	0.059
		PLACEBO	4	5.2	5.2	-3.1	20.02				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.9	-51.9	11.61	-50.9	(-97.1, -4.7)	17.97	0.037*
		UPA 15 MG QD	3	5.2	3.2	-40.9	12.93	-39.9	(-92.2, 12.5)	20.38	0.108
		UPA 7.5 MG QD	2	6.3	4.0	-34.1	14.07	-33.1	(-83.7, 17.6)	19.70	0.154
		PLACEBO	2	6.4	6.1	-1.0	14.32				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.297

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 7											
	ALL										
		UPA 30 MG QD	40	6.2	1.6	-73.5	6.80	-63.6	(-81.5, -45.7)	9.05	<0.001***
		UPA 15 MG QD	35	6.3	2.8	-49.6	7.11	-39.7	(-58.1, -21.3)	9.30	<0.001***
		UPA 7.5 MG QD	35	6.7	3.6	-42.2	7.26	-32.3	(-50.7, -13.9)	9.31	<0.001***
		PLACEBO	29	6.5	5.4	-9.9	7.85				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.2	1.7	-73.9	7.02	-56.0	(-76.7, -35.3)	10.45	<0.001***
		UPA 15 MG QD	25	6.6	2.8	-56.1	7.39	-38.2	(-59.4, -17.0)	10.68	<0.001***
		UPA 7.5 MG QD	26	6.8	3.9	-41.1	7.26	-23.2	(-44.2, -2.2)	10.58	0.031*
		PLACEBO	23	6.8	5.3	-17.9	7.71				
	EU/AUS										
		UPA 30 MG QD	9	6.1	1.2	-80.9	13.86	-98.3	(-151.2, -45.4)	25.51	<0.001***
		UPA 15 MG QD	7	5.9	2.7	-40.3	15.69	-57.7	(-112.5, -2.9)	26.42	0.040*
		UPA 7.5 MG QD	7	6.2	2.9	-53.4	15.75	-70.8	(-126.2, -15.5)	26.67	0.014*
		PLACEBO	4	4.8	5.9	17.4	21.24				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.0	-66.9	12.75	-60.1	(-110.8, -9.3)	19.75	0.029*
		UPA 15 MG QD	3	5.2	3.3	-36.1	14.21	-29.4	(-86.9, 28.2)	22.39	0.247
		UPA 7.5 MG QD	2	6.3	2.9	-52.7	15.46	-46.0	(-101.6, 9.7)	21.64	0.087
		PLACEBO	2	6.4	6.1	-6.8	15.74				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.489

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 8											
	ALL										
		UPA 30 MG QD	40	6.2	1.6	-72.9	6.79	-66.2	(-84.0, -48.3)	9.03	<0.001***
		UPA 15 MG QD	34	6.4	2.9	-48.5	7.20	-41.8	(-60.3, -23.4)	9.33	<0.001***
		UPA 7.5 MG QD	34	6.8	3.7	-42.5	7.30	-35.8	(-54.3, -17.3)	9.35	<0.001***
		PLACEBO	29	6.5	5.5	-6.7	7.84				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.3	1.6	-76.1	7.10	-59.2	(-80.1, -38.2)	10.57	<0.001***
		UPA 15 MG QD	25	6.6	3.0	-52.4	7.48	-35.4	(-56.9, -14.0)	10.81	0.001**
		UPA 7.5 MG QD	25	7.0	4.0	-42.1	7.51	-25.1	(-46.6, -3.7)	10.81	0.022*
		PLACEBO	23	6.8	5.3	-17.0	7.80				
	EU/AUS										
		UPA 30 MG QD	9	6.1	1.5	-77.3	13.00	-104.0	(-154.0, -54.0)	24.03	<0.001***
		UPA 15 MG QD	6	6.4	2.4	-56.3	16.01	-83.0	(-137.2, -28.9)	26.03	0.004**
		UPA 7.5 MG QD	7	6.2	2.9	-57.0	14.76	-83.7	(-136.0, -31.5)	25.13	0.003**
		PLACEBO	4	4.8	5.9	26.7	20.11				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.1	-65.2	12.98	-72.2	(-123.9, -20.6)	20.10	0.016*
		UPA 15 MG QD	3	5.2	3.3	-36.5	14.46	-43.6	(-102.1, 15.0)	22.78	0.114
		UPA 7.5 MG QD	2	6.3	3.1	-48.3	15.73	-55.4	(-112.0, 1.3)	22.02	0.054
		PLACEBO	2	6.4	6.9	7.0	16.01				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.469

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 9											
	ALL										
		UPA 30 MG QD	40	6.2	1.6	-73.1	6.55	-65.6	(-82.8, -48.4)	8.71	<0.001***
		UPA 15 MG QD	34	6.4	2.9	-49.6	6.94	-42.2	(-60.0, -24.4)	9.00	<0.001***
		UPA 7.5 MG QD	36	6.8	3.7	-41.9	6.89	-34.4	(-52.0, -16.8)	8.92	<0.001***
		PLACEBO	29	6.5	5.5	-7.5	7.55				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.2	1.5	-77.4	7.05	-60.0	(-80.8, -39.2)	10.49	<0.001***
		UPA 15 MG QD	25	6.6	2.9	-54.7	7.42	-37.4	(-58.6, -16.1)	10.73	<0.001***
		UPA 7.5 MG QD	26	6.9	3.9	-42.8	7.30	-25.5	(-46.5, -4.4)	10.62	0.018*
		PLACEBO	23	6.8	5.4	-17.4	7.74				
	EU/AUS										
		UPA 30 MG QD	9	6.1	1.6	-76.8	11.12	-101.2	(-143.7, -58.6)	20.53	<0.001***
		UPA 15 MG QD	6	6.4	2.6	-57.3	13.66	-81.7	(-127.8, -35.6)	22.23	0.001**
		UPA 7.5 MG QD	8	6.5	3.1	-55.2	11.87	-79.6	(-123.6, -35.6)	21.23	0.001**
		PLACEBO	4	4.8	5.9	24.4	17.25				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.1	-63.4	10.84	-63.4	(-106.6, -20.3)	16.79	0.013*
		UPA 15 MG QD	3	5.2	3.4	-37.5	12.08	-37.5	(-86.4, 11.5)	19.03	0.106
		UPA 7.5 MG QD	2	6.3	3.4	-43.1	13.14	-43.1	(-90.4, 4.2)	18.40	0.066
		PLACEBO	2	6.4	6.3	0.0	13.38				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.542

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 10											
	ALL										
		UPA 30 MG QD	39	6.2	1.8	-72.2	6.56	-60.8	(-78.3, -43.3)	8.85	<0.001***
		UPA 15 MG QD	34	6.4	2.8	-52.0	6.87	-40.6	(-58.6, -22.6)	9.08	<0.001***
		UPA 7.5 MG QD	35	6.7	3.6	-45.6	6.87	-34.2	(-52.1, -16.3)	9.06	<0.001***
		PLACEBO	27	6.5	5.7	-11.4	7.71				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.2	2.0	-71.3	7.09	-55.3	(-76.5, -34.1)	10.69	<0.001***
		UPA 15 MG QD	25	6.6	2.8	-54.7	7.48	-38.7	(-60.4, -17.0)	10.93	<0.001***
		UPA 7.5 MG QD	25	6.8	4.1	-41.0	7.49	-25.0	(-46.7, -3.3)	10.93	0.024*
		PLACEBO	22	6.7	5.5	-16.0	7.97				
	EU/AUS										
		UPA 30 MG QD	8	6.0	1.1	-83.9	9.36	-99.4	(-136.8, -62.0)	17.93	<0.001***
		UPA 15 MG QD	6	6.4	2.6	-56.2	10.81	-71.8	(-111.1, -32.4)	18.85	0.001**
		UPA 7.5 MG QD	8	6.5	2.4	-64.7	9.38	-80.3	(-118.0, -42.5)	18.09	<0.001***
		PLACEBO	3	5.6	6.6	15.5	15.36				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.3	-63.2	17.76	-57.4	(-128.1, 13.3)	27.50	0.091
		UPA 15 MG QD	3	5.2	3.4	-33.2	19.78	-27.4	(-107.6, 52.7)	31.18	0.419
		UPA 7.5 MG QD	2	6.3	2.9	-53.7	21.53	-47.9	(-125.4, 29.6)	30.14	0.173
		PLACEBO	2	6.4	6.2	-5.8	21.91				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.471

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 11											
	ALL										
		UPA 30 MG QD	39	6.2	1.9	-69.9	6.62	-54.9	(-72.4, -37.4)	8.83	<0.001***
		UPA 15 MG QD	33	6.5	2.6	-55.6	6.97	-40.6	(-58.6, -22.5)	9.12	<0.001***
		UPA 7.5 MG QD	34	6.7	3.7	-46.0	6.97	-31.0	(-49.0, -13.0)	9.10	<0.001***
		PLACEBO	28	6.6	5.5	-15.0	7.69				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.2	2.1	-69.8	6.95	-49.9	(-70.5, -29.4)	10.34	<0.001***
		UPA 15 MG QD	24	6.6	2.5	-59.8	7.46	-39.9	(-61.1, -18.8)	10.67	<0.001***
		UPA 7.5 MG QD	24	6.8	4.1	-41.5	7.48	-21.7	(-42.8, -0.5)	10.67	0.045*
		PLACEBO	23	6.8	5.3	-19.9	7.63				
	EU/AUS										
		UPA 30 MG QD	8	6.0	1.4	-78.2	10.26	-89.2	(-130.2, -48.3)	19.63	<0.001***
		UPA 15 MG QD	6	6.4	2.3	-61.0	11.83	-72.0	(-115.1, -29.0)	20.64	0.002**
		UPA 7.5 MG QD	8	6.5	2.4	-66.3	10.27	-77.4	(-118.7, -36.0)	19.81	<0.001***
		PLACEBO	3	5.6	6.5	11.0	16.83				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.0	-66.9	24.35	-58.9	(-155.8, 38.1)	37.71	0.179
		UPA 15 MG QD	3	5.2	3.5	-31.5	27.13	-23.4	(-133.3, 86.5)	42.76	0.608
		UPA 7.5 MG QD	2	6.3	2.8	-54.1	29.52	-46.0	(-152.3, 60.2)	41.33	0.316
		PLACEBO	2	6.4	6.1	-8.1	30.05				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.406

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 12											
	ALL										
		UPA 30 MG QD	40	6.2	2.0	-70.6	6.91	-52.3	(-70.6, -34.0)	9.24	<0.001***
		UPA 15 MG QD	34	6.4	2.6	-55.3	7.28	-37.0	(-55.8, -18.1)	9.54	<0.001***
		UPA 7.5 MG QD	36	6.8	3.5	-46.9	7.22	-28.6	(-47.3, -9.9)	9.45	0.003**
		PLACEBO	28	6.6	5.3	-18.3	8.08				
	US/PR/CANADA										
		UPA 30 MG QD	29	6.3	2.2	-68.2	7.26	-46.0	(-67.6, -24.3)	10.91	<0.001***
		UPA 15 MG QD	25	6.6	2.6	-56.9	7.78	-34.7	(-57.0, -12.4)	11.25	0.003**
		UPA 7.5 MG QD	26	6.9	3.9	-41.3	7.65	-19.1	(-41.2, 3.0)	11.14	0.089
		PLACEBO	23	6.8	5.1	-22.2	8.12				
	EU/AUS										
		UPA 30 MG QD	8	6.0	1.4	-78.5	10.60	-93.4	(-135.7, -51.1)	20.29	<0.001***
		UPA 15 MG QD	6	6.4	2.3	-60.0	12.23	-74.9	(-119.4, -30.4)	21.34	0.002**
		UPA 7.5 MG QD	8	6.5	2.4	-63.9	10.62	-78.9	(-121.6, -36.1)	20.48	<0.001***
		PLACEBO	3	5.6	6.7	14.9	17.39				
	JAPAN										
		UPA 30 MG QD	3	6.3	1.7	-71.7	22.02	-59.7	(-147.4, 27.9)	34.09	0.140
		UPA 15 MG QD	3	5.2	3.4	-33.4	24.53	-21.4	(-120.8, 77.9)	38.65	0.603
		UPA 7.5 MG QD	2	6.3	2.6	-57.2	26.69	-45.2	(-141.3, 50.8)	37.36	0.280
		PLACEBO	2	6.4	5.8	-11.9	27.17				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.441

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 13											
	ALL										
		UPA 30 MG QD	39	6.4	2.1	-71.0	6.88	-55.7	(-73.9, -37.5)	9.20	<0.001***
		UPA 15 MG QD	33	6.5	2.4	-58.8	7.22	-43.5	(-62.3, -24.6)	9.53	<0.001***
		UPA 7.5 MG QD	33	6.7	3.5	-47.9	7.32	-32.6	(-51.5, -13.7)	9.55	<0.001***
		PLACEBO	27	6.6	5.5	-15.3	8.05				
	US/PR/CANADA										
		UPA 30 MG QD	29	6.3	2.2	-68.6	7.15	-52.9	(-74.5, -31.3)	10.88	<0.001***
		UPA 15 MG QD	24	6.6	2.5	-59.1	7.83	-43.5	(-66.0, -21.0)	11.32	<0.001***
		UPA 7.5 MG QD	24	6.9	3.9	-41.3	7.85	-25.6	(-48.1, -3.2)	11.32	0.026*
		PLACEBO	22	6.8	5.5	-15.6	8.18				
	EU/AUS										
		UPA 30 MG QD	7	6.7	1.5	-77.6	11.46	-92.9	(-137.7, -48.2)	21.30	<0.001***
		UPA 15 MG QD	6	6.4	1.8	-67.4	12.28	-82.7	(-128.0, -37.4)	21.57	0.001**
		UPA 7.5 MG QD	7	6.2	2.1	-67.0	11.37	-82.3	(-126.3, -38.3)	20.94	<0.001***
		PLACEBO	3	5.6	6.8	15.3	17.66				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.0	-65.2	15.69	-31.3	(-93.8, 31.2)	24.30	0.254
		UPA 15 MG QD	3	5.2	3.5	-33.9	17.48	-0.0	(-70.8, 70.8)	27.55	1.000
		UPA 7.5 MG QD	2	6.3	3.0	-49.8	19.02	-15.9	(-84.3, 52.6)	26.63	0.577
		PLACEBO	2	6.4	4.2	-33.9	19.36				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.328

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 14											
	ALL										
		UPA 30 MG QD	37	6.3	1.8	-72.9	7.55	-57.0	(-77.1, -36.8)	10.18	<0.001***
		UPA 15 MG QD	34	6.4	2.7	-51.6	7.75	-35.7	(-56.1, -15.2)	10.34	<0.001***
		UPA 7.5 MG QD	33	6.7	3.3	-46.9	7.92	-30.9	(-51.6, -10.3)	10.42	0.004**
		PLACEBO	26	6.6	5.4	-16.0	8.80				
	US/PR/CANADA										
		UPA 30 MG QD	27	6.1	1.8	-74.9	8.13	-56.7	(-81.1, -32.2)	12.29	<0.001***
		UPA 15 MG QD	25	6.6	2.7	-54.2	8.39	-35.9	(-60.6, -11.2)	12.43	0.005**
		UPA 7.5 MG QD	24	6.9	3.6	-44.7	8.59	-26.4	(-51.3, -1.5)	12.54	0.038*
		PLACEBO	21	6.8	5.4	-18.3	9.17				
	EU/AUS										
		UPA 30 MG QD	7	6.7	1.6	-75.8	11.61	-81.9	(-127.2, -36.6)	21.56	0.001**
		UPA 15 MG QD	6	6.4	1.7	-68.7	12.42	-74.9	(-120.7, -29.0)	21.82	0.003**
		UPA 7.5 MG QD	7	6.2	2.5	-58.5	11.51	-64.7	(-109.1, -20.3)	21.15	0.007**
		PLACEBO	3	5.6	6.4	6.2	17.86				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.2	-59.3	15.01	-29.4	(-89.2, 30.3)	23.25	0.261
		UPA 15 MG QD	3	5.2	4.4	-20.5	16.73	9.4	(-58.3, 77.2)	26.36	0.735
		UPA 7.5 MG QD	2	6.3	2.5	-55.1	18.20	-25.2	(-90.7, 40.3)	25.48	0.369
		PLACEBO	2	6.4	4.1	-29.9	18.53				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.412

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 15											
	ALL										
		UPA 30 MG QD	38	6.3	1.9	-72.2	7.79	-56.6	(-77.7, -35.6)	10.63	<0.001***
		UPA 15 MG QD	34	6.4	2.6	-51.5	8.06	-35.9	(-57.4, -14.4)	10.86	0.001**
		UPA 7.5 MG QD	32	6.7	3.3	-48.2	8.30	-32.6	(-54.5, -10.8)	11.02	0.004**
		PLACEBO	25	6.6	5.4	-15.5	9.26				
	US/PR/CANADA										
		UPA 30 MG QD	28	6.2	1.8	-74.5	8.17	-57.7	(-82.9, -32.6)	12.66	<0.001***
		UPA 15 MG QD	25	6.6	2.7	-53.6	8.60	-36.8	(-62.5, -11.2)	12.92	0.005**
		UPA 7.5 MG QD	23	7.0	3.7	-44.4	9.00	-27.6	(-53.8, -1.5)	13.15	0.038*
		PLACEBO	20	6.8	5.4	-16.8	9.63				
	EU/AUS										
		UPA 30 MG QD	7	6.7	1.8	-71.8	12.33	-84.7	(-132.8, -36.6)	22.90	0.002**
		UPA 15 MG QD	6	6.4	1.6	-70.1	13.19	-83.0	(-131.7, -34.3)	23.18	0.002**
		UPA 7.5 MG QD	7	6.2	2.2	-64.2	12.22	-77.0	(-124.2, -29.8)	22.46	0.003**
		PLACEBO	3	5.6	6.7	12.9	18.97				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.4	-55.2	11.76	-12.8	(-59.6, 34.0)	18.21	0.515
		UPA 15 MG QD	3	5.2	4.6	-20.5	13.10	21.9	(-31.1, 75.0)	20.64	0.336
		UPA 7.5 MG QD	2	6.3	2.7	-50.0	14.25	-7.5	(-58.8, 43.7)	19.95	0.721
		PLACEBO	2	6.4	3.1	-42.4	14.51				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.187

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 16											
	ALL										
		UPA 30 MG QD	36	6.4	2.3	-66.5	7.89	-54.6	(-76.4, -32.8)	11.01	<0.001***
		UPA 15 MG QD	33	6.3	2.6	-53.4	8.15	-41.5	(-63.7, -19.3)	11.21	<0.001***
		UPA 7.5 MG QD	30	6.6	3.4	-48.4	8.54	-36.5	(-59.2, -13.9)	11.43	0.002**
		PLACEBO	23	6.6	5.7	-11.9	9.54				
	US/PR/CANADA										
		UPA 30 MG QD	26	6.3	2.4	-65.9	8.40	-54.9	(-81.0, -28.8)	13.14	<0.001***
		UPA 15 MG QD	24	6.4	2.5	-55.2	8.72	-44.2	(-70.8, -17.7)	13.34	0.001**
		UPA 7.5 MG QD	22	6.8	3.9	-42.6	9.13	-31.6	(-58.6, -4.6)	13.58	0.022*
		PLACEBO	18	6.8	5.9	-11.0	10.08				
	EU/AUS										
		UPA 30 MG QD	7	6.7	2.0	-69.7	13.12	-85.0	(-136.2, -33.8)	24.26	0.003**
		UPA 15 MG QD	6	6.4	1.9	-67.0	13.96	-82.3	(-134.1, -30.6)	24.52	0.004**
		UPA 7.5 MG QD	6	5.8	1.7	-69.2	14.09	-84.5	(-135.4, -33.6)	24.14	0.003**
		PLACEBO	3	5.6	6.8	15.4	19.98				
	JAPAN										
		UPA 30 MG QD	3	6.3	2.4	-56.0	13.37	-12.8	(-66.0, 40.4)	20.70	0.563
		UPA 15 MG QD	3	5.2	4.4	-23.3	14.89	19.9	(-40.4, 80.2)	23.47	0.436
		UPA 7.5 MG QD	2	6.3	3.1	-43.6	16.20	-0.4	(-58.7, 57.9)	22.68	0.986
		PLACEBO	2	6.4	3.0	-43.2	16.49				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.186

[A] ACROSS THE STRATA, P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, AND TREATMENT IN THE MODEL.
WITHIN EACH STRATUM, P-VALUES WERE CALCULATED FROM ANCOVA WITH BASELINE VALUE AND THE TREATMENT IN THE MODEL.
@ P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, TREATMENT, INTERACTION OF STRATUM AND TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.
Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2__1.4.1

表 2.7.3.6-25. ベースライン時の POEM スコアが 4 以上であった被験者のうち，二重盲検投与期の来院時別での POEM スコアがベースラインから 4 以上改善した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo	276	89 (32.2) [26.7, 37.8]	0					
UPA 15 mg QD	278	241 (86.7) [82.7, 90.7]	0	54.4	54.4	[47.6, 61.2]	<0.001***	0.117
UPA 30 mg QD	280	246 (87.9) [84.0, 91.7]	0	55.6	55.6	[48.9, 62.3]	<0.001***	0.313
vIGA-AD 3 (Moderate)								
Placebo	153	55 (35.9) [28.3, 43.6]	0					
UPA 15 mg QD	151	127 (84.1) [78.3, 89.9]	0	48.2		[38.6, 57.7]	<0.001***	
UPA 30 mg QD	151	134 (88.7) [83.7, 93.8]	0	52.8		[43.7, 61.9]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	123	34 (27.6) [19.7, 35.5]	0					
UPA 15 mg QD	127	114 (89.8) [84.5, 95.0]	0	62.1		[52.6, 71.6]	<0.001***	
UPA 30 mg QD	129	112 (86.8) [81.0, 92.7]	0	59.2		[49.4, 69.0]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo	126	47 (37.3) [28.9, 45.7]	0					
UPA 15 mg QD	126	109 (86.5) [80.5, 92.5]	0	49.2		[38.9, 59.5]	<0.001***	
UPA 30 mg QD	126	113 (89.7) [84.4, 95.0]	0	52.4		[42.4, 62.4]	<0.001***	
Japan								
Placebo	14	3 (21.4) [0.0, 42.9]	0					
UPA 15 mg QD	15	13 (86.7) [69.5, 100.0]	0	65.2		[37.7, 92.8]	<0.001***	
UPA 30 mg QD	16	14 (87.5) [71.3, 100.0]	0	66.1		[39.2, 93.0]	<0.001***	
China								
Placebo	14	4 (28.6) [4.9, 52.2]	0					
UPA 15 mg QD	14	14 (100) [100.0, 100.0]	0	71.4		[47.8, 95.1]	<0.001***	
UPA 30 mg QD	17	15 (88.2) [72.9, 100.0]	0	59.7		[31.5, 87.9]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo	122	35 (28.7) [20.7, 36.7]	0					
UPA 15 mg QD	123	105 (85.4) [79.1, 91.6]	0	56.7		[46.5, 66.8]	<0.001***	
UPA 30 mg QD	121	104 (86.0) [79.8, 92.1]	0	57.3		[47.1, 67.4]	<0.001***	
Adolescent								
Placebo	38	14 (36.8) [21.5, 52.2]	0					
UPA 15 mg QD	41	34 (82.9) [71.4, 94.4]	0	46.1		[26.9, 65.3]	<0.001***	
UPA 30 mg QD	42	41 (97.6) [93.0, 100.0]	0	60.8		[44.8, 76.8]	<0.001***	
Adult								
Placebo	238	75 (31.5) [25.6, 37.4]	0					
UPA 15 mg QD	237	207 (87.3) [83.1, 91.6]	0	55.8		[48.6, 63.1]	<0.001***	
UPA 30 mg QD	238	205 (86.1) [81.7, 90.5]	0	54.6		[47.3, 62.0]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo	276	78 (28.3) [22.9, 33.6]	0					
UPA 15 mg QD	278	230 (82.7) [78.3, 87.2]	0	54.5	54.5	[47.6, 61.4]	<0.001***	0.858
UPA 30 mg QD	280	245 (87.5) [83.6, 91.4]	0	59.2	59.2	[52.7, 65.8]	<0.001***	0.088
vIGA-AD 3 (Moderate)								
Placebo	153	48 (31.4) [24.0, 38.7]	0					
UPA 15 mg QD	151	125 (82.8) [76.8, 88.8]	0	51.4		[41.9, 60.9]	<0.001***	
UPA 30 mg QD	151	129 (85.4) [79.8, 91.1]	0	54.1		[44.8, 63.3]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	123	30 (24.4) [16.8, 32.0]	0					
UPA 15 mg QD	127	105 (82.7) [76.1, 89.3]	0	58.3		[48.2, 68.3]	<0.001***	
UPA 30 mg QD	129	116 (89.9) [84.7, 95.1]	0	65.5		[56.3, 74.7]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
US/Puerto Rico/Canada								
Placebo	126	34 (27.0) [19.2, 34.7]	0					
UPA 15 mg QD	126	98 (77.8) [70.5, 85.0]	0	50.8		[40.2, 61.4]	<0.001***	
UPA 30 mg QD	126	109 (86.5) [80.5, 92.5]	0	59.5		[49.7, 69.3]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	15	12 (80.0) [59.8, 100.0]	0	80.0		[59.8, 100.0]	<0.001***	
UPA 30 mg QD	16	14 (87.5) [71.3, 100.0]	0	87.5		[71.3, 100.0]	<0.001***	
China								
Placebo	14	3 (21.4) [0.0, 42.9]	0					
UPA 15 mg QD	14	14 (100) [100.0, 100.0]	0	78.6		[57.1, 100.0]	<0.001***	
UPA 30 mg QD	17	15 (88.2) [72.9, 100.0]	0	66.8		[40.4, 93.2]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Other								
Placebo	122	41 (33.6) [25.2, 42.0]	0					
UPA 15 mg QD	123	106 (86.2) [80.1, 92.3]	0	52.6		[42.2, 62.9]	<0.001***	
UPA 30 mg QD	121	107 (88.4) [82.7, 94.1]	0	54.8		[44.7, 65.0]	<0.001***	
Adolescent								
Placebo	38	9 (23.7) [10.2, 37.2]	0					
UPA 15 mg QD	41	33 (80.5) [68.4, 92.6]	0	56.8		[38.6, 75.0]	<0.001***	
UPA 30 mg QD	42	40 (95.2) [88.8, 100.0]	0	71.6		[56.6, 86.5]	<0.001***	
Adult								
Placebo	238	69 (29.0) [23.2, 34.8]	0					
UPA 15 mg QD	237	197 (83.1) [78.4, 87.9]	0	54.1		[46.6, 61.6]	<0.001***	
UPA 30 mg QD	238	205 (86.1) [81.7, 90.5]	0	57.1		[49.9, 64.4]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	276	63 (22.8) [17.8, 27.8]	4					
UPA 15 mg QD	278	209 (75.0) [69.9, 80.1]	1	52.3	52.3	[45.2, 59.4]	<0.001***	0.645
UPA 30 mg QD	280	228 (81.4) [76.9, 86.0]	2	58.7	58.6	[51.9, 65.3]	<0.001***	0.410
vIGA-AD 3 (Moderate)								
Placebo	153	40 (26.2) [19.1, 33.2]	3					
UPA 15 mg QD	151	117 (77.5) [70.8, 84.1]	0	51.3		[41.6, 61.0]	<0.001***	
UPA 30 mg QD	151	120 (79.5) [73.0, 85.9]	1	53.3		[43.7, 62.8]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	123	23 (18.5) [11.6, 25.4]	1					
UPA 15 mg QD	127	92 (72.1) [64.3, 79.9]	1	53.6		[43.1, 64.0]	<0.001***	
UPA 30 mg QD	129	108 (83.7) [77.4, 90.1]	1	65.2		[55.8, 74.6]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	126	31 (24.2) [16.7, 31.7]	1					
UPA 15 mg QD	126	94 (74.6) [67.0, 82.2]	0	50.4		[39.7, 61.1]	<0.001***	
UPA 30 mg QD	126	103 (81.7) [75.0, 88.5]	0	57.5		[47.4, 67.6]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	15	12 (80.0) [59.8, 100.0]	0	80.0		[59.8, 100.0]	<0.001***	
UPA 30 mg QD	16	11 (68.8) [46.0, 91.5]	0	68.8		[46.0, 91.5]	<0.001***	
China								
Placebo	14	2 (14.3) [0.0, 32.6]	0					
UPA 15 mg QD	14	11 (78.6) [57.1, 100.0]	0	64.3		[36.0, 92.5]	<0.001***	
UPA 30 mg QD	17	13 (76.5) [56.3, 96.6]	0	62.2		[34.9, 89.4]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	122	30 (24.9) [17.1, 32.6]	3					
UPA 15 mg QD	123	92 (74.4) [66.7, 82.2]	1	49.6		[38.6, 60.6]	<0.001***	
UPA 30 mg QD	121	101 (83.5) [76.9, 90.1]	2	58.6		[48.4, 68.8]	<0.001***	
Adolescent								
Placebo	38	11 (29.0) [14.6, 43.5]	1					
UPA 15 mg QD	41	32 (78.0) [65.4, 90.7]	0	49.0		[29.8, 68.2]	<0.001***	
UPA 30 mg QD	42	36 (85.7) [75.1, 96.3]	0	56.7		[38.8, 74.6]	<0.001***	
Adult								
Placebo	238	52 (21.8) [16.5, 27.1]	3					
UPA 15 mg QD	237	177 (74.5) [68.9, 80.1]	1	52.7		[45.1, 60.4]	<0.001***	
UPA 30 mg QD	238	192 (80.7) [75.7, 85.7]	2	58.9		[51.6, 66.2]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__5.1.1

表 2.7.3.6-26. ベースライン時の POEM 睡眠項目スコアが 0 を超えていた被験者のうち，二重盲検投与期の来院時別での POEM 睡眠項目スコア 0 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo	264	9 (3.4) [1.2, 5.6]	0					
UPA 15 mg QD	272	79 (29.0) [23.6, 34.4]	0	25.6	25.6	[19.8, 31.3]	<0.001***	0.420
UPA 30 mg QD	270	108 (40.0) [34.2, 45.8]	0	36.6	36.6	[30.4, 42.8]	<0.001***	0.576
vIGA-AD 3 (Moderate)								
Placebo	146	7 (4.8) [1.3, 8.3]	0					
UPA 15 mg QD	148	42 (28.4) [21.1, 35.6]	0	23.6		[15.5, 31.6]	<0.001***	
UPA 30 mg QD	143	64 (44.8) [36.6, 52.9]	0	40.0		[31.1, 48.8]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	118	2 (1.7) [0.0, 4.0]	0					
UPA 15 mg QD	124	37 (29.8) [21.8, 37.9]	0	28.1		[19.8, 36.5]	<0.001***	
UPA 30 mg QD	127	44 (34.6) [26.4, 42.9]	0	33.0		[24.4, 41.5]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo	121	7 (5.8) [1.6, 9.9]	0					
UPA 15 mg QD	122	37 (30.3) [22.2, 38.5]	0	24.5		[15.4, 33.7]	<0.001***	
UPA 30 mg QD	120	51 (42.5) [33.7, 51.3]	0	36.7		[26.9, 46.5]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	14	4 (28.6) [4.9, 52.2]	0	28.6		[4.9, 52.2]	0.018*	
UPA 30 mg QD	14	7 (50.0) [23.8, 76.2]	0	50.0		[23.8, 76.2]	<0.001***	
China								
Placebo	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD	14	3 (21.4) [0.0, 42.9]	0	14.3		[-11.1, 39.7]	0.270	
UPA 30 mg QD	17	6 (35.3) [12.6, 58.0]	0	28.2		[1.7, 54.6]	0.037*	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo	115	1 (0.9) [0.0, 2.6]	0					
UPA 15 mg QD	122	35 (28.7) [20.7, 36.7]	0	27.8		[19.6, 36.0]	<0.001***	
UPA 30 mg QD	119	44 (37.0) [28.3, 45.6]	0	36.1		[27.3, 44.9]	<0.001***	
Adolescent								
Placebo	35	3 (8.6) [0.0, 17.8]	0					
UPA 15 mg QD	38	17 (44.7) [28.9, 60.5]	0	36.2		[17.8, 54.5]	<0.001***	
UPA 30 mg QD	40	19 (47.5) [32.0, 63.0]	0	38.9		[20.9, 57.0]	<0.001***	
Adult								
Placebo	229	6 (2.6) [0.6, 4.7]	0					
UPA 15 mg QD	234	62 (26.5) [20.8, 32.2]	0	23.9		[17.9, 29.9]	<0.001***	
UPA 30 mg QD	230	89 (38.7) [32.4, 45.0]	0	36.1		[29.4, 42.7]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo	264	21 (8.0) [4.7, 11.2]	0					
UPA 15 mg QD	272	125 (46.0) [40.0, 51.9]	0	38.0	38.0	[31.2, 44.7]	<0.001***	0.472
UPA 30 mg QD	270	157 (58.1) [52.3, 64.0]	0	50.2	50.1	[43.4, 56.8]	<0.001***	0.994
vIGA-AD 3 (Moderate)								
Placebo	146	12 (8.2) [3.8, 12.7]	0					
UPA 15 mg QD	148	69 (46.6) [38.6, 54.7]	0	38.4		[29.2, 47.6]	<0.001***	
UPA 30 mg QD	143	85 (59.4) [51.4, 67.5]	0	51.2		[42.0, 60.4]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	118	9 (7.6) [2.8, 12.4]	0					
UPA 15 mg QD	124	56 (45.2) [36.4, 53.9]	0	37.5		[27.6, 47.5]	<0.001***	
UPA 30 mg QD	127	72 (56.7) [48.1, 65.3]	0	49.1		[39.2, 58.9]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
US/Puerto Rico/Canada								
Placebo	121	9 (7.4) [2.8, 12.1]	0					
UPA 15 mg QD	122	53 (43.4) [34.6, 52.2]	0	36.0		[26.0, 46.0]	<0.001***	
UPA 30 mg QD	120	75 (62.5) [53.8, 71.2]	0	55.1		[45.2, 64.9]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	14	5 (35.7) [10.6, 60.8]	0	35.7		[10.6, 60.8]	0.005**	
UPA 30 mg QD	14	5 (35.7) [10.6, 60.8]	0	35.7		[10.6, 60.8]	0.005**	
China								
Placebo	14	2 (14.3) [0.0, 32.6]	0					
UPA 15 mg QD	14	7 (50.0) [23.8, 76.2]	0	35.7		[3.7, 67.7]	0.029*	
UPA 30 mg QD	17	8 (47.1) [23.3, 70.8]	0	32.8		[2.8, 62.8]	0.032*	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Other								
Placebo	115	10 (8.7) [3.5, 13.8]	0					
UPA 15 mg QD	122	60 (49.2) [40.3, 58.1]	0	40.5		[30.2, 50.7]	<0.001***	
UPA 30 mg QD	119	69 (58.0) [49.1, 66.9]	0	49.3		[39.0, 59.5]	<0.001***	
Adolescent								
Placebo	35	4 (11.4) [0.9, 22.0]	0					
UPA 15 mg QD	38	17 (44.7) [28.9, 60.5]	0	33.3		[14.3, 52.3]	0.001**	
UPA 30 mg QD	40	25 (62.5) [47.5, 77.5]	0	51.1		[32.7, 69.4]	<0.001***	
Adult								
Placebo	229	17 (7.4) [4.0, 10.8]	0					
UPA 15 mg QD	234	108 (46.2) [39.8, 52.5]	0	38.7		[31.5, 46.0]	<0.001***	
UPA 30 mg QD	230	132 (57.4) [51.0, 63.8]	0	50.0		[42.7, 57.2]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	264	18 (6.9) [3.8, 9.9]	4					
UPA 15 mg QD	272	123 (45.4) [39.4, 51.3]	1	38.5	38.5	[31.9, 45.2]	<0.001***	0.194
UPA 30 mg QD	270	168 (62.1) [56.3, 67.9]	2	55.3	55.1	[48.6, 61.6]	<0.001***	0.792
vIGA-AD 3 (Moderate)								
Placebo	146	11 (7.5) [3.3, 11.8]	3					
UPA 15 mg QD	148	67 (45.3) [37.3, 53.3]	0	37.7		[28.6, 46.8]	<0.001***	
UPA 30 mg QD	143	89 (62.5) [54.6, 70.5]	1	55.0		[45.9, 64.0]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	118	7 (6.0) [1.7, 10.3]	1					
UPA 15 mg QD	124	56 (45.5) [36.7, 54.3]	1	39.4		[29.6, 49.2]	<0.001***	
UPA 30 mg QD	127	78 (61.7) [53.2, 70.1]	1	55.6		[46.1, 65.2]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	121	6 (5.0) [1.1, 8.8]	1					
UPA 15 mg QD	122	51 (41.8) [33.1, 50.6]	0	36.8		[27.3, 46.4]	<0.001***	
UPA 30 mg QD	120	81 (67.5) [59.1, 75.9]	0	62.5		[53.3, 71.8]	<0.001***	
Japan								
Placebo	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD	14	4 (28.6) [4.9, 52.2]	0	21.4		[-5.8, 48.7]	0.123	
UPA 30 mg QD	14	8 (57.1) [31.2, 83.1]	0	50.0		[20.8, 79.2]	0.001**	
China								
Placebo	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD	14	8 (57.1) [31.2, 83.1]	0	50.0		[20.8, 79.2]	0.001**	
UPA 30 mg QD	17	9 (52.9) [29.2, 76.7]	0	45.8		[18.5, 73.1]	0.001**	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	115	10 (8.8) [3.6, 14.0]	3					
UPA 15 mg QD	122	60 (49.5) [40.6, 58.4]	1		40.7	[30.4, 51.0]	<0.001***	
UPA 30 mg QD	119	70 (58.6) [49.6, 67.5]	2		49.8	[39.5, 60.1]	<0.001***	
Adolescent								
Placebo	35	3 (8.6) [0.0, 17.8]	1					
UPA 15 mg QD	38	14 (36.8) [21.5, 52.2]	0		28.3	[10.3, 46.2]	0.002**	
UPA 30 mg QD	40	29 (72.5) [58.7, 86.3]	0		63.9	[47.3, 80.6]	<0.001***	
Adult								
Placebo	229	15 (6.6) [3.4, 9.8]	3					
UPA 15 mg QD	234	109 (46.7) [40.3, 53.1]	1		40.1	[33.0, 47.3]	<0.001***	
UPA 30 mg QD	230	139 (60.3) [54.0, 66.7]	2		53.7	[46.6, 60.8]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__5.2.1

表 2.7.3.6-27.　二重盲検投与期の来院時別での POEM スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo	263	21.4	19.3	-8.34	[-12.48, -4.20]	2.109				
UPA 15 mg QD	272	21.2	10.2	-52.63	[-56.68, -48.57]	2.067	-44.28	[-49.36, -39.20]	2.588	<0.001***
UPA 30 mg QD	272	21.3	8.4	-60.67	[-64.71, -56.63]	2.059	-52.33	[-57.41, -47.25]	2.587	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	148	20.4	18.1	-9.21	[-14.07, -4.35]	2.472				
UPA 15 mg QD	147	20.3	9.7	-51.58	[-56.44, -46.72]	2.474	-42.37	[-49.24, -35.50]	3.497	<0.001***
UPA 30 mg QD	147	20.4	7.4	-62.20	[-67.07, -57.33]	2.477	-52.99	[-59.87, -46.12]	3.499	<0.001***
vIGA-AD 4 (Severe)										
Placebo	115	22.7	20.7	-5.51	[-10.99, -0.03]	2.787				
UPA 15 mg QD	125	22.3	10.7	-52.18	[-57.43, -46.93]	2.668	-46.67	[-54.26, -39.08]	3.859	<0.001***
UPA 30 mg QD	125	22.4	9.6	-57.24	[-62.48, -52.01]	2.662	-51.73	[-59.31, -44.16]	3.853	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	120	21.5	18.5	-12.57	[-17.96, -7.18]	2.742				
UPA 15 mg QD	125	21.5	10.7	-50.65	[-55.94, -45.36]	2.690	-38.08	[-45.64, -30.53]	3.841	<0.001***
UPA 30 mg QD	122	21.6	8.0	-61.57	[-66.91, -56.24]	2.713	-49.00	[-56.59, -41.42]	3.857	<0.001***
Japan										
Placebo	11	20.5	20.3	4.01	[-13.87, 21.89]	8.834				
UPA 15 mg QD	15	18.6	9.1	-49.20	[-64.37, -34.03]	7.494	-53.21	[-76.71, -29.72]	11.610	<0.001***
UPA 30 mg QD	16	18.8	9.4	-51.44	[-66.12, -36.76]	7.253	-55.45	[-78.61, -32.29]	11.443	<0.001***
China										
Placebo	14	21.4	19.4	-10.62	[-23.23, 2.00]	6.248				
UPA 15 mg QD	14	23.1	11.0	-50.97	[-63.58, -38.36]	6.245	-40.35	[-58.28, -22.42]	8.879	<0.001***
UPA 30 mg QD	17	22.5	9.1	-57.37	[-68.76, -45.98]	5.642	-46.75	[-63.78, -29.73]	8.431	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo	118	21.4	20.0	-3.30	[-8.89, 2.30]	2.845				
UPA 15 mg QD	118	21.0	9.7	-53.45	[-59.02, -47.89]	2.829	-50.15	[-58.05, -42.26]	4.012	<0.001***
UPA 30 mg QD	117	21.2	8.6	-59.62	[-65.22, -54.02]	2.848	-56.32	[-64.24, -48.41]	4.024	<0.001***
Adolescent										
Placebo	37	19.3	17.0	-8.05	[-21.01, 4.90]	6.540				
UPA 15 mg QD	40	20.6	9.2	-52.97	[-65.25, -40.69]	6.200	-44.92	[-62.81, -27.03]	9.032	<0.001***
UPA 30 mg QD	42	21.5	7.4	-64.42	[-76.58, -52.25]	6.140	-56.36	[-74.28, -38.45]	9.043	<0.001***
Adult										
Placebo	226	21.7	19.6	-7.75	[-11.42, -4.08]	1.869				
UPA 15 mg QD	232	21.3	10.4	-51.61	[-55.23, -48.00]	1.841	-43.86	[-49.02, -38.71]	2.624	<0.001***
UPA 30 mg QD	230	21.3	8.6	-58.92	[-62.55, -55.29]	1.847	-51.17	[-56.33, -46.01]	2.628	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo	160	20.4	15.8	-16.37	[-21.94, -10.80]	2.840				
UPA 15 mg QD	260	21.3	8.2	-62.81	[-67.52, -58.10]	2.400	-46.44	[-53.18, -39.71]	3.431	<0.001***
UPA 30 mg QD	267	21.4	6.2	-71.25	[-75.91, -66.58]	2.377	-54.88	[-61.58, -48.17]	3.416	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	102	19.6	15.6	-13.51	[-20.16, -6.86]	3.384				
UPA 15 mg QD	142	20.3	7.8	-62.50	[-68.37, -56.62]	2.989	-48.98	[-57.86, -40.11]	4.515	<0.001***
UPA 30 mg QD	140	20.6	6.0	-70.15	[-76.06, -64.25]	3.003	-56.64	[-65.53, -47.75]	4.524	<0.001***
vIGA-AD 4 (Severe)										
Placebo	58	21.8	16.1	-19.84	[-28.17, -11.50]	4.240				
UPA 15 mg QD	118	22.5	8.5	-61.50	[-67.81, -55.19]	3.208	-41.67	[-52.12, -31.21]	5.317	<0.001***
UPA 30 mg QD	127	22.4	6.4	-70.73	[-76.86, -64.59]	3.117	-50.89	[-61.24, -40.54]	5.263	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo	77	20.8	16.7	-12.36	[-20.20, -4.51]	3.989				
UPA 15 mg QD	116	21.6	9.1	-59.31	[-66.03, -52.59]	3.415	-46.96	[-57.28, -36.63]	5.252	<0.001***
UPA 30 mg QD	122	21.6	5.9	-72.39	[-78.99, -65.79]	3.356	-60.03	[-70.29, -49.78]	5.214	<0.001***
Japan										
Placebo	2	16.0	15.0	-4.21	[-42.90, 34.47]	18.926				
UPA 15 mg QD	15	18.6	9.6	-49.66	[-64.53, -34.80]	7.247	-45.45	[-86.83, -4.07]	20.254	0.032*
UPA 30 mg QD	14	19.4	6.4	-67.42	[-82.67, -52.17]	7.448	-63.20	[-104.76, -21.65]	20.345	0.004**
China										
Placebo	8	20.3	17.0	-21.14	[-42.54, 0.26]	10.584				
UPA 15 mg QD	14	23.1	8.1	-64.41	[-81.00, -47.81]	8.184	-43.27	[-70.43, -16.10]	13.430	0.003**
UPA 30 mg QD	17	22.5	7.4	-65.75	[-80.78, -50.73]	7.408	-44.61	[-70.78, -18.45]	12.933	0.001**

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo	73	20.1	14.8	-19.50	[-27.03, -11.97]	3.831				
UPA 15 mg QD	115	21.1	7.0	-66.13	[-72.48, -59.77]	3.231	-46.63	[-56.48, -36.77]	5.012	<0.001***
UPA 30 mg QD	114	21.4	6.4	-69.40	[-75.78, -63.02]	3.245	-49.90	[-59.77, -40.02]	5.021	<0.001***
Adolescent										
Placebo	20	17.4	12.5	-16.71	[-34.60, 1.17]	9.043				
UPA 15 mg QD	41	20.7	8.9	-57.84	[-72.00, -43.69]	7.142	-41.13	[-63.98, -18.28]	11.545	0.001**
UPA 30 mg QD	40	21.4	5.2	-73.50	[-87.70, -59.30]	7.164	-56.78	[-79.75, -33.81]	11.609	<0.001***
Adult										
Placebo	140	20.8	16.3	-16.05	[-21.34, -10.76]	2.694				
UPA 15 mg QD	219	21.4	8.0	-62.79	[-67.21, -58.38]	2.247	-46.74	[-53.63, -39.86]	3.508	<0.001***
UPA 30 mg QD	227	21.5	6.4	-69.72	[-74.06, -65.37]	2.214	-53.67	[-60.51, -46.82]	3.487	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo	123	19.9	15.6	-15.34	[-21.73, -8.94]	3.257				
UPA 15 mg QD	237	21.2	7.9	-59.88	[-64.97, -54.80]	2.590	-44.55	[-52.22, -36.87]	3.907	<0.001***
UPA 30 mg QD	253	21.5	6.2	-69.72	[-74.71, -64.74]	2.539	-54.39	[-62.00, -46.78]	3.876	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	81	19.2	15.7	-11.51	[-19.00, -4.02]	3.812				
UPA 15 mg QD	133	20.2	7.5	-60.44	[-66.70, -54.18]	3.183	-48.94	[-58.70, -39.17]	4.966	<0.001***
UPA 30 mg QD	133	20.5	5.6	-69.49	[-75.76, -63.23]	3.186	-57.98	[-67.75, -48.22]	4.969	<0.001***
vIGA-AD 4 (Severe)										
Placebo	42	21.1	15.5	-20.70	[-31.03, -10.37]	5.252				
UPA 15 mg QD	104	22.5	8.4	-57.43	[-64.61, -50.26]	3.644	-36.73	[-49.31, -24.16]	6.393	<0.001***
UPA 30 mg QD	120	22.6	6.7	-68.26	[-75.08, -61.44]	3.466	-47.56	[-59.94, -35.18]	6.293	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	60	20.5	16.5	-12.65	[-21.42, -3.89]	4.456				
UPA 15 mg QD	106	21.4	7.8	-59.91	[-67.01, -52.81]	3.609	-47.26	[-58.54, -35.98]	5.735	<0.001***
UPA 30 mg QD	115	21.6	5.1	-73.74	[-80.66, -66.82]	3.515	-61.09	[-72.25, -49.92]	5.676	<0.001***
Japan										
Placebo	1	11.0	13.0	21.68	[-24.19, 67.55]	22.514				
UPA 15 mg QD	13	18.4	8.0	-56.04	[-71.67, -40.42]	7.631	-77.73	[-126.08, -29.37]	23.765	0.003**
UPA 30 mg QD	14	19.4	8.1	-58.39	[-73.64, -43.15]	7.441	-80.08	[-128.32, -31.84]	23.709	0.002**
China										
Placebo	7	19.6	17.6	-11.69	[-36.81, 13.43]	12.459				
UPA 15 mg QD	14	23.1	9.4	-57.16	[-76.80, -37.53]	9.685	-45.47	[-77.38, -13.57]	15.807	0.006**
UPA 30 mg QD	16	22.6	9.1	-56.69	[-74.72, -38.66]	8.900	-45.00	[-75.91, -14.08]	15.318	0.005**

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo	55	19.4	14.5	-18.85	[-28.13, -9.56]	4.720				
UPA 15 mg QD	104	21.1	7.8	-59.19	[-66.41, -51.97]	3.669	-40.34	[-52.10, -28.58]	5.978	<0.001***
UPA 30 mg QD	108	21.5	6.6	-66.89	[-74.03, -59.74]	3.631	-48.04	[-59.76, -36.32]	5.957	<0.001***
Adolescent										
Placebo	17	17.8	13.4	-17.13	[-34.91, 0.65]	8.993				
UPA 15 mg QD	37	20.5	7.9	-56.84	[-70.94, -42.74]	7.113	-39.71	[-62.43, -16.98]	11.487	0.001**
UPA 30 mg QD	40	21.3	5.4	-73.40	[-87.34, -59.47]	7.028	-56.27	[-78.99, -33.55]	11.483	<0.001***
Adult										
Placebo	106	20.2	16.0	-15.10	[-21.54, -8.66]	3.279				
UPA 15 mg QD	200	21.3	7.9	-59.53	[-64.51, -54.54]	2.538	-44.43	[-52.57, -36.28]	4.146	<0.001***
UPA 30 mg QD	213	21.5	6.3	-67.92	[-72.78, -63.05]	2.477	-52.82	[-60.89, -44.75]	4.109	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__5.3.1

表 2.7.3.6-28.　二重盲検投与期の来院時別での POEM スコアのベースラインからの変化量（MMRM，ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo	263	21.4	19.3	-2.3	[-3.1, -1.6]	0.40				
UPA 15 mg QD	272	21.2	10.2	-11.3	[-12.0, -10.5]	0.40	-8.9	[-9.9, -7.9]	0.50	<0.001***
UPA 30 mg QD	272	21.3	8.4	-13.1	[-13.9, -12.4]	0.39	-10.8	[-11.8, -9.8]	0.50	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	148	20.4	18.1	-2.2	[-3.2, -1.3]	0.48				
UPA 15 mg QD	147	20.3	9.7	-10.5	[-11.4, -9.5]	0.48	-8.2	[-9.5, -6.9]	0.67	<0.001***
UPA 30 mg QD	147	20.4	7.4	-12.9	[-13.8, -11.9]	0.48	-10.6	[-11.9, -9.3]	0.67	<0.001***
vIGA-AD 4 (Severe)										
Placebo	115	22.7	20.7	-1.8	[-2.9, -0.7]	0.54				
UPA 15 mg QD	125	22.3	10.7	-11.6	[-12.6, -10.6]	0.52	-9.8	[-11.3, -8.3]	0.75	<0.001***
UPA 30 mg QD	125	22.4	9.6	-12.8	[-13.8, -11.8]	0.52	-11.0	[-12.5, -9.5]	0.75	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	120	21.5	18.5	-3.0	[-4.1, -1.9]	0.55				
UPA 15 mg QD	125	21.5	10.7	-10.8	[-11.8, -9.7]	0.54	-7.7	[-9.2, -6.2]	0.77	<0.001***
UPA 30 mg QD	122	21.6	8.0	-13.4	[-14.5, -12.3]	0.54	-10.4	[-11.9, -8.9]	0.77	<0.001***
Japan										
Placebo	11	20.5	20.3	0.6	[-2.8, 3.9]	1.64				
UPA 15 mg QD	15	18.6	9.1	-9.7	[-12.5, -6.9]	1.39	-10.2	[-14.6, -5.9]	2.15	<0.001***
UPA 30 mg QD	16	18.8	9.4	-9.4	[-12.1, -6.7]	1.35	-9.9	[-14.2, -5.6]	2.12	<0.001***
China										
Placebo	14	21.4	19.4	-2.5	[-5.5, 0.6]	1.51				
UPA 15 mg QD	14	23.1	11.0	-11.7	[-14.7, -8.7]	1.50	-9.2	[-13.5, -4.9]	2.14	<0.001***
UPA 30 mg QD	17	22.5	9.1	-13.3	[-16.0, -10.5]	1.36	-10.8	[-14.9, -6.7]	2.03	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo	118	21.4	20.0	-1.3	[-2.3, -0.2]	0.52				
UPA 15 mg QD	118	21.0	9.7	-11.2	[-12.3, -10.2]	0.52	-10.0	[-11.4, -8.5]	0.74	<0.001***
UPA 30 mg QD	117	21.2	8.6	-12.6	[-13.6, -11.5]	0.52	-11.3	[-12.8, -9.9]	0.74	<0.001***
Adolescent										
Placebo	37	19.3	17.0	-2.9	[-5.0, -0.9]	1.03				
UPA 15 mg QD	40	20.6	9.2	-11.2	[-13.1, -9.2]	0.98	-8.2	[-11.1, -5.4]	1.42	<0.001***
UPA 30 mg QD	42	21.5	7.4	-13.5	[-15.4, -11.5]	0.97	-10.5	[-13.3, -7.7]	1.42	<0.001***
Adult										
Placebo	226	21.7	19.6	-1.9	[-2.7, -1.2]	0.38				
UPA 15 mg QD	232	21.3	10.4	-10.9	[-11.7, -10.2]	0.38	-9.0	[-10.1, -8.0]	0.53	<0.001***
UPA 30 mg QD	230	21.3	8.6	-12.7	[-13.4, -12.0]	0.38	-10.8	[-11.8, -9.7]	0.54	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo	160	20.4	15.8	-4.6	[-5.7, -3.6]	0.54				
UPA 15 mg QD	260	21.3	8.2	-13.4	[-14.2, -12.5]	0.45	-8.7	[-10.0, -7.4]	0.65	<0.001***
UPA 30 mg QD	267	21.4	6.2	-15.5	[-16.4, -14.6]	0.45	-10.8	[-12.1, -9.6]	0.65	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	102	19.6	15.6	-3.8	[-5.0, -2.6]	0.62				
UPA 15 mg QD	142	20.3	7.8	-12.5	[-13.6, -11.4]	0.54	-8.7	[-10.3, -7.1]	0.82	<0.001***
UPA 30 mg QD	140	20.6	6.0	-14.5	[-15.5, -13.4]	0.54	-10.7	[-12.3, -9.1]	0.82	<0.001***
vIGA-AD 4 (Severe)										
Placebo	58	21.8	16.1	-5.3	[-7.0, -3.6]	0.86				
UPA 15 mg QD	118	22.5	8.5	-13.8	[-15.0, -12.5]	0.63	-8.5	[-10.6, -6.4]	1.07	<0.001***
UPA 30 mg QD	127	22.4	6.4	-16.0	[-17.2, -14.8]	0.61	-10.8	[-12.8, -8.7]	1.06	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo	77	20.8	16.7	-3.8	[-5.3, -2.4]	0.75				
UPA 15 mg QD	116	21.6	9.1	-12.5	[-13.8, -11.3]	0.64	-8.7	[-10.6, -6.8]	0.98	<0.001***
UPA 30 mg QD	122	21.6	5.9	-15.7	[-17.0, -14.5]	0.62	-11.9	[-13.8, -10.0]	0.98	<0.001***
Japan										
Placebo	2	16.0	15.0	-1.1	[-8.7, 6.4]	3.68				
UPA 15 mg QD	15	18.6	9.6	-9.1	[-12.0, -6.3]	1.41	-8.0	[-16.0, 0.0]	3.94	0.051
UPA 30 mg QD	14	19.4	6.4	-12.9	[-15.9, -9.9]	1.45	-11.8	[-19.8, -3.7]	3.95	0.006**
China										
Placebo	8	20.3	17.0	-4.0	[-9.0, 0.9]	2.46				
UPA 15 mg QD	14	23.1	8.1	-14.5	[-18.4, -10.7]	1.88	-10.5	[-16.8, -4.2]	3.10	0.002**
UPA 30 mg QD	17	22.5	7.4	-15.1	[-18.5, -11.6]	1.70	-11.0	[-17.1, -5.0]	2.99	0.001**

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo	73	20.1	14.8	-5.2	[-6.6, -3.7]	0.72				
UPA 15 mg QD	115	21.1	7.0	-13.9	[-15.1, -12.8]	0.60	-8.8	[-10.6, -6.9]	0.94	<0.001***
UPA 30 mg QD	114	21.4	6.4	-14.9	[-16.1, -13.7]	0.60	-9.7	[-11.6, -7.9]	0.94	<0.001***
Adolescent										
Placebo	20	17.4	12.5	-5.9	[-8.9, -2.9]	1.51				
UPA 15 mg QD	41	20.7	8.9	-11.6	[-13.9, -9.4]	1.12	-5.7	[-9.5, -2.0]	1.89	0.003**
UPA 30 mg QD	40	21.4	5.2	-15.7	[-17.9, -13.4]	1.13	-9.7	[-13.5, -6.0]	1.90	<0.001***
Adult										
Placebo	140	20.8	16.3	-4.2	[-5.2, -3.1]	0.53				
UPA 15 mg QD	219	21.4	8.0	-13.3	[-14.2, -12.5]	0.44	-9.2	[-10.5, -7.8]	0.69	<0.001***
UPA 30 mg QD	227	21.5	6.4	-15.1	[-15.9, -14.2]	0.43	-10.9	[-12.3, -9.6]	0.69	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo	123	19.9	15.6	-4.3	[-5.5, -3.1]	0.61				
UPA 15 mg QD	237	21.2	7.9	-13.2	[-14.1, -12.2]	0.48	-8.9	[-10.3, -7.4]	0.73	<0.001***
UPA 30 mg QD	253	21.5	6.2	-15.3	[-16.2, -14.4]	0.47	-11.0	[-12.4, -9.5]	0.72	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	81	19.2	15.7	-3.5	[-4.8, -2.1]	0.69				
UPA 15 mg QD	133	20.2	7.5	-12.5	[-13.6, -11.3]	0.57	-9.0	[-10.8, -7.2]	0.90	<0.001***
UPA 30 mg QD	133	20.5	5.6	-14.6	[-15.7, -13.5]	0.57	-11.2	[-12.9, -9.4]	0.90	<0.001***
vIGA-AD 4 (Severe)										
Placebo	42	21.1	15.5	-5.1	[-7.1, -3.1]	1.02				
UPA 15 mg QD	104	22.5	8.4	-13.4	[-14.8, -12.1]	0.70	-8.4	[-10.8, -5.9]	1.23	<0.001***
UPA 30 mg QD	120	22.6	6.7	-15.5	[-16.8, -14.2]	0.66	-10.4	[-12.8, -8.0]	1.21	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	60	20.5	16.5	-3.7	[-5.4, -2.1]	0.84				
UPA 15 mg QD	106	21.4	7.8	-13.1	[-14.4, -11.7]	0.67	-9.3	[-11.5, -7.2]	1.07	<0.001***
UPA 30 mg QD	115	21.6	5.1	-16.2	[-17.5, -14.9]	0.65	-12.5	[-14.6, -10.4]	1.06	<0.001***
Japan										
Placebo	1	11.0	13.0	1.6	[-7.7, 10.8]	4.53				
UPA 15 mg QD	13	18.4	8.0	-10.3	[-13.4, -7.2]	1.49	-11.9	[-21.6, -2.1]	4.77	0.018*
UPA 30 mg QD	14	19.4	8.1	-11.3	[-14.2, -8.3]	1.44	-12.8	[-22.5, -3.1]	4.76	0.011*
China										
Placebo	7	19.6	17.6	-2.2	[-7.6, 3.2]	2.70				
UPA 15 mg QD	14	23.1	9.4	-13.3	[-17.5, -9.0]	2.09	-11.1	[-18.0, -4.2]	3.42	0.002**
UPA 30 mg QD	16	22.6	9.1	-13.0	[-16.9, -9.1]	1.92	-10.8	[-17.5, -4.1]	3.31	0.002**

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo	55	19.4	14.5	-5.0	[-6.7, -3.3]	0.86				
UPA 15 mg QD	104	21.1	7.8	-13.0	[-14.3, -11.7]	0.66	-8.1	[-10.2, -5.9]	1.08	<0.001***
UPA 30 mg QD	108	21.5	6.6	-14.5	[-15.7, -13.2]	0.65	-9.5	[-11.6, -7.4]	1.08	<0.001***
Adolescent										
Placebo	17	17.8	13.4	-5.0	[-8.0, -2.0]	1.50				
UPA 15 mg QD	37	20.5	7.9	-12.2	[-14.4, -9.9]	1.12	-7.2	[-10.9, -3.5]	1.88	<0.001***
UPA 30 mg QD	40	21.3	5.4	-15.4	[-17.5, -13.2]	1.10	-10.4	[-14.1, -6.7]	1.87	<0.001***
Adult										
Placebo	106	20.2	16.0	-4.0	[-5.2, -2.8]	0.63				
UPA 15 mg QD	200	21.3	7.9	-13.0	[-14.0, -12.1]	0.49	-9.0	[-10.6, -7.5]	0.79	<0.001***
UPA 30 mg QD	213	21.5	6.3	-14.9	[-15.8, -14.0]	0.47	-10.9	[-12.5, -9.4]	0.79	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__5.4.1

表 2.7.3.6-29.　ベースライン時の POEM スコアが 4 以上であった被験者のうち，二重盲検投与期の来院時別での POEM スコアがベースラインから 4 以上改善した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo + TCS	301	129 (42.9) [37.3, 48.4]	0					
UPA 15 mg QD + TCS	297	241 (81.1) [76.7, 85.6]	0	38.3	38.3	[31.2, 45.4]	<0.001***	0.878
UPA 30 mg QD + TCS	292	257 (88.0) [84.3, 91.7]	0	45.2	45.0	[38.4, 51.7]	<0.001***	0.121
vIGA-AD 3 (Moderate)								
Placebo + TCS	139	52 (37.4) [29.4, 45.5]	0					
UPA 15 mg QD + TCS	140	108 (77.1) [70.2, 84.1]	0	39.7		[29.1, 50.4]	<0.001***	
UPA 30 mg QD + TCS	137	122 (89.1) [83.8, 94.3]	0	51.6		[42.0, 61.2]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	162	77 (47.5) [39.8, 55.2]	0					
UPA 15 mg QD + TCS	157	133 (84.7) [79.1, 90.3]	0	37.2		[27.7, 46.7]	<0.001***	
UPA 30 mg QD + TCS	155	135 (87.1) [81.8, 92.4]	0	39.6		[30.2, 48.9]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	108	59 (54.6) [45.2, 64.0]	0					
UPA 15 mg QD + TCS	107	86 (80.4) [72.8, 87.9]	0	25.7		[13.7, 37.8]	<0.001***	
UPA 30 mg QD + TCS	104	91 (87.5) [81.1, 93.9]	0	32.9		[21.5, 44.2]	<0.001***	
Japan								
Placebo + TCS	18	6 (33.3) [11.6, 55.1]	0					
UPA 15 mg QD + TCS	16	13 (81.3) [62.1, 100.0]	0	47.9		[18.9, 76.9]	0.001**	
UPA 30 mg QD + TCS	17	15 (88.2) [72.9, 100.0]	0	54.9		[28.3, 81.5]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
China								
Placebo + TCS	18	7 (38.9) [16.4, 61.4]	0					
UPA 15 mg QD + TCS	17	14 (82.4) [64.2, 100.0]	0		43.5	[14.6, 72.4]	0.003**	
UPA 30 mg QD + TCS	16	14 (87.5) [71.3, 100.0]	0		48.6	[20.9, 76.4]	0.001**	
Other								
Placebo + TCS	157	57 (36.3) [28.8, 43.8]	0					
UPA 15 mg QD + TCS	157	128 (81.5) [75.5, 87.6]	0		45.2	[35.6, 54.9]	<0.001***	
UPA 30 mg QD + TCS	155	137 (88.4) [83.3, 93.4]	0		52.1	[43.0, 61.1]	<0.001***	
Adolescent								
Placebo + TCS	39	16 (41.0) [25.6, 56.5]	0					
UPA 15 mg QD + TCS	39	32 (82.1) [70.0, 94.1]	0		41.0	[21.4, 60.6]	<0.001***	
UPA 30 mg QD + TCS	35	26 (74.3) [59.8, 88.8]	0		33.3	[12.1, 54.4]	0.002**	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Adult								
Placebo + TCS	262	113 (43.1) [37.1, 49.1]	0					
UPA 15 mg QD + TCS	258	209 (81.0) [76.2, 85.8]	0	37.9		[30.2, 45.6]	<0.001***	
UPA 30 mg QD + TCS	257	231 (89.9) [86.2, 93.6]	0	46.8		[39.7, 53.8]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo + TCS	301	140 (46.5) [40.9, 52.1]	0					
UPA 15 mg QD + TCS	297	254 (85.5) [81.5, 89.5]	0	39.0	39.0	[32.1, 45.9]	<0.001***	0.048*
UPA 30 mg QD + TCS	292	266 (91.1) [87.8, 94.4]	0	44.6	44.6	[38.1, 51.0]	<0.001***	0.559
vIGA-AD 3 (Moderate)								
Placebo + TCS	139	69 (49.6) [41.3, 58.0]	0					
UPA 15 mg QD + TCS	140	116 (82.9) [76.6, 89.1]	0	33.2		[22.8, 43.6]	<0.001***	
UPA 30 mg QD + TCS	137	126 (92.0) [87.4, 96.5]	0	42.3		[32.9, 51.8]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	162	71 (43.8) [36.2, 51.5]	0					
UPA 15 mg QD + TCS	157	138 (87.9) [82.8, 93.0]	0	44.1		[34.9, 53.3]	<0.001***	
UPA 30 mg QD + TCS	155	140 (90.3) [85.7, 95.0]	0	46.5		[37.5, 55.4]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	108	59 (54.6) [45.2, 64.0]	0					
UPA 15 mg QD + TCS	107	98 (91.6) [86.3, 96.8]	0	37.0		[26.2, 47.7]	<0.001***	
UPA 30 mg QD + TCS	104	97 (93.3) [88.5, 98.1]	0	38.6		[28.1, 49.2]	<0.001***	
Japan								
Placebo + TCS	18	8 (44.4) [21.5, 67.4]	0					
UPA 15 mg QD + TCS	16	13 (81.3) [62.1, 100.0]	0	36.8		[6.9, 66.7]	0.016*	
UPA 30 mg QD + TCS	17	16 (94.1) [82.9, 100.0]	0	49.7		[24.1, 75.2]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
China								
Placebo + TCS	18	11 (61.1) [38.6, 83.6]	0					
UPA 15 mg QD + TCS	17	11 (64.7) [42.0, 87.4]	0	3.6		[-28.4, 35.6]	0.826	
UPA 30 mg QD + TCS	16	14 (87.5) [71.3, 100.0]	0	26.4		[-1.4, 54.1]	0.062	
Other								
Placebo + TCS	157	62 (39.5) [31.8, 47.1]	0					
UPA 15 mg QD + TCS	157	132 (84.1) [78.4, 89.8]	0	44.6		[35.0, 54.1]	<0.001***	
UPA 30 mg QD + TCS	155	139 (89.7) [84.9, 94.5]	0	50.2		[41.2, 59.2]	<0.001***	
Adolescent								
Placebo + TCS	39	20 (51.3) [35.6, 67.0]	0					
UPA 15 mg QD + TCS	39	30 (76.9) [63.7, 90.1]	0	25.6		[5.1, 46.2]	0.014*	
UPA 30 mg QD + TCS	35	32 (91.4) [82.2, 100.0]	0	40.1		[21.9, 58.4]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Adult								
Placebo + TCS	262	120 (45.8) [39.8, 51.8]	0					
UPA 15 mg QD + TCS	258	224 (86.8) [82.7, 90.9]	0	41.0		[33.7, 48.3]	<0.001***	
UPA 30 mg QD + TCS	257	234 (91.1) [87.6, 94.5]	0	45.2		[38.3, 52.2]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	301	117 (38.8) [33.3, 44.3]	2					
UPA 15 mg QD + TCS	297	234 (78.9) [74.3, 83.6]	2	40.2	40.2	[33.0, 47.4]	<0.001***	0.352
UPA 30 mg QD + TCS	292	244 (83.7) [79.4, 87.9]	2	44.9	44.9	[37.9, 51.8]	<0.001***	0.275
vIGA-AD 3 (Moderate)								
Placebo + TCS	139	57 (40.8) [32.6, 49.0]	2					
UPA 15 mg QD + TCS	140	108 (77.1) [70.2, 84.1]	0	36.4		[25.6, 47.1]	<0.001***	
UPA 30 mg QD + TCS	137	118 (86.1) [80.3, 91.9]	0	45.3		[35.3, 55.4]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	162	60 (37.0) [29.6, 44.5]	0					
UPA 15 mg QD + TCS	157	126 (80.5) [74.3, 86.7]	2	43.5		[33.8, 53.2]	<0.001***	
UPA 30 mg QD + TCS	155	126 (81.5) [75.4, 87.7]	2	44.5		[34.8, 54.1]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	108	53 (48.8) [39.3, 58.3]	2					
UPA 15 mg QD + TCS	107	88 (82.2) [75.0, 89.5]	0	33.4		[21.5, 45.4]	<0.001***	
UPA 30 mg QD + TCS	104	87 (84.0) [76.9, 91.1]	1	35.2		[23.4, 47.0]	<0.001***	
Japan								
Placebo + TCS	18	6 (33.3) [11.6, 55.1]	0					
UPA 15 mg QD + TCS	16	14 (87.5) [71.3, 100.0]	0	54.2		[27.0, 81.3]	<0.001***	
UPA 30 mg QD + TCS	17	14 (82.4) [64.2, 100.0]	0	49.0		[20.7, 77.4]	0.001**	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
China								
Placebo + TCS	18	13 (72.2) [51.5, 92.9]	0					
UPA 15 mg QD + TCS	17	12 (70.6) [48.9, 92.2]	0	-1.6		[-31.6, 28.3]	0.915	
UPA 30 mg QD + TCS	16	16 (100) [100.0, 100.0]	0	27.8		[7.1, 48.5]	0.009**	
Other								
Placebo + TCS	157	45 (28.7) [21.6, 35.7]	0					
UPA 15 mg QD + TCS	157	120 (76.7) [70.0, 83.3]	2	48.0		[38.3, 57.7]	<0.001***	
UPA 30 mg QD + TCS	155	127 (81.9) [75.9, 88.0]	1	53.3		[44.0, 62.6]	<0.001***	
Adolescent								
Placebo + TCS	39	17 (43.6) [28.0, 59.2]	0					
UPA 15 mg QD + TCS	39	27 (69.2) [54.7, 83.7]	0	25.6		[4.4, 46.9]	0.018*	
UPA 30 mg QD + TCS	35	27 (77.1) [63.2, 91.1]	0	33.6		[12.7, 54.4]	0.002**	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Adult								
Placebo + TCS	262	100 (38.1) [32.2, 43.9]	2					
UPA 15 mg QD + TCS	258	207 (80.4) [75.5, 85.2]	2		42.3	[34.7, 50.0]	<0.001***	
UPA 30 mg QD + TCS	257	217 (84.6) [80.1, 89.0]	2		46.5	[39.2, 53.9]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2__5.1.1

表 2.7.3.6-30. ベースライン時の POEM 睡眠項目スコアが 0 を超えていた被験者のうち，二重盲検投与期の来院時別での POEM 睡眠項目スコア 0 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo + TCS	286	20 (7.0) [4.0, 9.9]	0					
UPA 15 mg QD + TCS	285	74 (26.0) [20.9, 31.1]	0	19.0	19.0	[13.1, 24.8]	<0.001***	0.969
UPA 30 mg QD + TCS	282	103 (36.5) [30.9, 42.1]	0	29.5	29.6	[23.2, 35.9]	<0.001***	0.817
vIGA-AD 3 (Moderate)								
Placebo + TCS	130	9 (6.9) [2.6, 11.3]	0					
UPA 15 mg QD + TCS	134	31 (23.1) [16.0, 30.3]	0	16.2		[7.8, 24.6]	<0.001***	
UPA 30 mg QD + TCS	131	45 (34.4) [26.2, 42.5]	0	27.4		[18.2, 36.7]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	156	11 (7.1) [3.0, 11.1]	0					
UPA 15 mg QD + TCS	151	43 (28.5) [21.3, 35.7]	0	21.4		[13.2, 29.7]	<0.001***	
UPA 30 mg QD + TCS	151	58 (38.4) [30.7, 46.2]	0	31.4		[22.6, 40.1]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	103	10 (9.7) [4.0, 15.4]	0					
UPA 15 mg QD + TCS	102	25 (24.5) [16.2, 32.9]	0	14.8		[4.7, 24.9]	0.004**	
UPA 30 mg QD + TCS	102	35 (34.3) [25.1, 43.5]	0	24.6		[13.8, 35.4]	<0.001***	
Japan								
Placebo + TCS	15	0	0					
UPA 15 mg QD + TCS	14	7 (50.0) [23.8, 76.2]	0	50.0		[23.8, 76.2]	<0.001***	
UPA 30 mg QD + TCS	17	4 (23.5) [3.4, 43.7]	0	23.5		[3.4, 43.7]	0.022*	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
China								
Placebo + TCS	17	0	0					
UPA 15 mg QD + TCS	16	5 (31.3) [8.5, 54.0]	0	31.3		[8.5, 54.0]	0.007**	
UPA 30 mg QD + TCS	16	5 (31.3) [8.5, 54.0]	0	31.3		[8.5, 54.0]	0.007**	
Other								
Placebo + TCS	151	10 (6.6) [2.7, 10.6]	0					
UPA 15 mg QD + TCS	153	37 (24.2) [17.4, 31.0]	0	17.6		[9.7, 25.4]	<0.001***	
UPA 30 mg QD + TCS	147	59 (40.1) [32.2, 48.1]	0	33.5		[24.7, 42.4]	<0.001***	
Adolescent								
Placebo + TCS	37	2 (5.4) [0.0, 12.7]	0					
UPA 15 mg QD + TCS	35	8 (22.9) [8.9, 36.8]	0	17.5		[1.7, 33.2]	0.029*	
UPA 30 mg QD + TCS	31	13 (41.9) [24.6, 59.3]	0	36.5		[17.7, 55.4]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Adult								
Placebo + TCS	249	18 (7.2) [4.0, 10.4]	0					
UPA 15 mg QD + TCS	250	66 (26.4) [20.9, 31.9]	0	19.2		[12.8, 25.5]	<0.001***	
UPA 30 mg QD + TCS	251	90 (35.9) [29.9, 41.8]	0	28.6		[21.9, 35.4]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo + TCS	286	39 (13.6) [9.7, 17.6]	0					
UPA 15 mg QD + TCS	285	125 (43.9) [38.1, 49.6]	0	30.2	30.2	[23.2, 37.2]	<0.001***	0.784
UPA 30 mg QD + TCS	282	159 (56.4) [50.6, 62.2]	0	42.7	42.7	[35.7, 49.6]	<0.001***	0.394
vIGA-AD 3 (Moderate)								
Placebo + TCS	130	18 (13.8) [7.9, 19.8]	0					
UPA 15 mg QD + TCS	134	59 (44.0) [35.6, 52.4]	0	30.2		[19.9, 40.5]	<0.001***	
UPA 30 mg QD + TCS	131	85 (64.9) [56.7, 73.1]	0	51.0		[40.9, 61.1]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	156	21 (13.5) [8.1, 18.8]	0					
UPA 15 mg QD + TCS	151	66 (43.7) [35.8, 51.6]	0	30.2		[20.7, 39.8]	<0.001***	
UPA 30 mg QD + TCS	151	74 (49.0) [41.0, 57.0]	0	35.5		[25.9, 45.2]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	103	20 (19.4) [11.8, 27.1]	0					
UPA 15 mg QD + TCS	102	47 (46.1) [36.4, 55.8]	0	26.7		[14.3, 39.0]	<0.001***	
UPA 30 mg QD + TCS	102	55 (53.9) [44.2, 63.6]	0	34.5		[22.2, 46.8]	<0.001***	
Japan								
Placebo + TCS	15	2 (13.3) [0.0, 30.5]	0					
UPA 15 mg QD + TCS	14	8 (57.1) [31.2, 83.1]	0	43.8		[12.7, 74.9]	0.006**	
UPA 30 mg QD + TCS	17	8 (47.1) [23.3, 70.8]	0	33.7		[4.4, 63.0]	0.024*	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
China								
Placebo + TCS	17	0	0					
UPA 15 mg QD + TCS	16	7 (43.8) [19.4, 68.1]	0	43.8		[19.4, 68.1]	<0.001***	
UPA 30 mg QD + TCS	16	5 (31.3) [8.5, 54.0]	0	31.3		[8.5, 54.0]	0.007**	
Other								
Placebo + TCS	151	17 (11.3) [6.2, 16.3]	0					
UPA 15 mg QD + TCS	153	63 (41.2) [33.4, 49.0]	0	29.9		[20.6, 39.2]	<0.001***	
UPA 30 mg QD + TCS	147	91 (61.9) [54.1, 69.8]	0	50.6		[41.3, 60.0]	<0.001***	
Adolescent								
Placebo + TCS	37	4 (10.8) [0.8, 20.8]	0					
UPA 15 mg QD + TCS	35	16 (45.7) [29.2, 62.2]	0	34.9		[15.6, 54.2]	<0.001***	
UPA 30 mg QD + TCS	31	18 (58.1) [40.7, 75.4]	0	47.3		[27.2, 67.3]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Adult								
Placebo + TCS	249	35 (14.1) [9.7, 18.4]	0					
UPA 15 mg QD + TCS	250	109 (43.6) [37.5, 49.7]	0	29.5		[22.0, 37.1]	<0.001***	
UPA 30 mg QD + TCS	251	141 (56.2) [50.0, 62.3]	0	42.1		[34.6, 49.6]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	286	34 (11.9) [8.2, 15.7]	2					
UPA 15 mg QD + TCS	285	125 (43.8) [38.0, 49.5]	2	31.8	31.7	[24.9, 38.4]	<0.001***	0.638
UPA 30 mg QD + TCS	282	146 (51.7) [45.9, 57.6]	2	39.8	39.6	[32.7, 46.5]	<0.001***	0.192
vIGA-AD 3 (Moderate)								
Placebo + TCS	130	14 (10.9) [5.5, 16.3]	2					
UPA 15 mg QD + TCS	134	60 (44.8) [36.4, 53.2]	0	33.9		[23.9, 43.9]	<0.001***	
UPA 30 mg QD + TCS	131	77 (58.8) [50.3, 67.2]	0	47.9		[37.9, 57.9]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	156	20 (12.8) [7.6, 18.1]	0					
UPA 15 mg QD + TCS	151	65 (42.9) [34.9, 50.8]	2	30.0		[20.5, 39.6]	<0.001***	
UPA 30 mg QD + TCS	151	69 (45.6) [37.6, 53.6]	2	32.8		[23.2, 42.4]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	103	19 (18.6) [11.1, 26.2]	2					
UPA 15 mg QD + TCS	102	54 (52.9) [43.3, 62.6]	0	34.3		[22.1, 46.6]	<0.001***	
UPA 30 mg QD + TCS	102	52 (51.4) [41.7, 61.2]	1	32.8		[20.5, 45.2]	<0.001***	
Japan								
Placebo + TCS	15	0	0					
UPA 15 mg QD + TCS	14	10 (71.4) [47.8, 95.1]	0	71.4		[47.8, 95.1]	<0.001***	
UPA 30 mg QD + TCS	17	11 (64.7) [42.0, 87.4]	0	64.7		[42.0, 87.4]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
China								
Placebo + TCS	17	2 (11.8) [0.0, 27.1]	0					
UPA 15 mg QD + TCS	16	6 (37.5) [13.8, 61.2]	0	25.7		[-2.5, 54.0]	0.074	
UPA 30 mg QD + TCS	16	5 (31.3) [8.5, 54.0]	0	19.5		[-7.9, 46.9]	0.163	
Other								
Placebo + TCS	151	13 (8.6) [4.1, 13.1]	0					
UPA 15 mg QD + TCS	153	55 (35.8) [28.1, 43.4]	2	27.2		[18.3, 36.0]	<0.001***	
UPA 30 mg QD + TCS	147	77 (52.7) [44.6, 60.8]	1	44.1		[34.8, 53.3]	<0.001***	
Adolescent								
Placebo + TCS	37	1 (2.7) [0.0, 7.9]	0					
UPA 15 mg QD + TCS	35	7 (20.0) [6.7, 33.3]	0	17.3		[3.1, 31.5]	0.017*	
UPA 30 mg QD + TCS	31	14 (45.2) [27.6, 62.7]	0	42.5		[24.2, 60.7]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Adult								
Placebo + TCS	249	33 (13.3) [9.1, 17.6]	2					
UPA 15 mg QD + TCS	250	118 (47.1) [40.9, 53.3]	2	33.8		[26.3, 41.3]	<0.001***	
UPA 30 mg QD + TCS	251	132 (52.5) [46.3, 58.8]	2	39.2		[31.7, 46.7]	<0.001***	

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2__5.2.1

表 2.7.3.6-31. 二重盲検投与期の来院時別での POEM スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo + TCS	292	21.1	17.7	-15.10	[-19.10, -11.10]	2.038				
UPA 15 mg QD + TCS	294	21.0	10.4	-50.14	[-54.12, -46.16]	2.029	-35.04	[-39.91, -30.16]	2.485	<0.001***
UPA 30 mg QD + TCS	286	21.6	8.8	-58.93	[-62.96, -54.90]	2.055	-43.83	[-48.74, -38.91]	2.504	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	134	20.0	17.1	-11.78	[-17.24, -6.31]	2.780				
UPA 15 mg QD + TCS	137	20.3	10.0	-48.84	[-54.24, -43.44]	2.746	-37.07	[-44.75, -29.38]	3.908	<0.001***
UPA 30 mg QD + TCS	135	19.8	7.7	-60.42	[-65.86, -54.98]	2.766	-48.64	[-56.35, -40.93]	3.922	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	158	22.0	18.2	-16.38	[-20.77, -11.99]	2.233				
UPA 15 mg QD + TCS	157	21.6	10.9	-49.50	[-53.92, -45.08]	2.250	-33.12	[-39.34, -26.90]	3.164	<0.001***
UPA 30 mg QD + TCS	151	23.2	9.9	-56.47	[-60.97, -51.96]	2.294	-40.09	[-46.39, -33.78]	3.208	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	106	21.2	16.4	-22.30	[-27.63, -16.98]	2.705				
UPA 15 mg QD + TCS	106	21.2	10.3	-50.75	[-56.07, -45.43]	2.704	-28.44	[-35.97, -20.92]	3.825	<0.001***
UPA 30 mg QD + TCS	100	21.6	8.2	-60.93	[-66.41, -55.45]	2.785	-38.62	[-46.26, -30.98]	3.883	<0.001***
Japan										
Placebo + TCS	18	19.8	17.7	-12.12	[-24.73, 0.49]	6.270				
UPA 15 mg QD + TCS	16	19.4	8.7	-52.97	[-66.36, -39.58]	6.658	-40.85	[-59.24, -22.45]	9.144	<0.001***
UPA 30 mg QD + TCS	17	21.1	10.4	-51.90	[-64.99, -38.81]	6.508	-39.78	[-57.97, -21.60]	9.041	<0.001***
China										
Placebo + TCS	17	23.0	19.5	-0.03	[-21.75, 21.68]	10.785				
UPA 15 mg QD + TCS	17	21.3	10.5	-52.31	[-73.90, -30.73]	10.721	-52.28	[-83.00, -21.56]	15.261	0.001**
UPA 30 mg QD + TCS	16	21.1	10.0	-57.52	[-79.80, -35.23]	11.068	-57.48	[-88.74, -26.22]	15.529	0.001**

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo + TCS	151	20.8	18.4	-10.14	[-14.89, -5.38]	2.420				
UPA 15 mg QD + TCS	155	21.0	10.7	-47.84	[-52.53, -43.14]	2.390	-37.70	[-44.38, -31.02]	3.400	<0.001***
UPA 30 mg QD + TCS	153	21.7	8.9	-57.60	[-62.32, -52.87]	2.405	-47.46	[-54.17, -40.75]	3.415	<0.001***
Adolescent										
Placebo + TCS	37	19.4	16.6	-14.42	[-24.30, -4.53]	4.987				
UPA 15 mg QD + TCS	38	19.4	8.5	-53.37	[-63.12, -43.62]	4.919	-38.95	[-52.83, -25.07]	7.002	<0.001***
UPA 30 mg QD + TCS	34	17.9	7.0	-56.90	[-67.25, -46.56]	5.217	-42.49	[-56.82, -28.16]	7.229	<0.001***
Adult										
Placebo + TCS	255	21.3	17.8	-14.22	[-17.92, -10.52]	1.884				
UPA 15 mg QD + TCS	256	21.2	10.7	-48.71	[-52.40, -45.01]	1.881	-34.49	[-39.71, -29.27]	2.661	<0.001***
UPA 30 mg QD + TCS	252	22.1	9.1	-58.43	[-62.15, -54.71]	1.897	-44.21	[-49.46, -38.96]	2.676	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo + TCS	233	21.1	15.8	-23.02	[-27.50, -18.54]	2.282				
UPA 15 mg QD + TCS	283	21.0	8.6	-59.72	[-63.94, -55.50]	2.150	-36.70	[-42.16, -31.24]	2.781	<0.001***
UPA 30 mg QD + TCS	280	21.6	6.1	-72.08	[-76.32, -67.85]	2.159	-49.06	[-54.54, -43.58]	2.791	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	117	20.0	15.6	-19.62	[-25.69, -13.54]	3.091				
UPA 15 mg QD + TCS	131	20.3	8.0	-59.58	[-65.36, -53.80]	2.939	-39.96	[-48.35, -31.58]	4.265	<0.001***
UPA 30 mg QD + TCS	132	19.8	4.8	-74.78	[-80.56, -69.01]	2.937	-55.16	[-63.55, -46.78]	4.264	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	116	22.3	16.1	-24.63	[-29.91, -19.35]	2.685				
UPA 15 mg QD + TCS	152	21.6	9.0	-58.09	[-62.85, -53.32]	2.425	-33.45	[-40.56, -26.35]	3.615	<0.001***
UPA 30 mg QD + TCS	148	23.2	7.3	-68.54	[-73.38, -63.71]	2.461	-43.91	[-51.08, -36.75]	3.646	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	93	21.3	15.1	-28.27	[-34.32, -22.21]	3.078				
UPA 15 mg QD + TCS	107	21.2	7.7	-63.50	[-69.18, -57.82]	2.887	-35.24	[-43.54, -26.93]	4.220	<0.001***
UPA 30 mg QD + TCS	101	21.8	6.4	-69.81	[-75.66, -63.95]	2.975	-41.54	[-49.96, -33.11]	4.281	<0.001***
Japan										
Placebo + TCS	12	18.8	12.3	-32.06	[-48.39, -15.73]	8.098				
UPA 15 mg QD + TCS	15	19.4	6.6	-61.70	[-76.78, -46.62]	7.456	-29.64	[-51.85, -7.44]	10.999	0.010**
UPA 30 mg QD + TCS	16	20.7	5.1	-76.83	[-91.50, -62.16]	7.252	-44.77	[-66.76, -22.78]	10.894	<0.001***
China										
Placebo + TCS	17	23.0	18.8	-2.74	[-24.41, 18.93]	10.761				
UPA 15 mg QD + TCS	14	21.4	11.7	-42.96	[-65.72, -20.19]	11.330	-40.22	[-71.74, -8.69]	15.675	0.014*
UPA 30 mg QD + TCS	16	21.1	8.3	-65.48	[-87.71, -43.24]	11.042	-62.74	[-93.93, -31.54]	15.494	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo + TCS	111	20.9	16.3	-19.09	[-24.67, -13.51]	2.841				
UPA 15 mg QD + TCS	147	21.0	9.1	-56.90	[-61.90, -51.89]	2.546	-37.81	[-45.30, -30.31]	3.813	<0.001***
UPA 30 mg QD + TCS	147	21.6	5.8	-72.80	[-77.80, -67.79]	2.549	-53.71	[-61.21, -46.20]	3.819	<0.001***
Adolescent										
Placebo + TCS	30	20.2	14.6	-27.77	[-38.44, -17.10]	5.380				
UPA 15 mg QD + TCS	35	19.3	7.7	-56.56	[-66.48, -46.65]	4.997	-28.80	[-43.35, -14.24]	7.337	<0.001***
UPA 30 mg QD + TCS	35	18.2	5.5	-69.04	[-79.04, -59.04]	5.038	-41.28	[-55.94, -26.61]	7.391	<0.001***
Adult										
Placebo + TCS	203	21.3	16.0	-21.35	[-25.68, -17.02]	2.205				
UPA 15 mg QD + TCS	248	21.3	8.7	-59.18	[-63.18, -55.17]	2.039	-37.83	[-43.72, -31.93]	3.002	<0.001***
UPA 30 mg QD + TCS	245	22.1	6.2	-71.73	[-75.76, -67.70]	2.054	-50.38	[-56.30, -44.46]	3.015	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo + TCS	201	21.3	15.8	-21.73	[-26.65, -16.81]	2.507				
UPA 15 mg QD + TCS	273	20.9	8.9	-56.88	[-61.37, -52.39]	2.288	-35.15	[-41.17, -29.12]	3.071	<0.001***
UPA 30 mg QD + TCS	269	21.6	7.2	-66.80	[-71.32, -62.29]	2.302	-45.07	[-51.12, -39.02]	3.083	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	102	20.1	15.5	-17.66	[-24.27, -11.05]	3.362				
UPA 15 mg QD + TCS	128	20.1	8.1	-56.85	[-62.91, -50.79]	3.081	-39.19	[-48.16, -30.22]	4.560	<0.001***
UPA 30 mg QD + TCS	132	19.8	5.9	-68.87	[-74.88, -62.86]	3.057	-51.21	[-60.15, -42.28]	4.544	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	99	22.5	16.0	-23.99	[-30.07, -17.91]	3.093				
UPA 15 mg QD + TCS	145	21.6	9.5	-55.15	[-60.44, -49.85]	2.692	-31.16	[-39.21, -23.10]	4.098	<0.001***
UPA 30 mg QD + TCS	137	23.3	8.5	-63.82	[-69.23, -58.40]	2.754	-39.83	[-47.97, -31.68]	4.144	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	21.3	14.4	-29.69	[-36.75, -22.64]	3.584				
UPA 15 mg QD + TCS	104	21.1	7.7	-62.47	[-68.79, -56.16]	3.209	-32.78	[-42.25, -23.31]	4.810	<0.001***
UPA 30 mg QD + TCS	96	21.8	7.2	-66.32	[-72.88, -59.75]	3.334	-36.62	[-46.26, -26.99]	4.895	<0.001***
Japan										
Placebo + TCS	11	18.5	13.0	-22.14	[-42.96, -1.32]	10.310				
UPA 15 mg QD + TCS	15	19.4	6.5	-61.15	[-79.51, -42.80]	9.063	-39.01	[-66.75, -11.28]	13.717	0.007**
UPA 30 mg QD + TCS	16	20.7	6.6	-68.58	[-86.40, -50.77]	8.797	-46.45	[-73.89, -19.00]	13.579	0.001**
China										
Placebo + TCS	17	23.0	17.3	-9.79	[-29.35, 9.78]	9.714				
UPA 15 mg QD + TCS	14	21.4	9.1	-56.58	[-76.99, -36.17]	10.154	-46.79	[-75.17, -18.41]	14.107	0.002**
UPA 30 mg QD + TCS	16	21.1	7.8	-65.06	[-85.12, -45.00]	9.958	-55.27	[-83.46, -27.08]	13.995	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo + TCS	93	21.2	17.0	-15.24	[-21.63, -8.85]	3.250				
UPA 15 mg QD + TCS	140	20.9	10.0	-50.82	[-56.32, -45.33]	2.795	-35.58	[-44.01, -27.16]	4.285	<0.001***
UPA 30 mg QD + TCS	141	21.6	7.2	-66.13	[-71.62, -60.64]	2.792	-50.89	[-59.32, -42.46]	4.286	<0.001***
Adolescent										
Placebo + TCS	27	20.2	15.0	-21.93	[-34.27, -9.58]	6.220				
UPA 15 mg QD + TCS	35	19.3	9.3	-47.22	[-58.19, -36.25]	5.525	-25.29	[-41.80, -8.78]	8.316	0.003**
UPA 30 mg QD + TCS	32	18.1	6.8	-62.00	[-73.47, -50.54]	5.775	-40.08	[-56.96, -23.20]	8.506	<0.001***
Adult										
Placebo + TCS	174	21.4	15.9	-20.79	[-25.62, -15.95]	2.462				
UPA 15 mg QD + TCS	238	21.1	8.8	-57.27	[-61.59, -52.96]	2.199	-36.49	[-42.97, -30.01]	3.300	<0.001***
UPA 30 mg QD + TCS	237	22.1	7.3	-66.74	[-71.08, -62.40]	2.210	-45.96	[-52.45, -39.46]	3.310	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2__5.3.1

表 2.7.3.6-32.　二重盲検投与期の来院時別での POEM スコアのベースラインからの変化量（MMRM，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo + TCS	292	21.1	17.7	-3.6	[-4.4, -2.8]	0.40				
UPA 15 mg QD + TCS	294	21.0	10.4	-10.8	[-11.5, -10.0]	0.40	-7.1	[-8.1, -6.2]	0.49	<0.001***
UPA 30 mg QD + TCS	286	21.6	8.8	-12.7	[-13.5, -11.9]	0.40	-9.1	[-10.0, -8.1]	0.49	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	134	20.0	17.1	-2.9	[-3.9, -2.0]	0.50				
UPA 15 mg QD + TCS	137	20.3	10.0	-10.1	[-11.1, -9.1]	0.49	-7.1	[-8.5, -5.8]	0.70	<0.001***
UPA 30 mg QD + TCS	135	19.8	7.7	-12.3	[-13.2, -11.3]	0.50	-9.3	[-10.7, -7.9]	0.70	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	158	22.0	18.2	-4.0	[-4.9, -3.0]	0.49				
UPA 15 mg QD + TCS	157	21.6	10.9	-11.1	[-12.1, -10.1]	0.49	-7.1	[-8.5, -5.8]	0.69	<0.001***
UPA 30 mg QD + TCS	151	23.2	9.9	-12.9	[-13.9, -11.9]	0.50	-8.9	[-10.3, -7.5]	0.70	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	106	21.2	16.4	-5.0	[-6.1, -3.8]	0.56				
UPA 15 mg QD + TCS	106	21.2	10.3	-10.9	[-12.1, -9.8]	0.56	-6.0	[-7.6, -4.4]	0.80	<0.001***
UPA 30 mg QD + TCS	100	21.6	8.2	-13.3	[-14.4, -12.1]	0.58	-8.3	[-9.9, -6.7]	0.81	<0.001***
Japan										
Placebo + TCS	18	19.8	17.7	-2.1	[-4.7, 0.5]	1.31				
UPA 15 mg QD + TCS	16	19.4	8.7	-10.9	[-13.7, -8.1]	1.39	-8.8	[-12.7, -5.0]	1.91	<0.001***
UPA 30 mg QD + TCS	17	21.1	10.4	-10.1	[-12.8, -7.3]	1.36	-8.0	[-11.8, -4.2]	1.88	<0.001***
China										
Placebo + TCS	17	23.0	19.5	-2.7	[-5.9, 0.6]	1.63				
UPA 15 mg QD + TCS	17	21.3	10.5	-11.1	[-14.4, -7.9]	1.62	-8.5	[-13.1, -3.8]	2.30	0.001**
UPA 30 mg QD + TCS	16	21.1	10.0	-11.6	[-15.0, -8.2]	1.67	-8.9	[-13.7, -4.2]	2.34	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo + TCS	151	20.8	18.4	-2.7	[-3.7, -1.8]	0.49				
UPA 15 mg QD + TCS	155	21.0	10.7	-10.3	[-11.3, -9.4]	0.48	-7.6	[-9.0, -6.3]	0.68	<0.001***
UPA 30 mg QD + TCS	153	21.7	8.9	-12.5	[-13.4, -11.5]	0.48	-9.8	[-11.1, -8.4]	0.69	<0.001***
Adolescent										
Placebo + TCS	37	19.4	16.6	-2.6	[-4.4, -0.8]	0.91				
UPA 15 mg QD + TCS	38	19.4	8.5	-10.7	[-12.5, -8.9]	0.90	-8.1	[-10.6, -5.5]	1.28	<0.001***
UPA 30 mg QD + TCS	34	17.9	7.0	-11.5	[-13.4, -9.7]	0.95	-8.9	[-11.5, -6.3]	1.32	<0.001***
Adult										
Placebo + TCS	255	21.3	17.8	-3.6	[-4.3, -2.9]	0.38				
UPA 15 mg QD + TCS	256	21.2	10.7	-10.6	[-11.3, -9.9]	0.37	-7.0	[-8.0, -6.0]	0.53	<0.001***
UPA 30 mg QD + TCS	252	22.1	9.1	-12.7	[-13.5, -12.0]	0.38	-9.1	[-10.2, -8.1]	0.53	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo + TCS	233	21.1	15.8	-5.3	[-6.1, -4.4]	0.44				
UPA 15 mg QD + TCS	283	21.0	8.6	-12.7	[-13.5, -11.9]	0.42	-7.4	[-8.5, -6.4]	0.54	<0.001***
UPA 30 mg QD + TCS	280	21.6	6.1	-15.4	[-16.2, -14.6]	0.42	-10.2	[-11.2, -9.1]	0.54	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	117	20.0	15.6	-4.3	[-5.4, -3.3]	0.54				
UPA 15 mg QD + TCS	131	20.3	8.0	-12.2	[-13.2, -11.2]	0.51	-7.9	[-9.3, -6.4]	0.74	<0.001***
UPA 30 mg QD + TCS	132	19.8	4.8	-15.1	[-16.1, -14.1]	0.51	-10.8	[-12.2, -9.3]	0.74	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	116	22.3	16.1	-5.9	[-7.0, -4.8]	0.58				
UPA 15 mg QD + TCS	152	21.6	9.0	-12.9	[-13.9, -11.9]	0.52	-7.0	[-8.5, -5.5]	0.78	<0.001***
UPA 30 mg QD + TCS	148	23.2	7.3	-15.5	[-16.5, -14.5]	0.53	-9.6	[-11.1, -8.1]	0.79	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	93	21.3	15.1	-6.1	[-7.3, -4.8]	0.63				
UPA 15 mg QD + TCS	107	21.2	7.7	-13.6	[-14.8, -12.5]	0.60	-7.6	[-9.3, -5.8]	0.87	<0.001***
UPA 30 mg QD + TCS	101	21.8	6.4	-15.2	[-16.4, -14.0]	0.61	-9.1	[-10.8, -7.3]	0.88	<0.001***
Japan										
Placebo + TCS	12	18.8	12.3	-6.0	[-9.1, -2.9]	1.53				
UPA 15 mg QD + TCS	15	19.4	6.6	-12.8	[-15.6, -9.9]	1.39	-6.8	[-10.9, -2.6]	2.06	0.002**
UPA 30 mg QD + TCS	16	20.7	5.1	-15.3	[-18.0, -12.6]	1.35	-9.3	[-13.4, -5.2]	2.04	<0.001***
China										
Placebo + TCS	17	23.0	18.8	-3.4	[-6.9, 0.1]	1.74				
UPA 15 mg QD + TCS	14	21.4	11.7	-9.9	[-13.7, -6.1]	1.88	-6.5	[-11.7, -1.4]	2.57	0.014*
UPA 30 mg QD + TCS	16	21.1	8.3	-13.3	[-17.0, -9.7]	1.79	-10.0	[-15.0, -4.9]	2.51	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo + TCS	111	20.9	16.3	-4.6	[-5.7, -3.5]	0.56				
UPA 15 mg QD + TCS	147	21.0	9.1	-12.1	[-13.1, -11.1]	0.50	-7.4	[-8.9, -6.0]	0.75	<0.001***
UPA 30 mg QD + TCS	147	21.6	5.8	-15.6	[-16.6, -14.6]	0.50	-11.0	[-12.5, -9.5]	0.75	<0.001***
Adolescent										
Placebo + TCS	30	20.2	14.6	-5.0	[-6.9, -3.1]	0.96				
UPA 15 mg QD + TCS	35	19.3	7.7	-11.6	[-13.3, -9.8]	0.90	-6.5	[-9.1, -3.9]	1.31	<0.001***
UPA 30 mg QD + TCS	35	18.2	5.5	-13.3	[-15.1, -11.5]	0.91	-8.2	[-10.9, -5.6]	1.33	<0.001***
Adult										
Placebo + TCS	203	21.3	16.0	-5.1	[-6.0, -4.3]	0.43				
UPA 15 mg QD + TCS	248	21.3	8.7	-12.7	[-13.5, -11.9]	0.40	-7.6	[-8.7, -6.4]	0.59	<0.001***
UPA 30 mg QD + TCS	245	22.1	6.2	-15.6	[-16.4, -14.8]	0.40	-10.5	[-11.6, -9.3]	0.59	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo + TCS	201	21.3	15.8	-5.1	[-6.0, -4.1]	0.50				
UPA 15 mg QD + TCS	273	20.9	8.9	-12.2	[-13.1, -11.3]	0.45	-7.2	[-8.3, -6.0]	0.61	<0.001***
UPA 30 mg QD + TCS	269	21.6	7.2	-14.3	[-15.2, -13.4]	0.45	-9.2	[-10.4, -8.0]	0.61	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	102	20.1	15.5	-4.2	[-5.4, -3.0]	0.61				
UPA 15 mg QD + TCS	128	20.1	8.1	-11.8	[-12.9, -10.7]	0.56	-7.6	[-9.2, -6.0]	0.83	<0.001***
UPA 30 mg QD + TCS	132	19.8	5.9	-14.0	[-15.1, -12.9]	0.56	-9.8	[-11.4, -8.2]	0.83	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	99	22.5	16.0	-5.6	[-6.9, -4.3]	0.66				
UPA 15 mg QD + TCS	145	21.6	9.5	-12.3	[-13.5, -11.2]	0.58	-6.7	[-8.4, -5.0]	0.88	<0.001***
UPA 30 mg QD + TCS	137	23.3	8.5	-14.4	[-15.5, -13.2]	0.59	-8.7	[-10.5, -7.0]	0.89	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	21.3	14.4	-6.4	[-7.9, -4.9]	0.74				
UPA 15 mg QD + TCS	104	21.1	7.7	-13.5	[-14.8, -12.2]	0.67	-7.1	[-9.1, -5.1]	1.00	<0.001***
UPA 30 mg QD + TCS	96	21.8	7.2	-14.2	[-15.6, -12.9]	0.70	-7.8	[-9.8, -5.8]	1.02	<0.001***
Japan										
Placebo + TCS	11	18.5	13.0	-4.9	[-8.4, -1.4]	1.72				
UPA 15 mg QD + TCS	15	19.4	6.5	-13.0	[-16.0, -9.9]	1.51	-8.1	[-12.7, -3.5]	2.28	0.001**
UPA 30 mg QD + TCS	16	20.7	6.6	-13.8	[-16.8, -10.8]	1.46	-8.9	[-13.5, -4.3]	2.27	<0.001***
China										
Placebo + TCS	17	23.0	17.3	-4.9	[-8.0, -1.8]	1.53				
UPA 15 mg QD + TCS	14	21.4	9.1	-12.6	[-15.9, -9.2]	1.65	-7.7	[-12.2, -3.1]	2.25	0.001**
UPA 30 mg QD + TCS	16	21.1	7.8	-13.8	[-16.9, -10.6]	1.57	-8.9	[-13.3, -4.5]	2.20	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo + TCS	93	21.2	17.0	-3.8	[-5.1, -2.5]	0.66				
UPA 15 mg QD + TCS	140	20.9	10.0	-10.9	[-12.0, -9.8]	0.56	-7.1	[-8.8, -5.4]	0.86	<0.001***
UPA 30 mg QD + TCS	141	21.6	7.2	-14.2	[-15.3, -13.1]	0.56	-10.3	[-12.0, -8.7]	0.86	<0.001***
Adolescent										
Placebo + TCS	27	20.2	15.0	-4.3	[-6.5, -2.0]	1.12				
UPA 15 mg QD + TCS	35	19.3	9.3	-9.9	[-11.9, -7.9]	1.00	-5.7	[-8.7, -2.7]	1.50	<0.001***
UPA 30 mg QD + TCS	32	18.1	6.8	-11.8	[-13.9, -9.8]	1.05	-7.6	[-10.6, -4.5]	1.54	<0.001***
Adult										
Placebo + TCS	174	21.4	15.9	-5.0	[-6.0, -4.1]	0.49				
UPA 15 mg QD + TCS	238	21.1	8.8	-12.4	[-13.2, -11.5]	0.44	-7.3	[-8.6, -6.0]	0.66	<0.001***
UPA 30 mg QD + TCS	237	22.1	7.3	-14.5	[-15.4, -13.6]	0.44	-9.5	[-10.8, -8.2]	0.66	<0.001***

Note: POEM = Patient Oriented Eczema Measure; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2__5.4.1

表 2.7.3.6-33.　第 1 ピリオドの来院時別の POEM スコアのベースラインからの変化量（LOCF，OC，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	20.7	5.8	-15.1	1.17	-13.5	(-16.4, -10.6)	1.47	<0.001***
		UPA 15 MG QD	40	21.7	9.7	-11.8	1.18	-10.2	(-13.2, -7.3)	1.49	<0.001***
		UPA 7.5 MG QD	42	20.5	12.5	-8.5	1.20	-6.9	(-9.8, -4.0)	1.47	<0.001***
		PLACEBO	37	20.9	19.5	-1.6	1.25				
	US/PR/CANADA										
		UPA 30 MG QD	29	21.3	6.0	-15.5	1.21	-14.0	(-17.5, -10.5)	1.77	<0.001***
		UPA 15 MG QD	27	22.7	9.9	-12.3	1.26	-10.7	(-14.3, -7.2)	1.80	<0.001***
		UPA 7.5 MG QD	29	20.6	11.8	-9.3	1.22	-7.8	(-11.3, -4.2)	1.77	<0.001***
		PLACEBO	26	22.0	20.3	-1.5	1.28				
	EU/AUS										
		UPA 30 MG QD	10	19.4	6.0	-13.6	2.24	-13.8	(-20.4, -7.2)	3.26	<0.001***
		UPA 15 MG QD	10	18.9	9.6	-9.7	2.25	-9.9	(-16.6, -3.3)	3.27	0.004**
		UPA 7.5 MG QD	11	20.5	13.6	-6.5	2.15	-6.8	(-13.2, -0.3)	3.19	0.042*
		PLACEBO	9	20.0	20.1	0.2	2.37				
	JAPAN										
		UPA 30 MG QD	3	18.7	4.0	-14.4	2.89	-6.3	(-20.3, 7.7)	5.46	0.299
		UPA 15 MG QD	3	22.0	8.3	-11.4	3.29	-3.3	(-19.6, 13.0)	6.32	0.625
		UPA 7.5 MG QD	2	18.5	15.0	-3.3	3.54	4.7	(-10.1, 19.6)	5.79	0.450
		PLACEBO	2	11.5	7.5	-8.1	4.51				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.801

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	42	20.7	7.6	-12.3	1.40	-10.8	(-14.2, -7.3)	1.76	<0.001***
		UPA 15 MG QD	40	21.7	12.0	-8.6	1.41	-7.0	(-10.5, -3.5)	1.78	<0.001***
		UPA 7.5 MG QD	42	20.5	14.3	-5.5	1.43	-4.0	(-7.4, -0.5)	1.76	0.025*
		PLACEBO	37	20.9	18.5	-1.6	1.49				
	US/PR/CANADA										
		UPA 30 MG QD	29	21.3	7.5	-14.0	1.50	-11.9	(-16.2, -7.5)	2.18	<0.001***
		UPA 15 MG QD	27	22.7	11.4	-10.7	1.56	-8.6	(-13.0, -4.2)	2.22	<0.001***
		UPA 7.5 MG QD	29	20.6	14.1	-7.0	1.51	-4.9	(-9.2, -0.5)	2.19	0.028*
		PLACEBO	26	22.0	19.7	-2.1	1.59				
	EU/AUS										
		UPA 30 MG QD	10	19.4	8.2	-11.3	2.36	-9.1	(-16.0, -2.1)	3.43	0.012*
		UPA 15 MG QD	10	18.9	11.0	-8.2	2.37	-5.9	(-12.9, 1.1)	3.44	0.094
		UPA 7.5 MG QD	11	20.5	14.1	-6.2	2.26	-3.9	(-10.8, 2.9)	3.35	0.247
		PLACEBO	9	20.0	17.7	-2.2	2.49				
	JAPAN										
		UPA 30 MG QD	3	18.7	7.3	-11.2	2.42	-4.5	(-16.2, 7.2)	4.56	0.367
		UPA 15 MG QD	3	22.0	20.7	0.2	2.75	6.8	(-6.8, 20.4)	5.28	0.256
		UPA 7.5 MG QD	2	18.5	17.5	-0.9	2.96	5.7	(-6.7, 18.2)	4.84	0.288
		PLACEBO	2	11.5	7.5	-6.6	3.77				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.507

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	20.7	5.8	-15.1	1.17	-13.5	(-16.4, -10.6)	1.47	<0.001***
		UPA 15 MG QD	40	21.7	9.7	-11.8	1.18	-10.2	(-13.2, -7.3)	1.49	<0.001***
		UPA 7.5 MG QD	42	20.5	12.5	-8.5	1.20	-6.9	(-9.8, -4.0)	1.47	<0.001***
		PLACEBO	37	20.9	19.5	-1.6	1.25				
	US/PR/CANADA										
		UPA 30 MG QD	29	21.3	6.0	-15.5	1.21	-14.0	(-17.5, -10.5)	1.77	<0.001***
		UPA 15 MG QD	27	22.7	9.9	-12.3	1.26	-10.7	(-14.3, -7.2)	1.80	<0.001***
		UPA 7.5 MG QD	29	20.6	11.8	-9.3	1.22	-7.8	(-11.3, -4.2)	1.77	<0.001***
		PLACEBO	26	22.0	20.3	-1.5	1.28				
	EU/AUS										
		UPA 30 MG QD	10	19.4	6.0	-13.6	2.24	-13.8	(-20.4, -7.2)	3.26	<0.001***
		UPA 15 MG QD	10	18.9	9.6	-9.7	2.25	-9.9	(-16.6, -3.3)	3.27	0.004**
		UPA 7.5 MG QD	11	20.5	13.6	-6.5	2.15	-6.8	(-13.2, -0.3)	3.19	0.042*
		PLACEBO	9	20.0	20.1	0.2	2.37				
	JAPAN										
		UPA 30 MG QD	3	18.7	4.0	-14.4	2.89	-6.3	(-20.3, 7.7)	5.46	0.299
		UPA 15 MG QD	3	22.0	8.3	-11.4	3.29	-3.3	(-19.6, 13.0)	6.32	0.625
		UPA 7.5 MG QD	2	18.5	15.0	-3.3	3.54	4.7	(-10.1, 19.6)	5.79	0.450
		PLACEBO	2	11.5	7.5	-8.1	4.51				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.801

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 16											
	ALL										
		UPA 30 MG QD	40	20.7	7.1	-13.1	1.44	-10.4	(-14.2, -6.6)	1.94	<0.001***
		UPA 15 MG QD	37	22.1	12.1	-9.0	1.47	-6.3	(-10.2, -2.4)	1.97	0.002**
		UPA 7.5 MG QD	35	20.2	13.3	-6.6	1.55	-4.0	(-7.9, -0.0)	2.00	0.050*
		PLACEBO	27	21.2	17.9	-2.7	1.71				
	US/PR/CANADA										
		UPA 30 MG QD	29	21.3	7.5	-14.1	1.51	-11.0	(-15.6, -6.5)	2.30	<0.001***
		UPA 15 MG QD	27	22.7	11.4	-10.9	1.57	-7.8	(-12.5, -3.2)	2.33	0.001**
		UPA 7.5 MG QD	26	20.8	14.1	-7.2	1.60	-4.2	(-8.9, 0.5)	2.36	0.078
		PLACEBO	22	22.4	19.0	-3.0	1.73				
	EU/AUS										
		UPA 30 MG QD	8	19.1	5.6	-13.5	2.52	-10.8	(-20.9, -0.7)	4.83	0.038*
		UPA 15 MG QD	7	19.7	10.9	-8.5	2.70	-5.8	(-16.1, 4.5)	4.93	0.251
		UPA 7.5 MG QD	7	18.4	9.0	-9.8	2.70	-7.1	(-17.3, 3.2)	4.93	0.168
		PLACEBO	3	19.0	16.3	-2.7	4.12				
	JAPAN										
		UPA 30 MG QD	3	18.7	7.3	-11.2	2.42	-4.5	(-16.2, 7.2)	4.56	0.367
		UPA 15 MG QD	3	22.0	20.7	0.2	2.75	6.8	(-6.8, 20.4)	5.28	0.256
		UPA 7.5 MG QD	2	18.5	17.5	-0.9	2.96	5.7	(-6.7, 18.2)	4.84	0.288
		PLACEBO	2	11.5	7.5	-6.6	3.77				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.478

[A] ACROSS THE STRATA, P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, AND TREATMENT IN THE MODEL.
WITHIN EACH STRATUM, P-VALUES WERE CALCULATED FROM ANCOVA WITH BASELINE VALUE AND THE TREATMENT IN THE MODEL.
@ P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, TREATMENT, INTERACTION OF STRATUM AND TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.
Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2__1.14

表 2.7.3.6-34. ベースライン時の DLQI スコアが 4 以上であり，かつスクリーニング時に 16 歳以上であった被験者のうち，二重盲検投与期の来院時別での DLQI スコアがベースラインから 4 以上改善した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo	250	111 (44.4) [38.2, 50.6]	0					
UPA 15 mg QD	254	203 (79.9) [75.0, 84.8]	0	35.5	35.9	[28.1, 43.7]	<0.001***	0.357
UPA 30 mg QD	256	212 (82.8) [78.2, 87.4]	0	38.4	38.7	[31.1, 46.4]	<0.001***	0.488
vIGA-AD 3 (Moderate)								
Placebo	135	60 (44.4) [36.1, 52.8]	0					
UPA 15 mg QD	141	108 (76.6) [69.6, 83.6]	0	32.2		[21.2, 43.1]	<0.001***	
UPA 30 mg QD	134	113 (84.3) [78.2, 90.5]	0	39.9		[29.5, 50.3]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	115	51 (44.3) [35.3, 53.4]	0					
UPA 15 mg QD	113	95 (84.1) [77.3, 90.8]	0	39.7		[28.4, 51.0]	<0.001***	
UPA 30 mg QD	122	99 (81.1) [74.2, 88.1]	0	36.8		[25.4, 48.2]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo	111	50 (45.0) [35.8, 54.3]	0					
UPA 15 mg QD	115	95 (82.6) [75.7, 89.5]	0	37.6		[26.0, 49.1]	<0.001***	
UPA 30 mg QD	107	91 (85.0) [78.3, 91.8]	0	40.0		[28.5, 51.5]	<0.001***	
Japan								
Placebo	14	6 (42.9) [16.9, 68.8]	0					
UPA 15 mg QD	13	11 (84.6) [65.0, 100.0]	0	41.8		[9.3, 74.3]	0.012*	
UPA 30 mg QD	14	12 (85.7) [67.4, 100.0]	0	42.9		[11.1, 74.6]	0.008**	
China								
Placebo	14	8 (57.1) [31.2, 83.1]	0					
UPA 15 mg QD	13	12 (92.3) [77.8, 100.0]	0	35.2		[5.5, 64.9]	0.020*	
UPA 30 mg QD	17	14 (82.4) [64.2, 100.0]	0	25.2		[-6.4, 56.8]	0.118	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo	111	47 (42.3) [33.2, 51.5]	0					
UPA 15 mg QD	113	85 (75.2) [67.3, 83.2]	0	32.9		[20.7, 45.0]	<0.001***	
UPA 30 mg QD	118	95 (80.5) [73.4, 87.7]	0	38.2		[26.5, 49.8]	<0.001***	
Adolescent								
Placebo	14	3 (21.4) [0.0, 42.9]	0					
UPA 15 mg QD	20	13 (65.0) [44.1, 85.9]	0	43.6		[13.6, 73.6]	0.004**	
UPA 30 mg QD	21	17 (81.0) [64.2, 97.7]	0	59.5		[32.2, 86.8]	<0.001***	
Adult								
Placebo	236	108 (45.8) [39.4, 52.1]	0					
UPA 15 mg QD	234	190 (81.2) [76.2, 86.2]	0	35.4		[27.3, 43.5]	<0.001***	
UPA 30 mg QD	235	195 (83.0) [78.2, 87.8]	0	37.2		[29.2, 45.2]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo	250	93 (37.2) [31.2, 43.2]	0					
UPA 15 mg QD	254	208 (81.9) [77.2, 86.6]	0	44.7	44.6	[37.0, 52.2]	<0.001***	0.254
UPA 30 mg QD	256	225 (87.9) [83.9, 91.9]	0	50.7	50.8	[43.6, 57.9]	<0.001***	0.250
vIGA-AD 3 (Moderate)								
Placebo	135	55 (40.7) [32.5, 49.0]	0					
UPA 15 mg QD	141	114 (80.9) [74.4, 87.3]	0	40.1		[29.6, 50.6]	<0.001***	
UPA 30 mg QD	134	115 (85.8) [79.9, 91.7]	0	45.1		[34.9, 55.3]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	115	38 (33.0) [24.4, 41.6]	0					
UPA 15 mg QD	113	94 (83.2) [76.3, 90.1]	0	50.1		[39.1, 61.2]	<0.001***	
UPA 30 mg QD	122	110 (90.2) [84.9, 95.4]	0	57.1		[47.0, 67.2]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
US/Puerto Rico/Canada								
Placebo	111	40 (36.0) [27.1, 45.0]	0					
UPA 15 mg QD	115	91 (79.1) [71.7, 86.6]	0	43.1		[31.5, 54.7]	<0.001***	
UPA 30 mg QD	107	94 (87.9) [81.7, 94.0]	0	51.8		[40.9, 62.7]	<0.001***	
Japan								
Placebo	14	2 (14.3) [0.0, 32.6]	0					
UPA 15 mg QD	13	11 (84.6) [65.0, 100.0]	0	70.3		[43.5, 97.2]	<0.001***	
UPA 30 mg QD	14	12 (85.7) [67.4, 100.0]	0	71.4		[45.5, 97.4]	<0.001***	
China								
Placebo	14	5 (35.7) [10.6, 60.8]	0					
UPA 15 mg QD	13	12 (92.3) [77.8, 100.0]	0	56.6		[27.6, 85.6]	<0.001***	
UPA 30 mg QD	17	14 (82.4) [64.2, 100.0]	0	46.6		[15.7, 77.6]	0.003**	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Other								
Placebo	111	46 (41.4) [32.3, 50.6]	0					
UPA 15 mg QD	113	94 (83.2) [76.3, 90.1]	0	41.7		[30.3, 53.2]	<0.001***	
UPA 30 mg QD	118	105 (89.0) [83.3, 94.6]	0	47.5		[36.8, 58.3]	<0.001***	
Adolescent								
Placebo	14	5 (35.7) [10.6, 60.8]	0					
UPA 15 mg QD	20	19 (95.0) [85.4, 100.0]	0	59.3		[32.4, 86.1]	<0.001***	
UPA 30 mg QD	21	18 (85.7) [70.7, 100.0]	0	50.0		[20.8, 79.2]	0.001**	
Adult								
Placebo	236	88 (37.3) [31.1, 43.5]	0					
UPA 15 mg QD	234	189 (80.8) [75.7, 85.8]	0	43.5		[35.5, 51.5]	<0.001***	
UPA 30 mg QD	235	207 (88.1) [83.9, 92.2]	0	50.8		[43.4, 58.2]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	250	73 (29.0) [23.3, 34.7]	3					
UPA 15 mg QD	254	192 (75.4) [70.1, 80.8]	1	46.4	46.7	[39.0, 54.4]	<0.001***	0.735
UPA 30 mg QD	256	210 (82.0) [77.3, 86.7]	2	53.0	53.2	[45.9, 60.5]	<0.001***	0.146
vIGA-AD 3 (Moderate)								
Placebo	135	43 (31.9) [23.9, 39.8]	2					
UPA 15 mg QD	141	108 (76.6) [69.6, 83.6]	0	44.7		[34.2, 55.3]	<0.001***	
UPA 30 mg QD	134	108 (80.6) [73.9, 87.3]	1	48.7		[38.4, 59.1]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	115	30 (25.7) [17.6, 33.7]	1					
UPA 15 mg QD	113	84 (74.0) [65.9, 82.1]	1	48.3		[36.9, 59.7]	<0.001***	
UPA 30 mg QD	122	102 (83.6) [77.0, 90.2]	1	57.9		[47.5, 68.3]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	111	28 (25.6) [17.5, 33.8]	1					
UPA 15 mg QD	115	87 (75.7) [67.8, 83.5]	0	50.0		[38.7, 61.3]	<0.001***	
UPA 30 mg QD	107	87 (81.3) [73.9, 88.7]	0	55.7		[44.6, 66.7]	<0.001***	
Japan								
Placebo	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD	13	9 (69.2) [44.1, 94.3]	0	62.1		[33.6, 90.6]	<0.001***	
UPA 30 mg QD	14	11 (78.6) [57.1, 100.0]	0	71.4		[46.1, 96.8]	<0.001***	
China								
Placebo	14	5 (35.7) [10.6, 60.8]	0					
UPA 15 mg QD	13	11 (84.6) [65.0, 100.0]	0	48.9		[17.0, 80.8]	0.003**	
UPA 30 mg QD	17	15 (88.2) [72.9, 100.0]	0	52.5		[23.1, 81.9]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	111	38 (34.3) [25.4, 43.2]	2					
UPA 15 mg QD	113	85 (74.9) [66.9, 82.9]	1	40.6		[28.6, 52.6]	<0.001***	
UPA 30 mg QD	118	97 (82.2) [75.3, 89.1]	2	47.9		[36.6, 59.2]	<0.001***	
Adolescent								
Placebo	14	5 (35.7) [10.6, 60.8]	0					
UPA 15 mg QD	20	15 (75.0) [56.0, 94.0]	0	39.3		[7.8, 70.8]	0.014*	
UPA 30 mg QD	21	14 (66.7) [46.5, 86.8]	0	31.0		[-1.2, 63.1]	0.060	
Adult								
Placebo	236	68 (28.6) [22.8, 34.4]	3					
UPA 15 mg QD	234	177 (75.5) [70.0, 81.0]	1	46.9		[38.9, 54.9]	<0.001***	
UPA 30 mg QD	235	196 (83.4) [78.6, 88.2]	2	54.8		[47.3, 62.3]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__6.1.1

表 2.7.3.6-35. ベースライン時の DLQI スコアが 1 を超えており，かつスクリーニング時に 16 歳以上であった被験者のうち，二重盲検投与期の来院時別での DLQI スコア 0 又は 1 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo	252	2 (0.8) [0.0, 1.9]	0					
UPA 15 mg QD	258	43 (16.7) [12.1, 21.2]	0	15.9	15.9	[11.2, 20.6]	<0.001***	0.530
UPA 30 mg QD	261	61 (23.4) [18.2, 28.5]	0	22.6	22.6	[17.4, 27.9]	<0.001***	0.668
vIGA-AD 3 (Moderate)								
Placebo	137	2 (1.5) [0.0, 3.5]	0					
UPA 15 mg QD	143	27 (18.9) [12.5, 25.3]	0	17.4		[10.7, 24.1]	<0.001***	
UPA 30 mg QD	138	34 (24.6) [17.4, 31.8]	0	23.2		[15.7, 30.6]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	115	0	0					
UPA 15 mg QD	115	16 (13.9) [7.6, 20.2]	0	13.9		[7.6, 20.2]	<0.001***	
UPA 30 mg QD	123	27 (22.0) [14.6, 29.3]	0	22.0		[14.6, 29.3]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo	112	1 (0.9) [0.0, 2.6]	0					
UPA 15 mg QD	116	20 (17.2) [10.4, 24.1]	0	16.3		[9.3, 23.4]	<0.001***	
UPA 30 mg QD	110	28 (25.5) [17.3, 33.6]	0	24.6		[16.2, 32.9]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	14	0	0	0.0			NA	
UPA 30 mg QD	16	1 (6.3) [0.0, 18.1]	0	6.3		[-5.6, 18.1]	0.302	
China								
Placebo	14	0	0					
UPA 15 mg QD	13	0	0	0.0			NA	
UPA 30 mg QD	17	2 (11.8) [0.0, 27.1]	0	11.8		[-3.6, 27.1]	0.132	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo	112	1 (0.9) [0.0, 2.6]	0					
UPA 15 mg QD	115	23 (20.0) [12.7, 27.3]	0	19.1		[11.6, 26.6]	<0.001***	
UPA 30 mg QD	118	30 (25.4) [17.6, 33.3]	0	24.5		[16.5, 32.6]	<0.001***	
Adolescent								
Placebo	14	0	0					
UPA 15 mg QD	20	2 (10.0) [0.0, 23.1]	0	10.0		[-3.1, 23.1]	0.136	
UPA 30 mg QD	22	5 (22.7) [5.2, 40.2]	0	22.7		[5.2, 40.2]	0.011*	
Adult								
Placebo	238	2 (0.8) [0.0, 2.0]	0					
UPA 15 mg QD	238	41 (17.2) [12.4, 22.0]	0	16.4		[11.5, 21.3]	<0.001***	
UPA 30 mg QD	239	56 (23.4) [18.1, 28.8]	0	22.6		[17.1, 28.1]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo	252	11 (4.4) [1.8, 6.9]	0					
UPA 15 mg QD	258	79 (30.6) [25.0, 36.2]	0	26.3	26.2	[20.1, 32.4]	<0.001***	0.034*
UPA 30 mg QD	261	100 (38.3) [32.4, 44.2]	0	33.9	33.9	[27.5, 40.3]	<0.001***	0.003**
vIGA-AD 3 (Moderate)								
Placebo	137	5 (3.6) [0.5, 6.8]	0					
UPA 15 mg QD	143	46 (32.2) [24.5, 39.8]	0	28.5		[20.2, 36.8]	<0.001***	
UPA 30 mg QD	138	57 (41.3) [33.1, 49.5]	0	37.7		[28.9, 46.4]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	115	6 (5.2) [1.2, 9.3]	0					
UPA 15 mg QD	115	33 (28.7) [20.4, 37.0]	0	23.5		[14.3, 32.7]	<0.001***	
UPA 30 mg QD	123	43 (35.0) [26.5, 43.4]	0	29.7		[20.4, 39.1]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
US/Puerto Rico/Canada								
Placebo	112	2 (1.8) [0.0, 4.2]	0					
UPA 15 mg QD	116	34 (29.3) [21.0, 37.6]	0	27.5		[18.9, 36.2]	<0.001***	
UPA 30 mg QD	110	50 (45.5) [36.1, 54.8]	0	43.7		[34.0, 53.3]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	14	3 (21.4) [0.0, 42.9]	0	21.4		[-0.1, 42.9]	0.051	
UPA 30 mg QD	16	4 (25.0) [3.8, 46.2]	0	25.0		[3.8, 46.2]	0.021*	
China								
Placebo	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD	13	1 (7.7) [0.0, 22.2]	0	0.5		[-19.2, 20.3]	0.957	
UPA 30 mg QD	17	5 (29.4) [7.8, 51.1]	0	22.3		[-3.2, 47.8]	0.087	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Other								
Placebo	112	8 (7.1) [2.4, 11.9]	0					
UPA 15 mg QD	115	41 (35.7) [26.9, 44.4]	0	28.5		[18.5, 38.5]	<0.001***	
UPA 30 mg QD	118	41 (34.7) [26.2, 43.3]	0	27.6		[17.8, 37.4]	<0.001***	
Adolescent								
Placebo	14	3 (21.4) [0.0, 42.9]	0					
UPA 15 mg QD	20	5 (25.0) [6.0, 44.0]	0	3.6		[-25.1, 32.2]	0.807	
UPA 30 mg QD	22	7 (31.8) [12.4, 51.3]	0	10.4		[-18.6, 39.4]	0.483	
Adult								
Placebo	238	8 (3.4) [1.1, 5.7]	0					
UPA 15 mg QD	238	74 (31.1) [25.2, 37.0]	0	27.7		[21.4, 34.0]	<0.001***	
UPA 30 mg QD	239	93 (38.9) [32.7, 45.1]	0	35.6		[29.0, 42.1]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	252	11 (4.4) [1.9, 7.0]	3					
UPA 15 mg QD	258	78 (30.3) [24.7, 35.9]	1	25.9	25.9	[19.7, 32.1]	<0.001***	0.398
UPA 30 mg QD	261	108 (41.5) [35.5, 47.4]	2	37.0	37.3	[30.8, 43.8]	<0.001***	0.587
vIGA-AD 3 (Moderate)								
Placebo	137	6 (4.5) [1.0, 8.0]	2					
UPA 15 mg QD	143	45 (31.5) [23.9, 39.1]	0	27.0		[18.6, 35.4]	<0.001***	
UPA 30 mg QD	138	59 (42.8) [34.6, 51.1]	1	38.3		[29.4, 47.3]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	115	5 (4.3) [0.6, 8.1]	1					
UPA 15 mg QD	115	33 (28.8) [20.5, 37.1]	1	24.4		[15.3, 33.5]	<0.001***	
UPA 30 mg QD	123	49 (39.9) [31.2, 48.6]	1	35.6		[26.1, 45.0]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	112	4 (3.6) [0.1, 7.0]	1					
UPA 15 mg QD	116	34 (29.3) [21.0, 37.6]	0	25.7		[16.8, 34.7]	<0.001***	
UPA 30 mg QD	110	51 (46.4) [37.0, 55.7]	0	42.8		[32.9, 52.7]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	14	4 (28.6) [4.9, 52.2]	0	28.6		[4.9, 52.2]	0.018*	
UPA 30 mg QD	16	6 (37.5) [13.8, 61.2]	0	37.5		[13.8, 61.2]	0.002**	
China								
Placebo	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD	13	2 (15.4) [0.0, 35.0]	0	8.2		[-15.6, 32.0]	0.497	
UPA 30 mg QD	17	5 (29.4) [7.8, 51.1]	0	22.3		[-3.2, 47.8]	0.087	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	112	6 (5.5) [1.2, 9.7]	2					
UPA 15 mg QD	115	38 (33.1) [24.5, 41.7]	1	27.7		[18.0, 37.3]	<0.001***	
UPA 30 mg QD	118	46 (39.2) [30.3, 48.0]	2	33.7		[23.9, 43.5]	<0.001***	
Adolescent								
Placebo	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD	20	5 (25.0) [6.0, 44.0]	0	17.9		[-5.4, 41.1]	0.133	
UPA 30 mg QD	22	6 (27.3) [8.7, 45.9]	0	20.1		[-2.9, 43.1]	0.086	
Adult								
Placebo	238	10 (4.3) [1.7, 6.8]	3					
UPA 15 mg QD	238	73 (30.7) [24.8, 36.6]	1	26.5		[20.0, 32.9]	<0.001***	
UPA 30 mg QD	239	102 (42.8) [36.5, 49.0]	2	38.5		[31.7, 45.3]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__6.2.1

表 2.7.3.6-36. 二重盲検投与期の来院時別でのスクリーニング時に 16 歳以上の被験者における DLQI スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-045 試験

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo	240	16.9	13.6	-15.83	[-21.25, -10.41]	2.762				
UPA 15 mg QD	254	16.3	7.1	-52.98	[-58.19, -47.77]	2.655	-37.15	[-42.97, -31.33]	2.966	<0.001***
UPA 30 mg QD	253	16.4	6.1	-60.43	[-65.62, -55.23]	2.645	-44.60	[-50.42, -38.77]	2.968	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	133	15.9	12.4	-20.08	[-25.93, -14.23]	2.974				
UPA 15 mg QD	140	15.6	6.9	-54.24	[-59.93, -48.55]	2.895	-34.16	[-42.31, -26.00]	4.148	<0.001***
UPA 30 mg QD	134	14.6	4.9	-66.16	[-71.98, -60.34]	2.961	-46.08	[-54.34, -37.82]	4.202	<0.001***
vIGA-AD 4 (Severe)										
Placebo	107	18.1	14.9	-17.32	[-23.28, -11.36]	3.031				
UPA 15 mg QD	114	17.2	7.2	-57.75	[-63.53, -51.97]	2.937	-40.43	[-48.74, -32.12]	4.223	<0.001***
UPA 30 mg QD	119	18.5	7.3	-60.24	[-65.89, -54.60]	2.870	-42.92	[-51.12, -34.71]	4.172	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	107	16.2	12.6	-21.29	[-27.26, -15.33]	3.033				
UPA 15 mg QD	115	16.5	7.0	-58.63	[-64.40, -52.87]	2.930	-37.34	[-45.64, -29.04]	4.217	<0.001***
UPA 30 mg QD	106	16.1	5.1	-69.76	[-75.75, -63.78]	3.042	-48.47	[-56.92, -40.02]	4.296	<0.001***
Japan										
Placebo	11	16.5	14.7	-9.85	[-31.38, 11.68]	10.635				
UPA 15 mg QD	15	10.5	4.9	-44.65	[-63.29, -26.00]	9.216	-34.80	[-63.92, -5.68]	14.403	0.020*
UPA 30 mg QD	16	15.1	7.8	-48.56	[-66.21, -30.91]	8.714	-38.71	[-66.23, -11.18]	13.588	0.007**
China										
Placebo	14	19.2	15.4	-19.85	[-33.47, -6.23]	6.741				
UPA 15 mg QD	13	19.3	10.5	-47.60	[-61.74, -33.47]	6.995	-27.75	[-47.38, -8.13]	9.713	0.007**
UPA 30 mg QD	17	19.8	9.0	-52.75	[-65.12, -40.38]	6.121	-32.90	[-51.30, -14.49]	9.108	0.001**

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo	108	17.3	14.2	-17.30	[-23.91, -10.70]	3.358				
UPA 15 mg QD	111	16.5	7.0	-55.40	[-61.90, -48.90]	3.302	-38.10	[-47.36, -28.83]	4.710	<0.001***
UPA 30 mg QD	114	16.4	6.3	-61.00	[-67.42, -54.59]	3.260	-43.70	[-52.91, -34.49]	4.680	<0.001***
Adolescent										
Placebo	14	15.3	13.3	-12.47	[-30.24, 5.30]	8.861				
UPA 15 mg QD	21	14.5	7.3	-44.49	[-59.03, -29.94]	7.254	-32.01	[-54.97, -9.06]	11.447	0.007**
UPA 30 mg QD	22	16.6	6.8	-59.98	[-74.21, -45.75]	7.097	-47.51	[-70.29, -24.73]	11.359	<0.001***
Adult										
Placebo	226	17.0	13.6	-19.35	[-23.66, -15.05]	2.194				
UPA 15 mg QD	233	16.4	7.1	-56.96	[-61.19, -52.72]	2.157	-37.60	[-43.65, -31.56]	3.077	<0.001***
UPA 30 mg QD	231	16.4	6.0	-63.44	[-67.69, -59.19]	2.165	-44.09	[-50.14, -38.04]	3.082	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo	148	16.6	10.5	-25.81	[-32.61, -19.01]	3.464				
UPA 15 mg QD	241	16.1	5.4	-63.66	[-69.38, -57.95]	2.911	-37.85	[-45.33, -30.37]	3.810	<0.001***
UPA 30 mg QD	248	16.6	4.7	-68.73	[-74.39, -63.07]	2.882	-42.92	[-50.36, -35.48]	3.790	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	91	15.8	10.3	-25.12	[-33.15, -17.10]	4.080				
UPA 15 mg QD	134	15.3	5.5	-65.38	[-72.14, -58.63]	3.436	-40.26	[-50.75, -29.77]	5.333	<0.001***
UPA 30 mg QD	127	14.7	4.2	-71.46	[-78.39, -64.54]	3.520	-46.34	[-56.94, -35.74]	5.392	<0.001***
vIGA-AD 4 (Severe)										
Placebo	57	17.9	10.7	-35.07	[-43.43, -26.70]	4.251				
UPA 15 mg QD	107	17.2	5.3	-67.82	[-74.19, -61.46]	3.235	-32.76	[-43.27, -22.24]	5.343	<0.001***
UPA 30 mg QD	121	18.5	5.2	-71.89	[-77.90, -65.87]	3.056	-36.82	[-47.12, -26.52]	5.234	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo	69	16.6	11.4	-20.94	[-30.52, -11.37]	4.867				
UPA 15 mg QD	106	16.5	6.1	-65.51	[-73.46, -57.57]	4.036	-44.57	[-57.01, -32.13]	6.322	<0.001***
UPA 30 mg QD	106	16.1	4.0	-74.88	[-82.86, -66.90]	4.055	-53.94	[-66.41, -41.47]	6.335	<0.001***
Japan										
Placebo	2	15.5	7.0	-30.91	[-69.27, 7.45]	18.934				
UPA 15 mg QD	15	10.5	5.1	-41.76	[-60.84, -22.68]	9.327	-10.85	[-53.93, 32.22]	21.309	0.613
UPA 30 mg QD	14	16.4	5.5	-66.52	[-85.20, -47.84]	9.151	-35.61	[-77.94, 6.72]	20.910	0.097
China										
Placebo	8	18.6	15.5	-4.93	[-33.15, 23.28]	13.951				
UPA 15 mg QD	13	19.3	8.1	-59.50	[-82.81, -36.19]	11.469	-54.57	[-91.15, -17.99]	18.060	0.005**
UPA 30 mg QD	17	19.8	7.6	-59.09	[-79.48, -38.70]	10.032	-54.15	[-88.95, -19.36]	17.186	0.003**

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo	69	16.4	9.0	-40.27	[-47.44, -33.09]	3.647				
UPA 15 mg QD	107	16.1	4.4	-71.82	[-77.71, -65.93]	2.993	-31.56	[-40.84, -22.27]	4.719	<0.001***
UPA 30 mg QD	111	16.5	4.8	-70.91	[-76.67, -65.14]	2.930	-30.64	[-39.85, -21.43]	4.678	<0.001***
Adolescent										
Placebo	7	15.3	5.4	-35.44	[-69.29, -1.59]	16.810				
UPA 15 mg QD	21	14.5	5.0	-63.87	[-83.26, -44.47]	9.631	-28.43	[-67.44, 10.58]	19.371	0.149
UPA 30 mg QD	20	17.0	6.8	-61.63	[-81.46, -41.81]	9.850	-26.19	[-65.43, 13.05]	19.488	0.186
Adult										
Placebo	141	16.7	10.7	-28.42	[-34.26, -22.58]	2.974				
UPA 15 mg QD	220	16.3	5.4	-66.80	[-71.63, -61.96]	2.462	-38.38	[-45.96, -30.79]	3.861	<0.001***
UPA 30 mg QD	228	16.5	4.5	-72.38	[-77.14, -67.62]	2.423	-43.96	[-51.49, -36.42]	3.836	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo	113	16.5	10.7	-23.57	[-31.22, -15.92]	3.899				
UPA 15 mg QD	221	15.8	4.9	-63.16	[-69.20, -57.11]	3.079	-39.59	[-48.10, -31.08]	4.333	<0.001***
UPA 30 mg QD	233	16.4	4.2	-70.88	[-76.83, -64.94]	3.029	-47.31	[-55.76, -38.87]	4.300	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	72	15.8	11.0	-22.90	[-32.14, -13.65]	4.702				
UPA 15 mg QD	126	15.0	4.8	-65.81	[-73.10, -58.52]	3.705	-42.92	[-54.69, -31.14]	5.985	<0.001***
UPA 30 mg QD	120	14.5	3.4	-75.03	[-82.48, -67.57]	3.792	-52.13	[-64.01, -40.24]	6.043	<0.001***
vIGA-AD 4 (Severe)										
Placebo	41	17.9	10.3	-32.82	[-42.91, -22.73]	5.126				
UPA 15 mg QD	95	16.9	5.0	-66.13	[-73.12, -59.13]	3.552	-33.31	[-45.59, -21.03]	6.237	<0.001***
UPA 30 mg QD	113	18.5	5.0	-72.50	[-78.99, -66.01]	3.293	-39.68	[-51.67, -27.69]	6.091	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	54	16.4	11.5	-18.72	[-29.61, -7.83]	5.533				
UPA 15 mg QD	96	15.9	4.8	-66.67	[-75.29, -58.05]	4.379	-47.95	[-61.84, -34.06]	7.056	<0.001***
UPA 30 mg QD	99	16.0	3.6	-75.14	[-83.72, -66.55]	4.361	-56.42	[-70.29, -42.55]	7.045	<0.001***
Japan										
Placebo	1	15.0	11.0	-19.56	[-83.16, 44.04]	30.844				
UPA 15 mg QD	13	10.2	3.4	-67.36	[-85.43, -49.29]	8.770	-47.80	[-114.06, 18.46]	32.153	0.150
UPA 30 mg QD	14	16.4	6.3	-64.87	[-82.15, -47.60]	8.369	-45.31	[-111.07, 20.45]	31.888	0.168
China										
Placebo	7	19.0	14.9	-13.00	[-40.55, 14.56]	13.600				
UPA 15 mg QD	13	19.3	7.7	-58.45	[-79.40, -37.50]	10.300	-45.45	[-80.05, -10.85]	17.060	0.011*
UPA 30 mg QD	16	19.6	6.6	-64.70	[-83.36, -46.05]	9.183	-51.71	[-84.98, -18.44]	16.413	0.003**

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo	51	16.4	9.4	-36.78	[-46.10, -27.45]	4.738				
UPA 15 mg QD	99	16.0	4.8	-66.25	[-73.25, -59.26]	3.554	-29.48	[-41.14, -17.82]	5.923	<0.001***
UPA 30 mg QD	104	16.3	4.1	-74.65	[-81.47, -67.84]	3.461	-37.88	[-49.43, -26.32]	5.867	<0.001***
Adolescent										
Placebo	7	15.3	8.4	-39.03	[-72.23, -5.82]	16.503				
UPA 15 mg QD	20	14.1	5.3	-56.37	[-76.23, -36.52]	9.865	-17.35	[-56.02, 21.33]	19.223	0.371
UPA 30 mg QD	20	16.4	6.5	-63.10	[-82.94, -43.26]	9.857	-24.08	[-62.75, 14.60]	19.226	0.217
Adult										
Placebo	106	16.6	10.9	-26.13	[-33.06, -19.20]	3.526				
UPA 15 mg QD	201	16.0	4.8	-67.00	[-72.28, -61.71]	2.691	-40.87	[-49.58, -32.16]	4.436	<0.001***
UPA 30 mg QD	213	16.4	4.0	-74.65	[-79.81, -69.50]	2.625	-48.52	[-57.16, -39.89]	4.396	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__6.3.1

表 2.7.3.6-37. 二重盲検投与期の来院時別でのスクリーニング時に 16 歳以上の被験者における DLQI スコアのベースラインからの変化量（MMRM, ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo	240	16.9	13.6	-2.8	[-3.6, -1.9]	0.44				
UPA 15 mg QD	254	16.3	7.1	-8.9	[-9.7, -8.1]	0.43	-6.2	[-7.1, -5.2]	0.48	<0.001***
UPA 30 mg QD	253	16.4	6.1	-10.0	[-10.8, -9.1]	0.42	-7.2	[-8.1, -6.3]	0.48	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	133	15.9	12.4	-3.1	[-4.0, -2.3]	0.44				
UPA 15 mg QD	140	15.6	6.9	-8.4	[-9.2, -7.6]	0.43	-5.3	[-6.5, -4.1]	0.61	<0.001***
UPA 30 mg QD	134	14.6	4.9	-9.9	[-10.8, -9.1]	0.44	-6.8	[-8.0, -5.6]	0.62	<0.001***
vIGA-AD 4 (Severe)										
Placebo	107	18.1	14.9	-3.1	[-4.1, -2.0]	0.54				
UPA 15 mg QD	114	17.2	7.2	-10.3	[-11.3, -9.3]	0.52	-7.2	[-8.7, -5.8]	0.75	<0.001***
UPA 30 mg QD	119	18.5	7.3	-10.8	[-11.8, -9.8]	0.51	-7.7	[-9.1, -6.2]	0.74	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	107	16.2	12.6	-3.7	[-4.7, -2.8]	0.49				
UPA 15 mg QD	115	16.5	7.0	-9.4	[-10.3, -8.4]	0.47	-5.6	[-7.0, -4.3]	0.68	<0.001***
UPA 30 mg QD	106	16.1	5.1	-11.0	[-12.0, -10.1]	0.49	-7.3	[-8.6, -5.9]	0.69	<0.001***
Japan										
Placebo	11	16.5	14.7	-0.2	[-2.9, 2.6]	1.35				
UPA 15 mg QD	15	10.5	4.9	-7.3	[-9.7, -4.9]	1.17	-7.1	[-10.9, -3.4]	1.84	<0.001***
UPA 30 mg QD	16	15.1	7.8	-6.4	[-8.7, -4.2]	1.10	-6.3	[-9.8, -2.8]	1.72	0.001**
China										
Placebo	14	19.2	15.4	-4.0	[-6.5, -1.4]	1.26				
UPA 15 mg QD	13	19.3	10.5	-8.9	[-11.5, -6.3]	1.30	-4.9	[-8.6, -1.3]	1.81	0.009**
UPA 30 mg QD	17	19.8	9.0	-10.6	[-12.9, -8.3]	1.14	-6.6	[-10.0, -3.2]	1.70	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo	108	17.3	14.2	-2.6	[-3.7, -1.6]	0.55				
UPA 15 mg QD	111	16.5	7.0	-9.4	[-10.4, -8.3]	0.54	-6.7	[-8.2, -5.2]	0.77	<0.001***
UPA 30 mg QD	114	16.4	6.3	-10.1	[-11.1, -9.0]	0.53	-7.4	[-8.9, -5.9]	0.76	<0.001***
Adolescent										
Placebo	14	15.3	13.3	-2.1	[-4.8, 0.6]	1.36				
UPA 15 mg QD	21	14.5	7.3	-7.8	[-10.0, -5.5]	1.11	-5.7	[-9.2, -2.1]	1.76	0.002**
UPA 30 mg QD	22	16.6	6.8	-9.2	[-11.4, -7.0]	1.09	-7.1	[-10.6, -3.6]	1.74	<0.001***
Adult										
Placebo	226	17.0	13.6	-3.2	[-3.9, -2.5]	0.35				
UPA 15 mg QD	233	16.4	7.1	-9.4	[-10.1, -8.7]	0.35	-6.2	[-7.2, -5.2]	0.50	<0.001***
UPA 30 mg QD	231	16.4	6.0	-10.4	[-11.1, -9.7]	0.35	-7.2	[-8.2, -6.2]	0.50	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo	148	16.6	10.5	-5.0	[-6.0, -4.0]	0.53				
UPA 15 mg QD	241	16.1	5.4	-10.5	[-11.4, -9.6]	0.45	-5.5	[-6.7, -4.4]	0.58	<0.001***
UPA 30 mg QD	248	16.6	4.7	-11.5	[-12.4, -10.6]	0.45	-6.5	[-7.6, -5.3]	0.57	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	91	15.8	10.3	-4.6	[-5.6, -3.5]	0.53				
UPA 15 mg QD	134	15.3	5.5	-9.9	[-10.8, -9.0]	0.46	-5.3	[-6.7, -4.0]	0.70	<0.001***
UPA 30 mg QD	127	14.7	4.2	-10.8	[-11.7, -9.9]	0.47	-6.2	[-7.6, -4.8]	0.71	<0.001***
vIGA-AD 4 (Severe)										
Placebo	57	17.9	10.7	-6.5	[-8.1, -5.0]	0.77				
UPA 15 mg QD	107	17.2	5.3	-12.1	[-13.2, -10.9]	0.59	-5.5	[-7.4, -3.6]	0.97	<0.001***
UPA 30 mg QD	121	18.5	5.2	-13.0	[-14.1, -11.9]	0.56	-6.4	[-8.3, -4.6]	0.95	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo	69	16.6	11.4	-4.7	[-6.0, -3.4]	0.66				
UPA 15 mg QD	106	16.5	6.1	-10.4	[-11.5, -9.3]	0.55	-5.7	[-7.4, -4.0]	0.86	<0.001***
UPA 30 mg QD	106	16.1	4.0	-12.2	[-13.3, -11.1]	0.56	-7.5	[-9.2, -5.8]	0.86	<0.001***
Japan										
Placebo	2	15.5	7.0	-4.9	[-10.0, 0.1]	2.47				
UPA 15 mg QD	15	10.5	5.1	-7.0	[-9.2, -4.9]	1.04	-2.1	[-7.6, 3.4]	2.71	0.442
UPA 30 mg QD	14	16.4	5.5	-9.3	[-11.5, -7.2]	1.04	-4.4	[-9.8, 1.0]	2.66	0.109
China										
Placebo	8	18.6	15.5	-2.9	[-7.9, 2.1]	2.47				
UPA 15 mg QD	13	19.3	8.1	-11.3	[-15.3, -7.3]	1.97	-8.4	[-14.8, -2.0]	3.16	0.012*
UPA 30 mg QD	17	19.8	7.6	-12.0	[-15.5, -8.5]	1.73	-9.1	[-15.2, -3.0]	3.01	0.005**

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo	69	16.4	9.0	-6.6	[-7.8, -5.4]	0.62				
UPA 15 mg QD	107	16.1	4.4	-11.8	[-12.8, -10.8]	0.52	-5.2	[-6.8, -3.6]	0.81	<0.001***
UPA 30 mg QD	111	16.5	4.8	-11.7	[-12.7, -10.7]	0.51	-5.1	[-6.7, -3.5]	0.80	<0.001***
Adolescent										
Placebo	7	15.3	5.4	-9.9	[-14.0, -5.9]	2.01				
UPA 15 mg QD	21	14.5	5.0	-10.0	[-12.4, -7.7]	1.16	-0.1	[-4.8, 4.6]	2.32	0.963
UPA 30 mg QD	20	17.0	6.8	-9.4	[-11.8, -7.1]	1.18	0.5	[-4.2, 5.2]	2.33	0.834
Adult										
Placebo	141	16.7	10.7	-5.1	[-6.0, -4.2]	0.46				
UPA 15 mg QD	220	16.3	5.4	-10.9	[-11.7, -10.2]	0.38	-5.8	[-7.0, -4.6]	0.59	<0.001***
UPA 30 mg QD	228	16.5	4.5	-12.0	[-12.8, -11.3]	0.38	-6.9	[-8.0, -5.7]	0.59	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo	113	16.5	10.7	-4.6	[-5.7, -3.4]	0.59				
UPA 15 mg QD	221	15.8	4.9	-10.7	[-11.6, -9.7]	0.47	-6.1	[-7.3, -4.8]	0.65	<0.001***
UPA 30 mg QD	233	16.4	4.2	-11.7	[-12.6, -10.8]	0.46	-7.1	[-8.4, -5.8]	0.64	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	72	15.8	11.0	-4.2	[-5.4, -3.0]	0.61				
UPA 15 mg QD	126	15.0	4.8	-10.2	[-11.2, -9.3]	0.48	-6.0	[-7.5, -4.5]	0.78	<0.001***
UPA 30 mg QD	120	14.5	3.4	-11.3	[-12.2, -10.3]	0.49	-7.0	[-8.6, -5.5]	0.79	<0.001***
vIGA-AD 4 (Severe)										
Placebo	41	17.9	10.3	-5.9	[-7.7, -4.1]	0.92				
UPA 15 mg QD	95	16.9	5.0	-11.9	[-13.2, -10.7]	0.64	-6.0	[-8.2, -3.8]	1.12	<0.001***
UPA 30 mg QD	113	18.5	5.0	-12.9	[-14.1, -11.8]	0.59	-7.0	[-9.1, -4.9]	1.09	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	54	16.4	11.5	-4.1	[-5.6, -2.6]	0.75				
UPA 15 mg QD	96	15.9	4.8	-10.9	[-12.0, -9.7]	0.59	-6.8	[-8.7, -4.9]	0.96	<0.001***
UPA 30 mg QD	99	16.0	3.6	-12.3	[-13.4, -11.1]	0.59	-8.2	[-10.1, -6.3]	0.95	<0.001***
Japan										
Placebo	1	15.0	11.0	-0.0	[-9.0, 9.0]	4.42				
UPA 15 mg QD	13	10.2	3.4	-7.8	[-10.8, -4.9]	1.41	-7.8	[-17.3, 1.6]	4.66	0.102
UPA 30 mg QD	14	16.4	6.3	-8.5	[-11.4, -5.7]	1.38	-8.5	[-18.0, 0.9]	4.62	0.074
China										
Placebo	7	19.0	14.9	-3.5	[-8.3, 1.3]	2.38				
UPA 15 mg QD	13	19.3	7.7	-11.7	[-15.4, -8.0]	1.82	-8.2	[-14.3, -2.1]	3.00	0.010**
UPA 30 mg QD	16	19.6	6.6	-12.7	[-16.0, -9.4]	1.62	-9.2	[-15.0, -3.3]	2.88	0.003**

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo	51	16.4	9.4	-6.4	[-7.9, -4.9]	0.76				
UPA 15 mg QD	99	16.0	4.8	-11.4	[-12.6, -10.3]	0.57	-5.1	[-7.0, -3.2]	0.95	<0.001***
UPA 30 mg QD	104	16.3	4.1	-12.1	[-13.2, -11.0]	0.56	-5.7	[-7.6, -3.9]	0.94	<0.001***
Adolescent										
Placebo	7	15.3	8.4	-6.9	[-11.7, -2.0]	2.40				
UPA 15 mg QD	20	14.1	5.3	-9.3	[-12.1, -6.4]	1.41	-2.4	[-8.0, 3.2]	2.78	0.391
UPA 30 mg QD	20	16.4	6.5	-9.2	[-12.1, -6.4]	1.41	-2.4	[-8.0, 3.2]	2.79	0.398
Adult										
Placebo	106	16.6	10.9	-4.9	[-5.9, -3.9]	0.53				
UPA 15 mg QD	201	16.0	4.8	-11.2	[-11.9, -10.4]	0.40	-6.3	[-7.6, -5.0]	0.66	<0.001***
UPA 30 mg QD	213	16.4	4.0	-12.3	[-13.0, -11.5]	0.39	-7.4	[-8.7, -6.1]	0.66	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__6.4.1

表 2.7.3.6-38. ベースライン時の CDLQI スコアが 1 を超えており，かつスクリーニング時に 16 歳未満であった被験者のうち，二重盲検投与期の来院時別での CDLQI スコア 0 又は 1 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo	25	1 (4.0) [0.0, 11.7]	0					
UPA 15 mg QD	20	2 (10.0) [0.0, 23.1]	0	6.0	6.8	[-10.6, 24.2]	0.443	0.031*
UPA 30 mg QD	20	7 (35.0) [14.1, 55.9]	0	31.0	30.1	[11.2, 49.0]	0.002**	0.007**
vIGA-AD 3 (Moderate)								
Placebo	16	0	0					
UPA 15 mg QD	9	2 (22.2) [0.0, 49.4]	0	22.2		[-4.9, 49.4]	0.109	
UPA 30 mg QD	14	7 (50.0) [23.8, 76.2]	0	50.0		[23.8, 76.2]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	9	1 (11.1) [0.0, 31.6]	0					
UPA 15 mg QD	11	0	0	-11.1		[-31.6, 9.4]	0.289	
UPA 30 mg QD	6	0	0	-11.1		[-31.6, 9.4]	0.289	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo	15	1 (6.7) [0.0, 19.3]	0					
UPA 15 mg QD	10	2 (20.0) [0.0, 44.8]	0	13.3		[-14.5, 41.2]	0.348	
UPA 30 mg QD	16	7 (43.8) [19.4, 68.1]	0	37.1		[9.7, 64.5]	0.008**	
Japan								
Placebo	0	0	0					
UPA 15 mg QD	0	0	0				NA	
UPA 30 mg QD	0	0	0				NA	
China								
Placebo	0	0	0					
UPA 15 mg QD	1	0	0				NA	
UPA 30 mg QD	0	0	0				NA	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo	10	0	0					
UPA 15 mg QD	9	0	0	0.0			NA	
UPA 30 mg QD	4	0	0	0.0			NA	
Adolescent								
Placebo	25	1 (4.0) [0.0, 11.7]	0					
UPA 15 mg QD	20	2 (10.0) [0.0, 23.1]	0	6.0		[-9.2, 21.2]	0.440	
UPA 30 mg QD	20	7 (35.0) [14.1, 55.9]	0	31.0		[8.7, 53.3]	0.006**	
Adult								
Placebo	0	0	0					
UPA 15 mg QD	0	0	0				NA	
UPA 30 mg QD	0	0	0				NA	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo	25	0	0					
UPA 15 mg QD	20	9 (45.0) [23.2, 66.8]	0	45.0	44.9	[22.8, 67.0]	<0.001***	NA
UPA 30 mg QD	20	14 (70.0) [49.9, 90.1]	0	70.0	69.9	[49.7, 90.0]	<0.001***	NA
vIGA-AD 3 (Moderate)								
Placebo	16	0	0					
UPA 15 mg QD	9	4 (44.4) [12.0, 76.9]	0	44.4		[12.0, 76.9]	0.007**	
UPA 30 mg QD	14	10 (71.4) [47.8, 95.1]	0	71.4		[47.8, 95.1]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	9	0	0					
UPA 15 mg QD	11	5 (45.5) [16.0, 74.9]	0	45.5		[16.0, 74.9]	0.002**	
UPA 30 mg QD	6	4 (66.7) [28.9, 100.0]	0	66.7		[28.9, 100.0]	0.001**	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
US/Puerto Rico/Canada								
Placebo	15	0	0					
UPA 15 mg QD	10	5 (50.0) [19.0, 81.0]	0	50.0		[19.0, 81.0]	0.002**	
UPA 30 mg QD	16	12 (75.0) [53.8, 96.2]	0	75.0		[53.8, 96.2]	<0.001***	
Japan								
Placebo	0	0	0					
UPA 15 mg QD	0	0	0				NA	
UPA 30 mg QD	0	0	0				NA	
China								
Placebo	0	0	0					
UPA 15 mg QD	1	1 (100) [100.0, 100.0]	0				NA	
UPA 30 mg QD	0	0	0				NA	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Other								
Placebo	10	0	0					
UPA 15 mg QD	9	3 (33.3) [2.5, 64.1]	0	33.3		[2.5, 64.1]	0.034*	
UPA 30 mg QD	4	2 (50.0) [1.0, 99.0]	0	50.0		[1.0, 99.0]	0.046*	
Adolescent								
Placebo	25	0	0					
UPA 15 mg QD	20	9 (45.0) [23.2, 66.8]	0	45.0		[23.2, 66.8]	<0.001***	
UPA 30 mg QD	20	14 (70.0) [49.9, 90.1]	0	70.0		[49.9, 90.1]	<0.001***	
Adult								
Placebo	0	0	0					
UPA 15 mg QD	0	0	0				NA	
UPA 30 mg QD	0	0	0				NA	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	25	1 (4.1) [0.0, 12.1]	1					
UPA 15 mg QD	20	6 (30.0) [9.9, 50.1]	0	25.9	25.3	[4.6, 46.0]	0.017*	0.316
UPA 30 mg QD	20	16 (80.0) [62.5, 97.5]	0	75.9	75.2	[55.9, 94.4]	<0.001***	0.647
vIGA-AD 3 (Moderate)								
Placebo	16	1 (6.5) [0.0, 18.7]	1					
UPA 15 mg QD	9	2 (22.2) [0.0, 49.4]	0	15.8		[-14.0, 45.6]	0.300	
UPA 30 mg QD	14	12 (85.7) [67.4, 100.0]	0	79.3		[57.2, 100.0]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	9	0	0					
UPA 15 mg QD	11	4 (36.4) [7.9, 64.8]	0	36.4		[7.9, 64.8]	0.012*	
UPA 30 mg QD	6	4 (66.7) [28.9, 100.0]	0	66.7		[28.9, 100.0]	0.001**	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	15	1 (6.7) [0.0, 19.3]	0					
UPA 15 mg QD	10	3 (30.0) [1.6, 58.4]	0	23.3		[-7.7, 54.4]	0.141	
UPA 30 mg QD	16	14 (87.5) [71.3, 100.0]	0	80.8		[60.3, 100.0]	<0.001***	
Japan								
Placebo	0	0	0					
UPA 15 mg QD	0	0	0				NA	
UPA 30 mg QD	0	0	0				NA	
China								
Placebo	0	0	0					
UPA 15 mg QD	1	1 (100) [100.0, 100.0]	0				NA	
UPA 30 mg QD	0	0	0				NA	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	10	0 (0.3) [0.0, 5.4]	1					
UPA 15 mg QD	9	2 (22.2) [0.0, 49.4]	0	21.9		[-5.7, 49.5]	0.120	
UPA 30 mg QD	4	2 (50.0) [1.0, 99.0]	0	49.7		[0.4, 98.9]	0.048*	
Adolescent								
Placebo	25	1 (4.1) [0.0, 12.1]	1					
UPA 15 mg QD	20	6 (30.0) [9.9, 50.1]	0	25.9		[4.3, 47.5]	0.019*	
UPA 30 mg QD	20	16 (80.0) [62.5, 97.5]	0	75.9		[56.6, 95.1]	<0.001***	
Adult								
Placebo	0	0	0					
UPA 15 mg QD	0	0	0				NA	
UPA 30 mg QD	0	0	0				NA	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2__7.1.1

表 2.7.3.6-39. 二重盲検投与期の来院時別でのスクリーニング時に 16 歳未満の被験者における CDLQI スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-045 試験

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo	24	12.7	9.0	-31.28	[-43.84, -18.72]	6.277				
UPA 15 mg QD	20	13.9	6.0	-53.98	[-67.60, -40.36]	6.806	-22.70	[-41.31, -4.10]	9.298	0.018*
UPA 30 mg QD	20	14.4	3.4	-76.32	[-90.47, -62.17]	7.073	-45.04	[-63.69, -26.40]	9.317	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	15	10.1	7.1	-29.53	[-46.18, -12.88]	8.194				
UPA 15 mg QD	9	11.9	7.8	-35.97	[-57.11, -14.83]	10.401	-6.44	[-33.40, 20.53]	13.269	0.631
UPA 30 mg QD	14	12.6	2.3	-77.36	[-94.40, -60.31]	8.386	-47.83	[-71.88, -23.77]	11.840	<0.001***
vIGA-AD 4 (Severe)										
Placebo	9	17.1	12.1	-34.42	[-53.23, -15.61]	9.071				
UPA 15 mg QD	11	15.5	4.5	-68.51	[-85.74, -51.27]	8.314	-34.09	[-59.66, -8.52]	12.334	0.011*
UPA 30 mg QD	6	18.5	5.8	-69.59	[-92.88, -46.29]	11.237	-35.17	[-65.04, -5.29]	14.409	0.023*

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	14	11.6	6.4	-42.56	[-58.76, -26.37]	7.987				
UPA 15 mg QD	10	11.8	5.3	-54.31	[-73.45, -35.18]	9.440	-11.75	[-36.79, 13.29]	12.350	0.348
UPA 30 mg QD	16	13.1	2.3	-78.16	[-93.33, -62.99]	7.482	-35.60	[-57.84, -13.36]	10.972	0.003**
Japan										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									
China										
Placebo	0									
UPA 15 mg QD	1	22.0	3.0	-86.36						
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo	10	14.2	12.5	-14.41	[-33.94, 5.11]	9.326				
UPA 15 mg QD	9	15.3	7.0	-51.44	[-71.73, -31.16]	9.687	-37.03	[-65.12, -8.95]	13.414	0.012*
UPA 30 mg QD	4	19.3	7.5	-60.33	[-92.07, -28.60]	15.163	-45.92	[-83.99, -7.85]	18.190	0.021*
Adolescent										
Placebo	24	12.7	9.0	-30.74	[-43.22, -18.26]	6.240				
UPA 15 mg QD	20	13.9	6.0	-54.20	[-67.83, -40.57]	6.815	-23.45	[-41.96, -4.95]	9.251	0.014*
UPA 30 mg QD	20	14.4	3.4	-75.03	[-88.69, -61.37]	6.828	-44.29	[-62.83, -25.74]	9.275	<0.001***
Adult										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo	13	11.7	7.4	-25.42	[-45.15, -5.69]	9.847				
UPA 15 mg QD	20	13.9	5.1	-61.00	[-77.26, -44.73]	8.067	-35.58	[-61.23, -9.92]	12.785	0.008**
UPA 30 mg QD	20	14.4	1.5	-87.71	[-104.41, -71.01]	8.294	-62.29	[-87.72, -36.85]	12.658	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	11	10.7	5.8	-28.18	[-49.10, -7.25]	10.264				
UPA 15 mg QD	9	11.9	5.1	-58.74	[-82.71, -34.78]	11.686	-30.57	[-62.42, 1.28]	15.573	0.059
UPA 30 mg QD	14	12.6	1.4	-83.82	[-103.12, -64.53]	9.411	-55.65	[-84.27, -27.03]	14.006	<0.001***
vIGA-AD 4 (Severe)										
Placebo	2	17.0	16.0	21.50	[-41.66, 84.67]	29.932				
UPA 15 mg QD	11	15.5	5.0	-62.63	[-91.54, -33.72]	12.957	-84.13	[-153.17, -15.09]	32.626	0.020*
UPA 30 mg QD	6	18.5	1.5	-92.45	[-131.57, -53.33]	17.531	-113.95	[-187.58, -40.32]	34.676	0.005**

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo	8	11.9	7.6	-29.60	[-56.35, -2.85]	13.127				
UPA 15 mg QD	10	11.8	5.3	-58.48	[-82.51, -34.46]	11.757	-28.89	[-64.82, 7.04]	17.614	0.111
UPA 30 mg QD	16	13.1	1.4	-85.13	[-104.16, -66.11]	9.310	-55.53	[-88.38, -22.69]	16.108	0.002**
Japan										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									
China										
Placebo	0									
UPA 15 mg QD	1	22.0	1.0	-95.45						
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo	5	11.4	7.0	-12.67	[-43.55, 18.20]	14.748				
UPA 15 mg QD	9	15.3	5.2	-61.39	[-87.24, -35.54]	11.994	-48.71	[-88.82, -8.61]	18.977	0.020*
UPA 30 mg QD	4	19.3	1.8	-89.38	[-129.05, -49.71]	18.506	-76.71	[-127.40, -26.01]	24.075	0.005**
Adolescent										
Placebo	13	11.7	7.4	-24.74	[-43.98, -5.50]	9.592				
UPA 15 mg QD	20	13.9	5.1	-61.21	[-77.20, -45.23]	7.940	-36.48	[-61.51, -11.45]	12.465	0.005**
UPA 30 mg QD	20	14.4	1.5	-86.41	[-102.42, -70.41]	7.951	-61.68	[-86.75, -36.60]	12.490	<0.001***
Adult										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo	10	10.4	5.2	-36.35	[-53.60, -19.10]	8.623				
UPA 15 mg QD	17	14.6	4.1	-65.14	[-80.37, -49.92]	7.535	-28.79	[-51.86, -5.72]	11.497	0.015*
UPA 30 mg QD	20	14.4	1.3	-92.02	[-107.21, -76.83]	7.512	-55.67	[-78.32, -33.02]	11.267	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	9	10.4	5.3	-38.00	[-59.59, -16.41]	10.582				
UPA 15 mg QD	8	11.6	5.1	-46.20	[-71.29, -21.11]	12.184	-8.20	[-41.33, 24.93]	16.159	0.616
UPA 30 mg QD	14	12.6	0.9	-91.43	[-111.18, -71.68]	9.568	-53.43	[-82.85, -24.01]	14.355	0.001**
vIGA-AD 4 (Severe)										
Placebo	1	10.0	4.0	-17.91	[-67.05, 31.22]	23.167				
UPA 15 mg QD	9	17.2	3.1	-80.72	[-100.81, -60.63]	8.733	-62.81	[-115.06, -10.56]	24.612	0.022*
UPA 30 mg QD	6	18.5	2.2	-89.06	[-115.02, -63.11]	11.096	-71.15	[-125.83, -16.47]	25.831	0.014*

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	6	10.3	5.0	-38.59	[-61.88, -15.30]	11.513				
UPA 15 mg QD	10	11.8	4.6	-60.96	[-82.79, -39.13]	10.653	-22.37	[-54.22, 9.49]	15.675	0.163
UPA 30 mg QD	16	13.1	1.0	-91.31	[-108.60, -74.01]	8.439	-52.71	[-81.72, -23.71]	14.296	0.001**
Japan										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									
China										
Placebo	0									
UPA 15 mg QD	1	22.0	0.0	-100.00		0.000				
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo	4	10.5	5.5	-34.34	[-64.51, -4.17]	13.828				
UPA 15 mg QD	6	18.0	3.8	-71.07	[-97.46, -44.67]	11.083	-36.72	[-75.74, 2.29]	17.686	0.063
UPA 30 mg QD	4	19.3	2.3	-86.23	[-122.97, -49.48]	14.517	-51.89	[-98.83, -4.95]	20.785	0.034*
Adolescent										
Placebo	10	10.4	5.2	-35.60	[-52.73, -18.47]	8.553				
UPA 15 mg QD	17	14.6	4.1	-65.32	[-80.54, -50.09]	7.538	-29.72	[-52.64, -6.80]	11.414	0.012*
UPA 30 mg QD	20	14.4	1.3	-90.72	[-105.45, -75.99]	7.273	-55.12	[-77.74, -32.51]	11.257	<0.001***
Adult										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　7.2.1

表 2.7.3.6-40. 二重盲検投与期の来院時別でのスクリーニング時に 16 歳未満の被験者における CDLQI スコアのベースラインからの変化量（MMRM, ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo	24	12.7	9.0	-4.3	[-6.2, -2.4]	0.96				
UPA 15 mg QD	20	13.9	6.0	-7.7	[-9.8, -5.7]	1.05	-3.5	[-6.3, -0.6]	1.43	0.019*
UPA 30 mg QD	20	14.4	3.4	-10.6	[-12.7, -8.4]	1.09	-6.3	[-9.1, -3.4]	1.43	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	15	10.1	7.1	-4.2	[-6.3, -2.1]	1.04				
UPA 15 mg QD	9	11.9	7.8	-3.9	[-6.6, -1.2]	1.32	0.3	[-3.1, 3.7]	1.68	0.859
UPA 30 mg QD	14	12.6	2.3	-9.6	[-11.7, -7.4]	1.06	-5.3	[-8.4, -2.3]	1.50	0.001**
vIGA-AD 4 (Severe)										
Placebo	9	17.1	12.1	-4.9	[-8.5, -1.3]	1.74				
UPA 15 mg QD	11	15.5	4.5	-11.7	[-15.0, -8.4]	1.60	-6.8	[-11.7, -1.9]	2.37	0.009**
UPA 30 mg QD	6	18.5	5.8	-11.9	[-16.4, -7.4]	2.16	-7.0	[-12.8, -1.3]	2.77	0.019*

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	14	11.6	6.4	-5.7	[-7.7, -3.7]	0.98				
UPA 15 mg QD	10	11.8	5.3	-6.9	[-9.2, -4.5]	1.16	-1.2	[-4.2, 1.9]	1.52	0.445
UPA 30 mg QD	16	13.1	2.3	-10.2	[-12.1, -8.4]	0.92	-4.5	[-7.3, -1.8]	1.35	0.002**
Japan										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									
China										
Placebo	0									
UPA 15 mg QD	1	22.0	3.0	-19.0		0.00				
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
Week 2 (Cont.)										
Other										
Placebo	10	14.2	12.5	-2.1	[-5.4, 1.3]	1.59				
UPA 15 mg QD	9	15.3	7.0	-8.4	[-11.9, -4.9]	1.66	-6.3	[-11.1, -1.5]	2.29	0.013*
UPA 30 mg QD	4	19.3	7.5	-10.7	[-16.2, -5.3]	2.59	-8.7	[-15.2, -2.2]	3.11	0.012*
Adolescent										
Placebo	24	12.7	9.0	-4.3	[-6.2, -2.4]	0.95				
UPA 15 mg QD	20	13.9	6.0	-7.8	[-9.8, -5.7]	1.04	-3.5	[-6.3, -0.7]	1.41	0.017*
UPA 30 mg QD	20	14.4	3.4	-10.5	[-12.6, -8.4]	1.04	-6.3	[-9.1, -3.4]	1.41	<0.001***
Adult										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo	13	11.7	7.4	-4.1	[-6.9, -1.4]	1.38				
UPA 15 mg QD	20	13.9	5.1	-8.6	[-10.9, -6.3]	1.13	-4.5	[-8.1, -0.9]	1.79	0.015*
UPA 30 mg QD	20	14.4	1.5	-12.5	[-14.8, -10.1]	1.17	-8.3	[-11.9, -4.8]	1.77	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	11	10.7	5.8	-5.0	[-7.1, -2.9]	1.04				
UPA 15 mg QD	9	11.9	5.1	-6.6	[-9.1, -4.1]	1.21	-1.6	[-4.9, 1.7]	1.60	0.334
UPA 30 mg QD	14	12.6	1.4	-10.4	[-12.4, -8.4]	0.98	-5.4	[-8.4, -2.5]	1.44	0.001**
vIGA-AD 4 (Severe)										
Placebo	2	17.0	16.0	5.0	[-4.9, 15.0]	4.73				
UPA 15 mg QD	11	15.5	5.0	-11.1	[-15.8, -6.4]	2.11	-16.2	[-27.1, -5.2]	5.18	0.006**
UPA 30 mg QD	6	18.5	1.5	-16.3	[-22.6, -9.9]	2.86	-21.3	[-33.0, -9.6]	5.52	0.001**

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo	8	11.9	7.6	-4.0	[-7.5, -0.5]	1.73				
UPA 15 mg QD	10	11.8	5.3	-6.9	[-10.0, -3.7]	1.55	-2.8	[-7.6, 1.9]	2.32	0.230
UPA 30 mg QD	16	13.1	1.4	-11.2	[-13.7, -8.6]	1.23	-7.1	[-11.4, -2.8]	2.12	0.002**
Japan										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									
China										
Placebo	0									
UPA 15 mg QD	1	22.0	1.0	-21.0		0.00				
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo	5	11.4	7.0	-2.7	[-7.6, 2.1]	2.34				
UPA 15 mg QD	9	15.3	5.2	-10.2	[-14.4, -6.0]	1.96	-7.4	[-13.8, -1.0]	3.05	0.026*
UPA 30 mg QD	4	19.3	1.8	-16.5	[-23.0, -10.0]	3.03	-13.7	[-21.9, -5.6]	3.90	0.002**
Adolescent										
Placebo	13	11.7	7.4	-4.1	[-6.8, -1.4]	1.35				
UPA 15 mg QD	20	13.9	5.1	-8.7	[-10.9, -6.4]	1.12	-4.5	[-8.0, -1.0]	1.76	0.013*
UPA 30 mg QD	20	14.4	1.5	-12.4	[-14.7, -10.2]	1.12	-8.3	[-11.8, -4.8]	1.76	<0.001***
Adult										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo	10	10.4	5.2	-5.1	[-7.7, -2.6]	1.26				
UPA 15 mg QD	17	14.6	4.1	-9.4	[-11.7, -7.2]	1.11	-4.3	[-7.7, -0.9]	1.69	0.015*
UPA 30 mg QD	20	14.4	1.3	-12.7	[-14.9, -10.4]	1.11	-7.5	[-10.9, -4.2]	1.65	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	9	10.4	5.3	-5.6	[-8.1, -3.0]	1.24				
UPA 15 mg QD	8	11.6	5.1	-5.3	[-8.3, -2.3]	1.44	0.3	[-3.6, 4.2]	1.90	0.882
UPA 30 mg QD	14	12.6	0.9	-11.0	[-13.3, -8.6]	1.13	-5.4	[-8.9, -1.9]	1.69	0.003**
vIGA-AD 4 (Severe)										
Placebo	1	10.0	4.0	-2.2	[-11.7, 7.3]	4.47				
UPA 15 mg QD	9	17.2	3.1	-13.6	[-17.6, -9.6]	1.77	-11.4	[-21.5, -1.3]	4.79	0.030*
UPA 30 mg QD	6	18.5	2.2	-15.6	[-20.8, -10.4]	2.27	-13.4	[-24.0, -2.8]	5.03	0.017*

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	6	10.3	5.0	-5.3	[-8.0, -2.5]	1.36				
UPA 15 mg QD	10	11.8	4.6	-7.6	[-10.2, -4.9]	1.28	-2.3	[-6.1, 1.5]	1.86	0.225
UPA 30 mg QD	16	13.1	1.0	-11.5	[-13.6, -9.5]	1.01	-6.3	[-9.7, -2.8]	1.70	0.001**
Japan										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									
China										
Placebo	0									
UPA 15 mg QD	1	22.0	0.0	-22.0						
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo	4	10.5	5.5	-4.6	[-10.0, 0.9]	2.52				
UPA 15 mg QD	6	18.0	3.8	-11.6	[-16.5, -6.8]	2.11	-7.1	[-14.3, 0.1]	3.27	0.052
UPA 30 mg QD	4	19.3	2.3	-16.0	[-22.7, -9.3]	2.81	-11.4	[-20.0, -2.8]	3.86	0.014*
Adolescent										
Placebo	10	10.4	5.2	-5.1	[-7.6, -2.6]	1.24				
UPA 15 mg QD	17	14.6	4.1	-9.4	[-11.7, -7.2]	1.10	-4.3	[-7.6, -0.9]	1.66	0.013*
UPA 30 mg QD	20	14.4	1.3	-12.6	[-14.8, -10.5]	1.07	-7.5	[-10.8, -4.2]	1.64	<0.001***
Adult										
Placebo	0									
UPA 15 mg QD	0									
UPA 30 mg QD	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　7.3.1

表 2.7.3.6-41. ベースライン時の DLQI スコアが 4 以上であり，かつスクリーニング時に 16 歳以上であった被験者のうち，二重盲検投与期の来院時別での DLQI スコアがベースラインから 4 以上改善した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo + TCS	269	142 (52.8) [46.8, 58.8]	0					
UPA 15 mg QD + TCS	266	223 (83.8) [79.4, 88.3]	0	31.0	31.3	[23.9, 38.6]	<0.001***	0.096
UPA 30 mg QD + TCS	269	233 (86.6) [82.5, 90.7]	0	33.8	33.7	[26.5, 40.9]	<0.001***	0.302
vIGA-AD 3 (Moderate)								
Placebo + TCS	124	62 (50.0) [41.2, 58.8]	0					
UPA 15 mg QD + TCS	129	102 (79.1) [72.0, 86.1]	0	29.1		[17.8, 40.3]	<0.001***	
UPA 30 mg QD + TCS	124	107 (86.3) [80.2, 92.3]	0	36.3		[25.6, 47.0]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	145	80 (55.2) [47.1, 63.3]	0					
UPA 15 mg QD + TCS	137	121 (88.3) [82.9, 93.7]	0	33.1		[23.4, 42.9]	<0.001***	
UPA 30 mg QD + TCS	145	126 (86.9) [81.4, 92.4]	0	31.7		[21.9, 41.5]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	94	56 (59.6) [49.7, 69.5]	0					
UPA 15 mg QD + TCS	92	76 (82.6) [74.9, 90.4]	0	23.0		[10.4, 35.6]	<0.001***	
UPA 30 mg QD + TCS	93	81 (87.1) [80.3, 93.9]	0	27.5		[15.5, 39.6]	<0.001***	
Japan								
Placebo + TCS	18	9 (50.0) [26.9, 73.1]	0					
UPA 15 mg QD + TCS	15	13 (86.7) [69.5, 100.0]	0	36.7		[7.9, 65.5]	0.013*	
UPA 30 mg QD + TCS	16	12 (75.0) [53.8, 96.2]	0	25.0		[-6.4, 56.4]	0.118	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
China								
Placebo + TCS	16	5 (31.3) [8.5, 54.0]	0					
UPA 15 mg QD + TCS	17	13 (76.5) [56.3, 96.6]	0	45.2		[14.8, 75.6]	0.004**	
UPA 30 mg QD + TCS	16	13 (81.3) [62.1, 100.0]	0	50.0		[20.3, 79.7]	0.001**	
Other								
Placebo + TCS	141	72 (51.1) [42.8, 59.3]	0					
UPA 15 mg QD + TCS	142	121 (85.2) [79.4, 91.0]	0	34.1		[24.0, 44.3]	<0.001***	
UPA 30 mg QD + TCS	144	127 (88.2) [82.9, 93.5]	0	37.1		[27.3, 46.9]	<0.001***	
Adolescent								
Placebo + TCS	13	4 (30.8) [5.7, 55.9]	0					
UPA 15 mg QD + TCS	15	14 (93.3) [80.7, 100.0]	0	62.6		[34.5, 90.6]	<0.001***	
UPA 30 mg QD + TCS	15	13 (86.7) [69.5, 100.0]	0	55.9		[25.5, 86.3]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Adult								
Placebo + TCS	256	138 (53.9) [47.8, 60.0]	0					
UPA 15 mg QD + TCS	251	209 (83.3) [78.6, 87.9]	0	29.4		[21.7, 37.0]	<0.001***	
UPA 30 mg QD + TCS	254	220 (86.6) [82.4, 90.8]	0	32.7		[25.3, 40.1]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo + TCS	269	138 (51.3) [45.3, 57.3]	0					
UPA 15 mg QD + TCS	266	225 (84.6) [80.2, 88.9]	0	33.3	33.4	[26.1, 40.7]	<0.001***	0.597
UPA 30 mg QD + TCS	269	238 (88.5) [84.7, 92.3]	0	37.2	36.9	[29.8, 44.0]	<0.001***	0.308
vIGA-AD 3 (Moderate)								
Placebo + TCS	124	66 (53.2) [44.4, 62.0]	0					
UPA 15 mg QD + TCS	129	107 (82.9) [76.5, 89.4]	0	29.7		[18.8, 40.6]	<0.001***	
UPA 30 mg QD + TCS	124	110 (88.7) [83.1, 94.3]	0	35.5		[25.1, 45.9]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	145	72 (49.7) [41.5, 57.8]	0					
UPA 15 mg QD + TCS	137	118 (86.1) [80.3, 91.9]	0	36.5		[26.5, 46.5]	<0.001***	
UPA 30 mg QD + TCS	145	128 (88.3) [83.0, 93.5]	0	38.6		[28.9, 48.3]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	94	60 (63.8) [54.1, 73.5]	0					
UPA 15 mg QD + TCS	92	80 (87.0) [80.1, 93.8]	0	23.1		[11.2, 35.0]	<0.001***	
UPA 30 mg QD + TCS	93	82 (88.2) [81.6, 94.7]	0	24.3		[12.6, 36.1]	<0.001***	
Japan								
Placebo + TCS	18	9 (50.0) [26.9, 73.1]	0					
UPA 15 mg QD + TCS	15	11 (73.3) [51.0, 95.7]	0	23.3		[-8.8, 55.5]	0.155	
UPA 30 mg QD + TCS	16	13 (81.3) [62.1, 100.0]	0	31.3		[1.3, 61.2]	0.041*	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
China								
Placebo + TCS	16	8 (50.0) [25.5, 74.5]	0					
UPA 15 mg QD + TCS	17	12 (70.6) [48.9, 92.2]	0	20.6		[-12.1, 53.3]	0.217	
UPA 30 mg QD + TCS	16	13 (81.3) [62.1, 100.0]	0	31.3		[0.2, 62.3]	0.049*	
Other								
Placebo + TCS	141	61 (43.3) [35.1, 51.4]	0					
UPA 15 mg QD + TCS	142	122 (85.9) [80.2, 91.6]	0	42.7		[32.7, 52.6]	<0.001***	
UPA 30 mg QD + TCS	144	130 (90.3) [85.4, 95.1]	0	47.0		[37.5, 56.5]	<0.001***	
Adolescent								
Placebo + TCS	13	4 (30.8) [5.7, 55.9]	0					
UPA 15 mg QD + TCS	15	12 (80.0) [59.8, 100.0]	0	49.2		[17.0, 81.5]	0.003**	
UPA 30 mg QD + TCS	15	15 (100) [100.0, 100.0]	0	69.2		[44.1, 94.3]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Adult								
Placebo + TCS	256	134 (52.3) [46.2, 58.5]	0					
UPA 15 mg QD + TCS	251	213 (84.9) [80.4, 89.3]	0	32.5		[25.0, 40.1]	<0.001***	
UPA 30 mg QD + TCS	254	223 (87.8) [83.8, 91.8]	0	35.5		[28.1, 42.8]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	269	111 (41.3) [35.4, 47.1]	1					
UPA 15 mg QD + TCS	266	215 (80.8) [76.1, 85.6]	2	39.6	39.7	[32.2, 47.2]	<0.001***	0.406
UPA 30 mg QD + TCS	269	228 (84.9) [80.6, 89.2]	2	43.6	43.7	[36.4, 51.0]	<0.001***	0.776
vIGA-AD 3 (Moderate)								
Placebo + TCS	124	53 (42.7) [34.0, 51.4]	1					
UPA 15 mg QD + TCS	129	100 (77.5) [70.3, 84.7]	0	34.8		[23.5, 46.1]	<0.001***	
UPA 30 mg QD + TCS	124	108 (87.1) [81.2, 93.0]	0	44.4		[33.8, 54.9]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	145	58 (40.0) [32.0, 48.0]	0					
UPA 15 mg QD + TCS	137	115 (83.9) [77.8, 90.1]	2	43.9		[33.9, 54.0]	<0.001***	
UPA 30 mg QD + TCS	145	120 (83.0) [76.8, 89.1]	2	43.0		[32.9, 53.1]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	94	51 (54.3) [44.2, 64.3]	1					
UPA 15 mg QD + TCS	92	77 (83.7) [76.1, 91.2]	0	29.4		[16.9, 42.0]	<0.001***	
UPA 30 mg QD + TCS	93	80 (86.4) [79.3, 93.4]	1	32.1		[19.8, 44.4]	<0.001***	
Japan								
Placebo + TCS	18	6 (33.3) [11.6, 55.1]	0					
UPA 15 mg QD + TCS	15	12 (80.0) [59.8, 100.0]	0	46.7		[16.9, 76.4]	0.002**	
UPA 30 mg QD + TCS	16	13 (81.3) [62.1, 100.0]	0	47.9		[18.9, 76.9]	0.001**	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
China								
Placebo + TCS	16	9 (56.3) [31.9, 80.6]	0					
UPA 15 mg QD + TCS	17	13 (76.5) [56.3, 96.6]	0	20.2		[-11.4, 51.8]	0.210	
UPA 30 mg QD + TCS	16	14 (87.5) [71.3, 100.0]	0	31.3		[2.0, 60.5]	0.036*	
Other								
Placebo + TCS	141	45 (31.9) [24.2, 39.6]	0					
UPA 15 mg QD + TCS	142	113 (79.6) [72.9, 86.2]	2	47.7		[37.5, 57.8]	<0.001***	
UPA 30 mg QD + TCS	144	121 (84.0) [78.0, 90.0]	1	52.1		[42.4, 61.9]	<0.001***	
Adolescent								
Placebo + TCS	13	5 (38.5) [12.0, 64.9]	0					
UPA 15 mg QD + TCS	15	11 (73.3) [51.0, 95.7]	0	34.9		[0.2, 69.5]	0.049*	
UPA 30 mg QD + TCS	15	13 (86.7) [69.5, 100.0]	0	48.2		[16.7, 79.8]	0.003**	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Adult								
Placebo + TCS	256	106 (41.4) [35.4, 47.4]	1					
UPA 15 mg QD + TCS	251	204 (81.3) [76.4, 86.1]	2	39.9		[32.1, 47.6]	<0.001***	
UPA 30 mg QD + TCS	254	215 (84.8) [80.3, 89.2]	2	43.4		[35.9, 50.9]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2__6.1.1

表 2.7.3.6-42.　ベースライン時の DLQI スコアが 1 を超えており，かつスクリーニング時に 16 歳以上であった被験者のうち，二重盲検投与期の来院時別での DLQI スコア 0 又は 1 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo + TCS	275	15 (5.5) [2.8, 8.1]	0					
UPA 15 mg QD + TCS	274	43 (15.7) [11.4, 20.0]	0	10.2	10.3	[5.2, 15.4]	<0.001***	0.830
UPA 30 mg QD + TCS	272	77 (28.3) [23.0, 33.7]	0	22.9	22.9	[16.8, 28.9]	<0.001***	0.456
vIGA-AD 3 (Moderate)								
Placebo + TCS	129	7 (5.4) [1.5, 9.3]	0					
UPA 15 mg QD + TCS	132	22 (16.7) [10.3, 23.0]	0	11.2		[3.8, 18.7]	0.003**	
UPA 30 mg QD + TCS	126	39 (31.0) [22.9, 39.0]	0	25.5		[16.6, 34.5]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	146	8 (5.5) [1.8, 9.2]	0					
UPA 15 mg QD + TCS	142	21 (14.8) [9.0, 20.6]	0	9.3		[2.4, 16.2]	0.008**	
UPA 30 mg QD + TCS	146	38 (26.0) [18.9, 33.1]	0	20.5		[12.5, 28.6]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	99	8 (8.1) [2.7, 13.4]	0					
UPA 15 mg QD + TCS	94	15 (16.0) [8.6, 23.4]	0	7.9		[-1.3, 17.0]	0.091	
UPA 30 mg QD + TCS	94	32 (34.0) [24.5, 43.6]	0	26.0		[15.0, 36.9]	<0.001***	
Japan								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	15	4 (26.7) [4.3, 49.0]	0	26.7		[4.3, 49.0]	0.020*	
UPA 30 mg QD + TCS	17	0	0	0.0			NA	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
China								
Placebo + TCS	16	1 (6.3) [0.0, 18.1]	0					
UPA 15 mg QD + TCS	17	0	0	-6.3		[-18.1, 5.6]	0.302	
UPA 30 mg QD + TCS	16	2 (12.5) [0.0, 28.7]	0	6.3		[-13.8, 26.3]	0.542	
Other								
Placebo + TCS	142	6 (4.2) [0.9, 7.5]	0					
UPA 15 mg QD + TCS	148	24 (16.2) [10.3, 22.2]	0	12.0		[5.2, 18.8]	0.001**	
UPA 30 mg QD + TCS	145	43 (29.7) [22.2, 37.1]	0	25.4		[17.3, 33.6]	<0.001***	
Adolescent								
Placebo + TCS	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD + TCS	17	2 (11.8) [0.0, 27.1]	0	4.6		[-15.8, 25.0]	0.657	
UPA 30 mg QD + TCS	15	4 (26.7) [4.3, 49.0]	0	19.5		[-6.6, 45.7]	0.143	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Adult								
Placebo + TCS	261	14 (5.4) [2.6, 8.1]	0					
UPA 15 mg QD + TCS	257	41 (16.0) [11.5, 20.4]	0	10.6		[5.3, 15.8]	<0.001***	
UPA 30 mg QD + TCS	257	73 (28.4) [22.9, 33.9]	0	23.0		[16.9, 29.2]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo + TCS	275	22 (8.0) [4.8, 11.2]	0					
UPA 15 mg QD + TCS	274	68 (24.8) [19.7, 29.9]	0	16.8	16.8	[10.8, 22.9]	<0.001***	0.143
UPA 30 mg QD + TCS	272	119 (43.8) [37.9, 49.6]	0	35.8	35.8	[29.1, 42.4]	<0.001***	0.410
vIGA-AD 3 (Moderate)								
Placebo + TCS	129	12 (9.3) [4.3, 14.3]	0					
UPA 15 mg QD + TCS	132	33 (25.0) [17.6, 32.4]	0	15.7		[6.8, 24.6]	0.001**	
UPA 30 mg QD + TCS	126	65 (51.6) [42.9, 60.3]	0	42.3		[32.2, 52.3]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	146	10 (6.8) [2.8, 10.9]	0					
UPA 15 mg QD + TCS	142	35 (24.6) [17.6, 31.7]	0	17.8		[9.6, 26.0]	<0.001***	
UPA 30 mg QD + TCS	146	54 (37.0) [29.2, 44.8]	0	30.1		[21.3, 39.0]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	99	9 (9.1) [3.4, 14.8]	0					
UPA 15 mg QD + TCS	94	31 (33.0) [23.5, 42.5]	0	23.9		[12.8, 35.0]	<0.001***	
UPA 30 mg QD + TCS	94	43 (45.7) [35.7, 55.8]	0	36.7		[25.1, 48.2]	<0.001***	
Japan								
Placebo + TCS	18	2 (11.1) [0.0, 25.6]	0					
UPA 15 mg QD + TCS	15	4 (26.7) [4.3, 49.0]	0	15.6		[-11.1, 42.2]	0.253	
UPA 30 mg QD + TCS	17	5 (29.4) [7.8, 51.1]	0	18.3		[-7.8, 44.4]	0.169	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
China								
Placebo + TCS	16	0	0					
UPA 15 mg QD + TCS	17	2 (11.8) [0.0, 27.1]	0	11.8		[-3.6, 27.1]	0.132	
UPA 30 mg QD + TCS	16	2 (12.5) [0.0, 28.7]	0	12.5		[-3.7, 28.7]	0.131	
Other								
Placebo + TCS	142	11 (7.7) [3.3, 12.1]	0					
UPA 15 mg QD + TCS	148	31 (20.9) [14.4, 27.5]	0	13.2		[5.3, 21.1]	0.001**	
UPA 30 mg QD + TCS	145	69 (47.6) [39.5, 55.7]	0	39.8		[30.6, 49.1]	<0.001***	
Adolescent								
Placebo + TCS	14	3 (21.4) [0.0, 42.9]	0					
UPA 15 mg QD + TCS	17	3 (17.6) [0.0, 35.8]	0	-3.8		[-31.9, 24.3]	0.792	
UPA 30 mg QD + TCS	15	6 (40.0) [15.2, 64.8]	0	18.6		[-14.2, 51.4]	0.267	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Adult								
Placebo + TCS	261	19 (7.3) [4.1, 10.4]	0					
UPA 15 mg QD + TCS	257	65 (25.3) [20.0, 30.6]	0	18.0		[11.8, 24.2]	<0.001***	
UPA 30 mg QD + TCS	257	113 (44.0) [37.9, 50.0]	0	36.7		[29.9, 43.5]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	275	16 (5.8) [3.1, 8.6]	2					
UPA 15 mg QD + TCS	274	71 (25.9) [20.7, 31.1]	2	20.1	20.2	[14.4, 26.1]	<0.001***	0.005**
UPA 30 mg QD + TCS	272	111 (40.9) [35.1, 46.8]	2	35.1	35.0	[28.6, 41.4]	<0.001***	0.530
vIGA-AD 3 (Moderate)								
Placebo + TCS	129	8 (6.2) [2.0, 10.4]	2					
UPA 15 mg QD + TCS	132	38 (28.8) [21.1, 36.5]	0	22.6		[13.8, 31.3]	<0.001***	
UPA 30 mg QD + TCS	126	62 (49.2) [40.5, 57.9]	0	43.0		[33.3, 52.7]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
vIGA-AD 4 (Severe)								
Placebo + TCS	146	8 (5.5) [1.8, 9.2]	0					
UPA 15 mg QD + TCS	142	33 (23.3) [16.3, 30.2]	2	17.8		[9.9, 25.7]	<0.001***	
UPA 30 mg QD + TCS	146	49 (33.8) [26.1, 41.5]	2	28.3		[19.7, 36.8]	<0.001***	
US/Puerto Rico/Canada								
Placebo + TCS	99	11 (11.1) [4.9, 17.4]	2					
UPA 15 mg QD + TCS	94	33 (35.1) [25.5, 44.8]	0	24.0		[12.5, 35.4]	<0.001***	
UPA 30 mg QD + TCS	94	41 (43.8) [33.7, 53.8]	1	32.6		[20.8, 44.4]	<0.001***	
Japan								
Placebo + TCS	18	1 (5.6) [0.0, 16.1]	0					
UPA 15 mg QD + TCS	15	8 (53.3) [28.1, 78.6]	0	47.8		[20.4, 75.2]	0.001**	
UPA 30 mg QD + TCS	17	7 (41.2) [17.8, 64.6]	0	35.6		[9.9, 61.3]	0.007**	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
China								
Placebo + TCS	16	0	0					
UPA 15 mg QD + TCS	17	2 (11.8) [0.0, 27.1]	0	11.8		[-3.6, 27.1]	0.132	
UPA 30 mg QD + TCS	16	2 (12.5) [0.0, 28.7]	0	12.5		[-3.7, 28.7]	0.131	
Other								
Placebo + TCS	142	4 (2.8) [0.1, 5.5]	0					
UPA 15 mg QD + TCS	148	28 (18.9) [12.6, 25.3]	2	16.1		[9.2, 23.0]	<0.001***	
UPA 30 mg QD + TCS	145	61 (42.2) [34.1, 50.2]	1	39.4		[30.9, 47.9]	<0.001***	
Adolescent								
Placebo + TCS	14	2 (14.3) [0.0, 32.6]	0					
UPA 15 mg QD + TCS	17	0	0	-14.3		[-32.6, 4.0]	0.127	
UPA 30 mg QD + TCS	15	6 (40.0) [15.2, 64.8]	0	25.7		[-5.1, 56.5]	0.102	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Adult								
Placebo + TCS	261	14 (5.4) [2.6, 8.1]	2					
UPA 15 mg QD + TCS	257	71 (27.6) [22.2, 33.1]	2	22.3		[16.1, 28.4]	<0.001***	
UPA 30 mg QD + TCS	257	105 (41.0) [34.9, 47.0]	2	35.6		[29.0, 42.2]	<0.001***	

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2__6.2.1

表 2.7.3.6-43. 二重盲検投与期の来院時別でのスクリーニング時に 16 歳以上の被験者における DLQI スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo + TCS	267	16.3	11.5	-23.48	[-30.50, -16.45]	3.582				
UPA 15 mg QD + TCS	271	16.5	6.7	-58.05	[-64.95, -51.15]	3.517	-34.58	[-41.78, -27.37]	3.671	<0.001***
UPA 30 mg QD + TCS	267	17.2	5.6	-66.43	[-73.38, -59.48]	3.542	-42.95	[-50.19, -35.71]	3.688	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	124	14.2	10.4	-16.42	[-24.74, -8.09]	4.236				
UPA 15 mg QD + TCS	129	14.8	6.2	-55.00	[-63.15, -46.86]	4.142	-38.59	[-50.23, -26.94]	5.922	<0.001***
UPA 30 mg QD + TCS	123	16.1	5.1	-66.28	[-74.64, -57.92]	4.252	-49.87	[-61.70, -38.04]	6.015	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	143	18.2	12.5	-27.93	[-34.17, -21.70]	3.172				
UPA 15 mg QD + TCS	142	18.0	7.1	-58.73	[-64.99, -52.48]	3.184	-30.80	[-39.64, -21.97]	4.495	<0.001***
UPA 30 mg QD + TCS	144	18.1	6.0	-64.18	[-70.40, -57.96]	3.166	-36.25	[-45.06, -27.44]	4.482	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	97	15.3	9.4	-30.87	[-39.55, -22.19]	4.410				
UPA 15 mg QD + TCS	93	16.1	6.2	-59.21	[-68.06, -50.36]	4.496	-28.34	[-40.74, -15.94]	6.300	<0.001***
UPA 30 mg QD + TCS	91	15.9	4.3	-70.68	[-79.64, -61.72]	4.551	-39.81	[-52.29, -27.33]	6.338	<0.001***
Japan										
Placebo + TCS	18	14.9	12.2	-16.87	[-34.26, 0.52]	8.641				
UPA 15 mg QD + TCS	15	12.5	5.1	-61.79	[-80.57, -43.00]	9.340	-44.92	[-70.69, -19.14]	12.813	0.001**
UPA 30 mg QD + TCS	17	14.2	5.8	-44.86	[-62.67, -27.05]	8.847	-27.99	[-52.81, -3.17]	12.331	0.028*
China										
Placebo + TCS	15	22.1	18.6	-18.77	[-33.84, -3.70]	7.480				
UPA 15 mg QD + TCS	17	19.6	10.6	-43.32	[-57.54, -29.09]	7.059	-24.55	[-45.38, -3.71]	10.342	0.022*
UPA 30 mg QD + TCS	16	21.1	11.7	-46.31	[-60.85, -31.76]	7.216	-27.54	[-48.48, -6.60]	10.392	0.011*

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo + TCS	137	16.6	12.2	-17.71	[-24.93, -10.49]	3.674				
UPA 15 mg QD + TCS	146	16.7	6.8	-56.47	[-63.47, -49.47]	3.562	-38.76	[-48.82, -28.71]	5.116	<0.001***
UPA 30 mg QD + TCS	143	17.9	5.6	-66.06	[-73.14, -58.98]	3.601	-48.35	[-58.47, -38.23]	5.150	<0.001***
Adolescent										
Placebo + TCS	13	10.7	7.9	-1.31	[-38.09, 35.46]	18.218				
UPA 15 mg QD + TCS	16	14.1	5.8	-53.70	[-86.15, -21.25]	16.082	-52.39	[-101.53, -3.24]	24.359	0.037*
UPA 30 mg QD + TCS	15	14.1	5.1	-64.24	[-98.25, -30.23]	16.840	-62.93	[-113.17, -12.69]	24.891	0.015*
Adult										
Placebo + TCS	254	16.6	11.7	-23.44	[-28.48, -18.39]	2.571				
UPA 15 mg QD + TCS	255	16.6	6.8	-57.07	[-62.11, -52.04]	2.566	-33.64	[-40.77, -26.51]	3.632	<0.001***
UPA 30 mg QD + TCS	252	17.4	5.6	-65.38	[-70.45, -60.31]	2.583	-41.95	[-49.10, -34.79]	3.645	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo + TCS	214	16.0	9.5	-32.84	[-39.87, -25.82]	3.579				
UPA 15 mg QD + TCS	261	16.5	5.5	-65.49	[-72.18, -58.79]	3.410	-32.64	[-39.60, -25.69]	3.542	<0.001***
UPA 30 mg QD + TCS	260	17.2	4.0	-76.36	[-83.04, -69.67]	3.406	-43.51	[-50.49, -36.54]	3.554	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	109	14.0	8.8	-27.03	[-35.04, -19.03]	4.070				
UPA 15 mg QD + TCS	123	14.9	5.0	-65.13	[-72.71, -57.56]	3.851	-38.10	[-49.12, -27.09]	5.601	<0.001***
UPA 30 mg QD + TCS	120	16.2	3.3	-76.22	[-83.94, -68.49]	3.927	-49.18	[-60.34, -38.03]	5.671	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	105	18.0	10.3	-36.30	[-42.64, -29.95]	3.228				
UPA 15 mg QD + TCS	138	17.9	6.0	-63.61	[-69.42, -57.80]	2.955	-27.31	[-35.92, -18.71]	4.376	<0.001***
UPA 30 mg QD + TCS	140	18.1	4.7	-74.12	[-79.90, -68.35]	2.937	-37.82	[-46.40, -29.24]	4.364	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	88	15.0	8.1	-38.82	[-46.22, -31.42]	3.758				
UPA 15 mg QD + TCS	94	16.2	5.0	-67.80	[-75.06, -60.54]	3.686	-28.98	[-39.36, -18.61]	5.267	<0.001***
UPA 30 mg QD + TCS	91	16.0	3.5	-76.72	[-84.11, -69.34]	3.749	-37.91	[-48.36, -27.45]	5.310	<0.001***
Japan										
Placebo + TCS	12	15.3	7.7	-42.10	[-59.82, -24.38]	8.804				
UPA 15 mg QD + TCS	15	11.1	4.3	-62.63	[-79.82, -45.44]	8.510	-20.53	[-45.47, 4.41]	12.374	0.104
UPA 30 mg QD + TCS	16	13.8	3.9	-65.65	[-82.08, -49.22]	8.126	-23.55	[-47.66, 0.55]	11.951	0.055
China										
Placebo + TCS	15	22.1	19.0	-15.81	[-34.96, 3.35]	9.496				
UPA 15 mg QD + TCS	14	20.2	10.3	-42.27	[-61.44, -23.11]	9.522	-26.47	[-53.64, 0.71]	13.487	0.056
UPA 30 mg QD + TCS	16	21.1	10.1	-55.18	[-73.68, -36.67]	9.173	-39.37	[-66.00, -12.74]	13.202	0.005**

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo + TCS	99	16.0	9.6	-27.83	[-35.65, -20.00]	3.980				
UPA 15 mg QD + TCS	138	16.9	5.5	-64.48	[-71.32, -57.64]	3.479	-36.65	[-47.04, -26.27]	5.285	<0.001***
UPA 30 mg QD + TCS	137	18.0	3.7	-77.37	[-84.25, -70.48]	3.502	-49.54	[-59.98, -39.10]	5.310	<0.001***
Adolescent										
Placebo + TCS	10	9.9	5.9	-42.48	[-62.71, -22.25]	10.026				
UPA 15 mg QD + TCS	13	14.5	4.2	-64.55	[-81.71, -47.39]	8.502	-22.07	[-49.08, 4.94]	13.388	0.107
UPA 30 mg QD + TCS	15	14.1	2.8	-79.62	[-96.59, -62.64]	8.380	-37.13	[-63.91, -10.36]	13.254	0.008**
Adult										
Placebo + TCS	204	16.3	9.7	-30.95	[-36.22, -25.67]	2.688				
UPA 15 mg QD + TCS	248	16.6	5.6	-64.43	[-69.35, -59.51]	2.506	-33.48	[-40.69, -26.27]	3.674	<0.001***
UPA 30 mg QD + TCS	245	17.4	4.1	-74.98	[-79.93, -70.02]	2.525	-44.03	[-51.27, -36.79]	3.689	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo + TCS	182	16.1	9.6	-31.65	[-38.85, -24.46]	3.666				
UPA 15 mg QD + TCS	250	16.3	5.3	-64.80	[-71.50, -58.11]	3.412	-33.15	[-40.27, -26.03]	3.625	<0.001***
UPA 30 mg QD + TCS	252	17.3	4.5	-73.72	[-80.38, -67.06]	3.395	-42.07	[-49.20, -34.94]	3.631	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	94	14.1	9.1	-23.85	[-32.12, -15.57]	4.205				
UPA 15 mg QD + TCS	120	14.6	4.6	-64.25	[-71.78, -56.72]	3.827	-40.40	[-51.58, -29.22]	5.682	<0.001***
UPA 30 mg QD + TCS	120	16.2	3.9	-72.50	[-80.13, -64.88]	3.873	-48.66	[-59.94, -37.38]	5.732	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	88	18.2	10.1	-37.50	[-44.18, -30.82]	3.398				
UPA 15 mg QD + TCS	130	17.8	6.0	-63.15	[-68.95, -57.35]	2.949	-25.66	[-34.50, -16.81]	4.499	<0.001***
UPA 30 mg QD + TCS	132	18.2	5.1	-72.40	[-78.17, -66.64]	2.929	-34.91	[-43.73, -26.09]	4.486	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	74	15.3	7.7	-39.06	[-47.28, -30.83]	4.176				
UPA 15 mg QD + TCS	91	16.1	4.3	-71.93	[-79.62, -64.25]	3.900	-32.88	[-44.14, -21.61]	5.716	<0.001***
UPA 30 mg QD + TCS	87	16.0	3.8	-74.89	[-82.74, -67.04]	3.982	-35.84	[-47.21, -24.46]	5.772	<0.001***
Japan										
Placebo + TCS	11	14.9	9.0	-23.72	[-45.21, -2.24]	10.628				
UPA 15 mg QD + TCS	14	11.9	4.4	-65.58	[-85.05, -46.11]	9.614	-41.86	[-71.06, -12.65]	14.443	0.006**
UPA 30 mg QD + TCS	16	13.8	3.7	-72.03	[-90.34, -53.72]	9.027	-48.31	[-76.50, -20.12]	13.928	0.001**
China										
Placebo + TCS	15	22.1	16.2	-30.14	[-46.75, -13.53]	8.234				
UPA 15 mg QD + TCS	14	20.2	8.9	-51.35	[-68.15, -34.55]	8.343	-21.20	[-44.91, 2.50]	11.763	0.078
UPA 30 mg QD + TCS	16	21.1	9.3	-59.69	[-75.73, -43.66]	7.949	-29.55	[-52.63, -6.46]	11.443	0.013*

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo + TCS	82	15.8	10.2	-25.26	[-33.19, -17.33]	4.033				
UPA 15 mg QD + TCS	131	16.5	5.7	-59.10	[-65.69, -52.51]	3.351	-33.85	[-44.15, -23.54]	5.240	<0.001***
UPA 30 mg QD + TCS	133	18.0	4.5	-72.23	[-78.83, -65.64]	3.352	-46.98	[-57.31, -36.64]	5.254	<0.001***
Adolescent										
Placebo + TCS	8	9.8	4.3	-47.52	[-72.98, -22.06]	12.381				
UPA 15 mg QD + TCS	13	14.5	4.5	-55.58	[-75.90, -35.25]	9.776	-8.06	[-41.02, 24.91]	15.994	0.619
UPA 30 mg QD + TCS	15	14.1	3.8	-73.10	[-92.56, -53.64]	9.247	-25.58	[-57.90, 6.74]	15.618	0.115
Adult										
Placebo + TCS	174	16.4	9.9	-29.63	[-35.08, -24.17]	2.780				
UPA 15 mg QD + TCS	237	16.4	5.4	-64.19	[-69.06, -59.31]	2.483	-34.56	[-41.88, -27.24]	3.727	<0.001***
UPA 30 mg QD + TCS	237	17.5	4.6	-72.59	[-77.48, -67.69]	2.493	-42.96	[-50.30, -35.63]	3.736	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　6.3.1

表 2.7.3.6-44. 二重盲検投与期の来院時別でのスクリーニング時に 16 歳以上の被験者における DLQI スコアのベースラインからの変化量（MMRM, ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo + TCS	267	16.3	11.5	-5.2	[-6.1, -4.2]	0.47				
UPA 15 mg QD + TCS	272	16.4	6.7	-10.0	[-10.9, -9.1]	0.46	-4.8	[-5.7, -3.9]	0.46	<0.001***
UPA 30 mg QD + TCS	267	17.2	5.6	-11.5	[-12.4, -10.6]	0.47	-6.3	[-7.2, -5.4]	0.47	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	124	14.2	10.4	-4.3	[-5.2, -3.5]	0.44				
UPA 15 mg QD + TCS	129	14.8	6.2	-8.6	[-9.5, -7.8]	0.43	-4.3	[-5.5, -3.1]	0.61	<0.001***
UPA 30 mg QD + TCS	123	16.1	5.1	-10.3	[-11.2, -9.5]	0.44	-6.0	[-7.2, -4.8]	0.62	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	143	18.2	12.5	-5.6	[-6.5, -4.6]	0.48				
UPA 15 mg QD + TCS	143	17.9	7.1	-10.9	[-11.8, -9.9]	0.48	-5.3	[-6.7, -4.0]	0.68	<0.001***
UPA 30 mg QD + TCS	144	18.1	6.0	-12.1	[-13.0, -11.1]	0.48	-6.5	[-7.9, -5.2]	0.68	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	97	15.3	9.4	-6.2	[-7.2, -5.2]	0.50				
UPA 15 mg QD + TCS	93	16.1	6.2	-9.7	[-10.7, -8.7]	0.51	-3.4	[-4.9, -2.0]	0.72	<0.001***
UPA 30 mg QD + TCS	91	15.9	4.3	-11.5	[-12.5, -10.5]	0.52	-5.3	[-6.7, -3.9]	0.72	<0.001***
Japan										
Placebo + TCS	18	14.9	12.2	-1.7	[-3.9, 0.5]	1.09				
UPA 15 mg QD + TCS	16	11.8	5.0	-7.9	[-10.2, -5.5]	1.15	-6.1	[-9.3, -2.9]	1.60	<0.001***
UPA 30 mg QD + TCS	17	14.2	5.8	-7.8	[-10.1, -5.6]	1.11	-6.1	[-9.2, -3.0]	1.55	<0.001***
China										
Placebo + TCS	15	22.1	18.6	-3.2	[-6.4, 0.1]	1.61				
UPA 15 mg QD + TCS	17	19.6	10.6	-9.5	[-12.6, -6.5]	1.52	-6.4	[-10.9, -1.9]	2.23	0.006**
UPA 30 mg QD + TCS	16	21.1	11.7	-9.4	[-12.6, -6.3]	1.55	-6.3	[-10.8, -1.8]	2.24	0.008**

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo + TCS	137	16.6	12.2	-4.7	[-5.6, -3.8]	0.46				
UPA 15 mg QD + TCS	146	16.7	6.8	-10.1	[-11.0, -9.2]	0.45	-5.4	[-6.7, -4.2]	0.64	<0.001***
UPA 30 mg QD + TCS	143	17.9	5.6	-11.7	[-12.6, -10.8]	0.45	-7.0	[-8.3, -5.8]	0.65	<0.001***
Adolescent										
Placebo + TCS	13	10.7	7.9	-4.4	[-6.8, -2.1]	1.16				
UPA 15 mg QD + TCS	16	14.1	5.8	-7.6	[-9.7, -5.5]	1.02	-3.2	[-6.3, -0.0]	1.56	0.047*
UPA 30 mg QD + TCS	15	14.1	5.1	-8.3	[-10.5, -6.2]	1.06	-3.9	[-7.1, -0.7]	1.59	0.018*
Adult										
Placebo + TCS	254	16.6	11.7	-5.0	[-5.7, -4.3]	0.34				
UPA 15 mg QD + TCS	256	16.5	6.7	-9.9	[-10.6, -9.2]	0.34	-4.9	[-5.8, -4.0]	0.48	<0.001***
UPA 30 mg QD + TCS	252	17.4	5.6	-11.4	[-12.1, -10.8]	0.34	-6.4	[-7.4, -5.5]	0.48	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo + TCS	214	16.0	9.5	-6.6	[-7.5, -5.6]	0.50				
UPA 15 mg QD + TCS	261	16.5	5.5	-11.2	[-12.1, -10.3]	0.47	-4.6	[-5.6, -3.7]	0.50	<0.001***
UPA 30 mg QD + TCS	260	17.2	4.0	-13.0	[-13.9, -12.0]	0.47	-6.4	[-7.4, -5.4]	0.50	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	109	14.0	8.8	-5.7	[-6.6, -4.8]	0.47				
UPA 15 mg QD + TCS	123	14.9	5.0	-10.1	[-10.9, -9.2]	0.44	-4.4	[-5.6, -3.1]	0.64	<0.001***
UPA 30 mg QD + TCS	120	16.2	3.3	-12.0	[-12.9, -11.1]	0.45	-6.3	[-7.6, -5.1]	0.65	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	105	18.0	10.3	-7.0	[-8.1, -5.9]	0.55				
UPA 15 mg QD + TCS	138	17.9	6.0	-11.9	[-12.9, -10.9]	0.51	-4.9	[-6.4, -3.4]	0.75	<0.001***
UPA 30 mg QD + TCS	140	18.1	4.7	-13.5	[-14.4, -12.5]	0.50	-6.5	[-7.9, -5.0]	0.75	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	88	15.0	8.1	-7.3	[-8.3, -6.2]	0.54				
UPA 15 mg QD + TCS	94	16.2	5.0	-10.9	[-12.0, -9.9]	0.53	-3.7	[-5.2, -2.2]	0.75	<0.001***
UPA 30 mg QD + TCS	91	16.0	3.5	-12.3	[-13.4, -11.3]	0.54	-5.1	[-6.6, -3.6]	0.76	<0.001***
Japan										
Placebo + TCS	12	15.3	7.7	-5.1	[-7.6, -2.6]	1.22				
UPA 15 mg QD + TCS	15	11.1	4.3	-8.3	[-10.7, -5.9]	1.18	-3.2	[-6.6, 0.3]	1.71	0.071
UPA 30 mg QD + TCS	16	13.8	3.9	-9.9	[-12.2, -7.6]	1.13	-4.8	[-8.2, -1.5]	1.66	0.006**
China										
Placebo + TCS	15	22.1	19.0	-2.8	[-6.4, 0.9]	1.80				
UPA 15 mg QD + TCS	14	20.2	10.3	-10.1	[-13.7, -6.5]	1.79	-7.3	[-12.4, -2.2]	2.54	0.006**
UPA 30 mg QD + TCS	16	21.1	10.1	-11.0	[-14.5, -7.6]	1.73	-8.3	[-13.3, -3.3]	2.49	0.002**

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo + TCS	99	16.0	9.6	-6.4	[-7.4, -5.4]	0.51				
UPA 15 mg QD + TCS	138	16.9	5.5	-11.4	[-12.3, -10.5]	0.45	-5.0	[-6.3, -3.7]	0.68	<0.001***
UPA 30 mg QD + TCS	137	18.0	3.7	-13.6	[-14.5, -12.7]	0.45	-7.1	[-8.5, -5.8]	0.68	<0.001***
Adolescent										
Placebo + TCS	10	9.9	5.9	-6.3	[-8.4, -4.2]	1.03				
UPA 15 mg QD + TCS	13	14.5	4.2	-9.2	[-11.0, -7.4]	0.87	-2.9	[-5.7, -0.2]	1.37	0.039*
UPA 30 mg QD + TCS	15	14.1	2.8	-10.7	[-12.4, -9.0]	0.84	-4.4	[-7.1, -1.7]	1.34	0.002**
Adult										
Placebo + TCS	204	16.3	9.7	-6.4	[-7.1, -5.6]	0.38				
UPA 15 mg QD + TCS	248	16.6	5.6	-11.1	[-11.8, -10.4]	0.35	-4.7	[-5.8, -3.7]	0.52	<0.001***
UPA 30 mg QD + TCS	245	17.4	4.1	-12.9	[-13.6, -12.2]	0.36	-6.5	[-7.5, -5.5]	0.52	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo + TCS	182	16.1	9.6	-6.3	[-7.3, -5.3]	0.52				
UPA 15 mg QD + TCS	251	16.2	5.3	-11.2	[-12.1, -10.3]	0.48	-4.9	[-5.9, -3.9]	0.52	<0.001***
UPA 30 mg QD + TCS	252	17.3	4.5	-12.5	[-13.5, -11.6]	0.48	-6.2	[-7.3, -5.2]	0.52	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	94	14.1	9.1	-5.0	[-6.0, -3.9]	0.52				
UPA 15 mg QD + TCS	120	14.6	4.6	-10.1	[-11.1, -9.2]	0.48	-5.1	[-6.5, -3.7]	0.71	<0.001***
UPA 30 mg QD + TCS	120	16.2	3.9	-11.6	[-12.5, -10.6]	0.49	-6.6	[-8.0, -5.2]	0.71	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	88	18.2	10.1	-7.2	[-8.3, -6.1]	0.58				
UPA 15 mg QD + TCS	131	17.7	5.9	-11.8	[-12.8, -10.8]	0.50	-4.6	[-6.1, -3.1]	0.76	<0.001***
UPA 30 mg QD + TCS	132	18.2	5.1	-13.0	[-14.0, -12.1]	0.50	-5.8	[-7.3, -4.3]	0.76	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	74	15.3	7.7	-7.1	[-8.3, -6.0]	0.58				
UPA 15 mg QD + TCS	91	16.1	4.3	-11.4	[-12.5, -10.3]	0.55	-4.3	[-5.8, -2.7]	0.80	<0.001***
UPA 30 mg QD + TCS	87	16.0	3.8	-12.0	[-13.1, -10.9]	0.56	-4.9	[-6.5, -3.3]	0.81	<0.001***
Japan										
Placebo + TCS	11	14.9	9.0	-3.4	[-6.0, -0.8]	1.29				
UPA 15 mg QD + TCS	15	11.1	4.1	-8.5	[-10.8, -6.1]	1.17	-5.0	[-8.6, -1.5]	1.76	0.007**
UPA 30 mg QD + TCS	16	13.8	3.7	-10.0	[-12.3, -7.7]	1.12	-6.6	[-10.0, -3.1]	1.70	<0.001***
China										
Placebo + TCS	15	22.1	16.2	-5.6	[-9.0, -2.1]	1.71				
UPA 15 mg QD + TCS	14	20.2	8.9	-11.5	[-15.0, -8.1]	1.73	-6.0	[-10.9, -1.1]	2.44	0.018*
UPA 30 mg QD + TCS	16	21.1	9.3	-11.8	[-15.1, -8.5]	1.65	-6.2	[-11.0, -1.4]	2.38	0.012*

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo + TCS	82	15.8	10.2	-5.7	[-6.8, -4.6]	0.57				
UPA 15 mg QD + TCS	131	16.5	5.7	-10.9	[-11.8, -10.0]	0.48	-5.2	[-6.7, -3.7]	0.75	<0.001***
UPA 30 mg QD + TCS	133	18.0	4.5	-12.9	[-13.8, -11.9]	0.48	-7.2	[-8.6, -5.7]	0.75	<0.001***
Adolescent										
Placebo + TCS	8	9.8	4.3	-6.8	[-9.5, -4.0]	1.34				
UPA 15 mg QD + TCS	13	14.5	4.5	-8.9	[-11.1, -6.7]	1.08	-2.2	[-5.7, 1.4]	1.74	0.220
UPA 30 mg QD + TCS	15	14.1	3.8	-9.7	[-11.7, -7.6]	1.01	-2.9	[-6.3, 0.5]	1.69	0.096
Adult										
Placebo + TCS	174	16.4	9.9	-6.1	[-6.9, -5.3]	0.40				
UPA 15 mg QD + TCS	238	16.3	5.3	-11.1	[-11.8, -10.4]	0.36	-5.0	[-6.1, -4.0]	0.54	<0.001***
UPA 30 mg QD + TCS	237	17.5	4.6	-12.5	[-13.2, -11.8]	0.36	-6.4	[-7.5, -5.3]	0.54	<0.001***

Note: DLQI = Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　6.4.1

表 2.7.3.6-45. ベースライン時の CDLQI スコアが 1 を超えており，かつスクリーニング時に 16 歳未満であった被験者のうち，二重盲検投与期の来院時別での CDLQI スコア 0 又は 1 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo + TCS	25	0	0					
UPA 15 mg QD + TCS	22	1 (4.5) [0.0, 13.2]	0	4.5	4.6	[-4.1, 13.2]	0.299	NA
UPA 30 mg QD + TCS	21	2 (9.5) [0.0, 22.1]	0	9.5	9.8	[-3.3, 22.9]	0.143	NA
vIGA-AD 3 (Moderate)								
Placebo + TCS	9	0	0					
UPA 15 mg QD + TCS	8	0	0	0.0			NA	
UPA 30 mg QD + TCS	12	1 (8.3) [0.0, 24.0]	0	8.3		[-7.3, 24.0]	0.296	
vIGA-AD 4 (Severe)								
Placebo + TCS	16	0	0					
UPA 15 mg QD + TCS	14	1 (7.1) [0.0, 20.6]	0	7.1		[-6.3, 20.6]	0.299	
UPA 30 mg QD + TCS	9	1 (11.1) [0.0, 31.6]	0	11.1		[-9.4, 31.6]	0.289	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	9	0	0					
UPA 15 mg QD + TCS	13	0	0	0.0			NA	
UPA 30 mg QD + TCS	11	0	0	0.0			NA	
Japan								
Placebo + TCS	0	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					
China								
Placebo + TCS	2	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo + TCS	14	0	0					
UPA 15 mg QD + TCS	9	1 (11.1) [0.0, 31.6]	0	11.1		[-9.4, 31.6]	0.289	
UPA 30 mg QD + TCS	10	2 (20.0) [0.0, 44.8]	0	20.0		[-4.8, 44.8]	0.114	
Adolescent								
Placebo + TCS	25	0	0					
UPA 15 mg QD + TCS	22	1 (4.5) [0.0, 13.2]	0	4.5		[-4.2, 13.2]	0.306	
UPA 30 mg QD + TCS	21	2 (9.5) [0.0, 22.1]	0	9.5		[-3.0, 22.1]	0.137	
Adult								
Placebo + TCS	0	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8								
All								
Placebo + TCS	25	0	0					
UPA 15 mg QD + TCS	22	4 (18.2) [2.1, 34.3]	0	18.2	18.1	[3.2, 33.0]	0.017*	NA
UPA 30 mg QD + TCS	21	4 (19.0) [2.3, 35.8]	0	19.0	19.6	[2.1, 37.1]	0.028*	NA
vIGA-AD 3 (Moderate)								
Placebo + TCS	9	0	0					
UPA 15 mg QD + TCS	8	3 (37.5) [4.0, 71.0]	0	37.5		[4.0, 71.0]	0.028*	
UPA 30 mg QD + TCS	12	2 (16.7) [0.0, 37.8]	0	16.7		[-4.4, 37.8]	0.121	
vIGA-AD 4 (Severe)								
Placebo + TCS	16	0	0					
UPA 15 mg QD + TCS	14	1 (7.1) [0.0, 20.6]	0	7.1		[-6.3, 20.6]	0.299	
UPA 30 mg QD + TCS	9	2 (22.2) [0.0, 49.4]	0	22.2		[-4.9, 49.4]	0.109	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	9	0	0					
UPA 15 mg QD + TCS	13	1 (7.7) [0.0, 22.2]	0	7.7		[-6.8, 22.2]	0.298	
UPA 30 mg QD + TCS	11	1 (9.1) [0.0, 26.1]	0	9.1		[-7.9, 26.1]	0.294	
Japan								
Placebo + TCS	0	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					
China								
Placebo + TCS	2	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 8 (Cont.)								
Other								
Placebo + TCS	14	0	0					
UPA 15 mg QD + TCS	9	3 (33.3) [2.5, 64.1]	0	33.3		[2.5, 64.1]	0.034*	
UPA 30 mg QD + TCS	10	3 (30.0) [1.6, 58.4]	0	30.0		[1.6, 58.4]	0.038*	
Adolescent								
Placebo + TCS	25	0	0					
UPA 15 mg QD + TCS	22	4 (18.2) [2.1, 34.3]	0	18.2		[2.1, 34.3]	0.027*	
UPA 30 mg QD + TCS	21	4 (19.0) [2.3, 35.8]	0	19.0		[2.3, 35.8]	0.026*	
Adult								
Placebo + TCS	0	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	25	0	0					
UPA 15 mg QD + TCS	22	3 (13.6) [0.0, 28.0]	0	13.6	13.6	[1.4, 25.7]	0.028*	NA
UPA 30 mg QD + TCS	21	4 (19.0) [2.3, 35.8]	0	19.0	19.6	[2.1, 37.1]	0.028*	NA
vIGA-AD 3 (Moderate)								
Placebo + TCS	9	0	0					
UPA 15 mg QD + TCS	8	3 (37.5) [4.0, 71.0]	0	37.5		[4.0, 71.0]	0.028*	
UPA 30 mg QD + TCS	12	2 (16.7) [0.0, 37.8]	0	16.7		[-4.4, 37.8]	0.121	
vIGA-AD 4 (Severe)								
Placebo + TCS	16	0	0					
UPA 15 mg QD + TCS	14	0	0	0.0			NA	
UPA 30 mg QD + TCS	9	2 (22.2) [0.0, 49.4]	0	22.2		[-4.9, 49.4]	0.109	

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	9	0	0					
UPA 15 mg QD + TCS	13	2 (15.4) [0.0, 35.0]	0	15.4		[-4.2, 35.0]	0.124	
UPA 30 mg QD + TCS	11	1 (9.1) [0.0, 26.1]	0	9.1		[-7.9, 26.1]	0.294	
Japan								
Placebo + TCS	0	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					
China								
Placebo + TCS	2	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo + TCS	14	0	0					
UPA 15 mg QD + TCS	9	1 (11.1) [0.0, 31.6]	0	11.1		[-9.4, 31.6]	0.289	
UPA 30 mg QD + TCS	10	3 (30.0) [1.6, 58.4]	0	30.0		[1.6, 58.4]	0.038*	
Adolescent								
Placebo + TCS	25	0	0					
UPA 15 mg QD + TCS	22	3 (13.6) [0.0, 28.0]	0	13.6		[-0.7, 28.0]	0.062	
UPA 30 mg QD + TCS	21	4 (19.0) [2.3, 35.8]	0	19.0		[2.3, 35.8]	0.026*	
Adult								
Placebo + TCS	0	0	0					
UPA 15 mg QD + TCS	0	0	0					
UPA 30 mg QD + TCS	0	0	0					

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　7.1.1

表 2.7.3.6-46. 二重盲検投与期の来院時別でのスクリーニング時に 16 歳未満の被験者における CDLQI スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo + TCS	24	14.1	10.9	-15.93	[-35.37, 3.52]	9.734				
UPA 15 mg QD + TCS	22	13.4	7.4	-37.84	[-58.25, -17.43]	10.213	-21.91	[-49.80, 5.98]	13.958	0.121
UPA 30 mg QD + TCS	21	11.6	5.4	-43.02	[-63.87, -22.18]	10.432	-27.10	[-55.84, 1.65]	14.386	0.064
vIGA-AD 3 (Moderate)										
Placebo + TCS	9	11.0	6.2	-33.55	[-68.90, 1.80]	17.171				
UPA 15 mg QD + TCS	8	12.8	6.3	-15.95	[-54.24, 22.33]	18.606	17.60	[-34.30, 69.50]	25.216	0.492
UPA 30 mg QD + TCS	12	8.6	5.5	-28.99	[-60.52, 2.54]	15.326	4.56	[-43.03, 52.15]	23.125	0.845
vIGA-AD 4 (Severe)										
Placebo + TCS	15	15.9	13.7	-8.27	[-25.88, 9.33]	8.679				
UPA 15 mg QD + TCS	14	13.8	8.1	-45.94	[-64.36, -27.53]	9.073	-37.67	[-63.24, -12.10]	12.605	0.005**
UPA 30 mg QD + TCS	9	15.7	5.2	-68.61	[-91.45, -45.77]	11.249	-60.34	[-89.15, -31.53]	14.195	<0.001***

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	8	12.9	12.3	-5.36	[-40.67, 29.95]	17.258				
UPA 15 mg QD + TCS	13	14.0	8.8	-25.54	[-53.04, 1.96]	13.442	-20.18	[-64.95, 24.59]	21.883	0.364
UPA 30 mg QD + TCS	11	12.5	6.5	-40.53	[-70.44, -10.62]	14.620	-35.17	[-81.42, 11.09]	22.607	0.131
Japan										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									
China										
Placebo + TCS	2	13.5	10.0							
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo + TCS	14	14.9	10.3	-24.09	[-50.75, 2.57]	13.033				
UPA 15 mg QD + TCS	9	12.6	5.3	-58.17	[-90.72, -25.62]	15.899	-34.08	[-76.27, 8.11]	20.618	0.109
UPA 30 mg QD + TCS	10	10.6	4.1	-42.81	[-74.32, -11.30]	15.405	-18.72	[-60.82, 23.38]	20.603	0.371
Adolescent										
Placebo + TCS	24	14.1	10.9	-16.47	[-35.62, 2.67]	9.585				
UPA 15 mg QD + TCS	22	13.4	7.4	-38.54	[-58.55, -18.53]	10.016	-22.07	[-49.73, 5.60]	13.848	0.116
UPA 30 mg QD + TCS	21	11.6	5.4	-42.90	[-63.57, -22.23]	10.348	-26.43	[-54.78, 1.93]	14.197	0.067
Adult										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo + TCS	20	14.7	9.5	-27.02	[-59.21, 5.17]	16.122				
UPA 15 mg QD + TCS	22	13.4	4.9	-61.62	[-93.19, -30.04]	15.793	-34.60	[-79.51, 10.31]	22.474	0.129
UPA 30 mg QD + TCS	21	11.6	4.4	-37.53	[-69.82, -5.24]	16.150	-10.51	[-56.27, 35.24]	22.906	0.648
vIGA-AD 3 (Moderate)										
Placebo + TCS	8	11.9	6.1	-40.79	[-115.85, 34.26]	36.537				
UPA 15 mg QD + TCS	8	12.8	3.5	-60.82	[-137.34, 15.69]	37.196	-20.03	[-127.16, 87.10]	52.099	0.704
UPA 30 mg QD + TCS	12	8.6	4.8	-16.03	[-78.62, 46.57]	30.438	24.76	[-73.00, 122.53]	47.598	0.607
vIGA-AD 4 (Severe)										
Placebo + TCS	12	16.5	11.7	-24.99	[-40.02, -9.95]	7.393				
UPA 15 mg QD + TCS	14	13.8	5.6	-57.66	[-72.11, -43.22]	7.082	-32.68	[-53.68, -11.68]	10.319	0.003**
UPA 30 mg QD + TCS	9	15.7	3.8	-73.07	[-90.93, -55.22]	8.747	-48.09	[-71.38, -24.79]	11.431	<0.001***

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	6	14.0	10.0	-32.10	[-58.73, -5.47]	12.967				
UPA 15 mg QD + TCS	13	14.0	5.9	-54.99	[-72.89, -37.09]	8.715	-22.89	[-54.95, 9.18]	15.611	0.154
UPA 30 mg QD + TCS	11	12.5	4.9	-50.99	[-70.47, -31.52]	9.484	-18.89	[-51.92, 14.13]	16.082	0.251
Japan										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									
China										
Placebo + TCS	2	13.5	11.5							
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo + TCS	12	15.2	8.8	-35.86	[-92.79, 21.06]	27.933				
UPA 15 mg QD + TCS	9	12.6	3.3	-73.75	[-142.53, -4.97]	33.633	-37.89	[-127.21, 51.43]	43.745	0.393
UPA 30 mg QD + TCS	10	10.6	3.8	-19.76	[-85.29, 45.76]	32.061	16.10	[-71.02, 103.21]	42.702	0.709
Adolescent										
Placebo + TCS	20	14.7	9.5	-27.56	[-59.53, 4.40]	16.012				
UPA 15 mg QD + TCS	22	13.4	4.9	-62.32	[-93.59, -31.04]	15.641	-34.75	[-79.45, 9.95]	22.372	0.125
UPA 30 mg QD + TCS	21	11.6	4.4	-37.41	[-69.54, -5.28]	16.071	-9.84	[-55.30, 35.61]	22.757	0.667
Adult										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo + TCS	19	14.3	9.6	-25.58	[-51.34, 0.17]	12.897				
UPA 15 mg QD + TCS	22	13.4	5.3	-57.87	[-82.93, -32.81]	12.531	-32.29	[-68.01, 3.44]	17.879	0.076
UPA 30 mg QD + TCS	18	11.8	3.9	-49.83	[-75.93, -23.72]	13.070	-24.24	[-61.14, 12.66]	18.481	0.194
vIGA-AD 3 (Moderate)										
Placebo + TCS	8	11.9	8.5	-21.23	[-77.96, 35.50]	27.621				
UPA 15 mg QD + TCS	8	12.8	3.9	-53.71	[-111.83, 4.41]	28.256	-32.48	[-113.55, 48.59]	39.420	0.418
UPA 30 mg QD + TCS	12	8.6	3.8	-33.88	[-81.50, 13.73]	23.160	-12.65	[-86.86, 61.56]	36.145	0.729
vIGA-AD 4 (Severe)										
Placebo + TCS	11	16.0	10.5	-34.66	[-51.71, -17.61]	8.319				
UPA 15 mg QD + TCS	14	13.8	6.1	-55.84	[-71.03, -40.65]	7.404	-21.18	[-44.12, 1.76]	11.193	0.069
UPA 30 mg QD + TCS	6	18.2	4.3	-79.50	[-102.77, -56.23]	11.375	-44.84	[-73.56, -16.13]	14.022	0.003**

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	6	14.0	8.5	-32.35	[-61.86, -2.84]	14.360				
UPA 15 mg QD + TCS	13	14.0	6.4	-51.16	[-71.00, -31.32]	9.654	-18.81	[-54.35, 16.73]	17.292	0.287
UPA 30 mg QD + TCS	10	12.8	4.4	-59.14	[-81.76, -36.53]	11.011	-26.79	[-64.00, 10.41]	18.108	0.151
Japan										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									
China										
Placebo + TCS	2	13.5	8.5							
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo + TCS	11	14.5	10.5	-26.95	[-70.44, 16.54]	21.348				
UPA 15 mg QD + TCS	9	12.6	3.8	-70.13	[-122.12, -18.13]	25.409	-43.18	[-111.02, 24.66]	33.219	0.204
UPA 30 mg QD + TCS	8	10.5	3.4	-36.01	[-86.23, 14.21]	24.603	-9.06	[-75.92, 57.79]	32.807	0.784
Adolescent										
Placebo + TCS	19	14.3	9.6	-26.05	[-51.65, -0.46]	12.818				
UPA 15 mg QD + TCS	22	13.4	5.3	-58.57	[-83.35, -33.79]	12.389	-32.52	[-68.11, 3.08]	17.813	0.073
UPA 30 mg QD + TCS	18	11.8	3.9	-49.57	[-75.56, -23.57]	13.011	-23.51	[-60.15, 13.12]	18.347	0.205
Adult										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　7.2.1

表 2.7.3.6-47. 二重盲検投与期の来院時別でのスクリーニング時に 16 歳未満の被験者における CDLQI スコアのベースラインからの変化量（MMRM, ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo + TCS	24	14.1	10.9	-2.5	[-4.4, -0.5]	0.98				
UPA 15 mg QD + TCS	22	13.4	7.4	-5.9	[-8.0, -3.9]	1.02	-3.4	[-6.3, -0.6]	1.40	0.017*
UPA 30 mg QD + TCS	21	11.6	5.4	-7.2	[-9.3, -5.1]	1.05	-4.7	[-7.6, -1.9]	1.44	0.002**
vIGA-AD 3 (Moderate)										
Placebo + TCS	9	11.0	6.2	-4.5	[-6.5, -2.5]	0.96				
UPA 15 mg QD + TCS	8	12.8	6.3	-4.9	[-7.1, -2.8]	1.04	-0.4	[-3.3, 2.5]	1.41	0.765
UPA 30 mg QD + TCS	12	8.6	5.5	-4.6	[-6.4, -2.8]	0.85	-0.1	[-2.8, 2.6]	1.29	0.941
vIGA-AD 4 (Severe)										
Placebo + TCS	15	15.9	13.7	-1.6	[-4.3, 1.2]	1.35				
UPA 15 mg QD + TCS	14	13.8	8.1	-6.6	[-9.4, -3.7]	1.41	-5.0	[-9.0, -1.0]	1.96	0.016*
UPA 30 mg QD + TCS	9	15.7	5.2	-10.2	[-13.7, -6.6]	1.75	-8.6	[-13.1, -4.1]	2.21	<0.001***

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean (Within Group, Change from Baseline)	[95% CI]	SE	LS Mean (Between Groups Difference, Compared to Placebo)	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	8	12.9	12.3	-0.6	[-4.2, 3.0]	1.76				
UPA 15 mg QD + TCS	13	14.0	8.8	-4.8	[-7.6, -1.9]	1.39	-4.2	[-8.8, 0.4]	2.24	0.073
UPA 30 mg QD + TCS	11	12.5	6.5	-6.6	[-9.7, -3.5]	1.51	-6.0	[-10.7, -1.2]	2.32	0.016*
Japan										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									
China										
Placebo + TCS	2	13.5	10.0	-3.5	[-8.7, 1.7]	0.66				
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group Change from Baseline [95% CI]	Within Group Change from Baseline SE	Between Groups Difference Compared to Placebo LS Mean	Between Groups Difference Compared to Placebo [95% CI]	Between Groups Difference Compared to Placebo SE	Between Groups Difference Compared to Placebo P-value
Week 2 (Cont.)										
Other										
Placebo + TCS	14	14.9	10.3	-3.2	[-5.7, -0.6]	1.26				
UPA 15 mg QD + TCS	9	12.6	5.3	-7.5	[-10.6, -4.3]	1.54	-4.3	[-8.4, -0.2]	1.99	0.040*
UPA 30 mg QD + TCS	10	10.6	4.1	-8.1	[-11.2, -5.1]	1.49	-5.0	[-9.0, -0.9]	1.99	0.019*
Adolescent										
Placebo + TCS	24	14.1	10.9	-2.4	[-4.3, -0.5]	0.97				
UPA 15 mg QD + TCS	22	13.4	7.4	-5.8	[-7.9, -3.8]	1.02	-3.4	[-6.2, -0.6]	1.41	0.018*
UPA 30 mg QD + TCS	21	11.6	5.4	-7.3	[-9.3, -5.2]	1.05	-4.8	[-7.7, -2.0]	1.43	0.001**
Adult										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo + TCS	20	14.7	9.5	-4.2	[-5.8, -2.6]	0.82				
UPA 15 mg QD + TCS	22	13.4	4.9	-8.5	[-10.1, -6.9]	0.81	-4.3	[-6.6, -2.0]	1.14	<0.001***
UPA 30 mg QD + TCS	21	11.6	4.4	-8.2	[-9.9, -6.6]	0.82	-4.0	[-6.4, -1.7]	1.18	0.001**
vIGA-AD 3 (Moderate)										
Placebo + TCS	8	11.9	6.1	-4.9	[-7.4, -2.5]	1.20				
UPA 15 mg QD + TCS	8	12.8	3.5	-7.7	[-10.2, -5.2]	1.22	-2.8	[-6.3, 0.7]	1.70	0.117
UPA 30 mg QD + TCS	12	8.6	4.8	-5.3	[-7.3, -3.2]	1.00	-0.4	[-3.6, 2.9]	1.58	0.826
vIGA-AD 4 (Severe)										
Placebo + TCS	12	16.5	11.7	-4.1	[-6.1, -2.0]	1.01				
UPA 15 mg QD + TCS	14	13.8	5.6	-9.0	[-11.0, -7.1]	0.96	-4.9	[-7.8, -2.1]	1.41	0.001**
UPA 30 mg QD + TCS	9	15.7	3.8	-11.6	[-14.0, -9.2]	1.18	-7.6	[-10.7, -4.4]	1.56	<0.001***

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group Change from Baseline [95% CI]	Within Group Change from Baseline SE	Between Groups Difference Compared to Placebo LS Mean	Between Groups Difference Compared to Placebo [95% CI]	Between Groups Difference Compared to Placebo SE	Between Groups Difference Compared to Placebo P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	6	14.0	10.0	-3.5	[-6.5, -0.5]	1.47				
UPA 15 mg QD + TCS	13	14.0	5.9	-7.7	[-9.8, -5.6]	1.02	-4.2	[-7.9, -0.6]	1.78	0.026*
UPA 30 mg QD + TCS	11	12.5	4.9	-8.2	[-10.5, -5.9]	1.11	-4.7	[-8.5, -0.9]	1.84	0.017*
Japan										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									
China										
Placebo + TCS	2	13.5	11.5	-2.0	[-7.2, 3.2]	0.66				
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group Change from Baseline [95% CI]	SE	Between Groups Difference Compared to Placebo LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo + TCS	12	15.2	8.8	-4.8	[-7.1, -2.5]	1.14				
UPA 15 mg QD + TCS	9	12.6	3.3	-9.5	[-12.1, -6.8]	1.30	-4.6	[-8.2, -1.1]	1.74	0.012*
UPA 30 mg QD + TCS	10	10.6	3.8	-8.4	[-11.0, -5.8]	1.27	-3.6	[-7.2, -0.0]	1.75	0.049*
Adolescent										
Placebo + TCS	20	14.7	9.5	-4.1	[-5.8, -2.5]	0.82				
UPA 15 mg QD + TCS	22	13.4	4.9	-8.4	[-10.0, -6.8]	0.80	-4.2	[-6.5, -1.9]	1.15	<0.001***
UPA 30 mg QD + TCS	21	11.6	4.4	-8.3	[-9.9, -6.6]	0.83	-4.1	[-6.5, -1.8]	1.18	0.001**
Adult										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo + TCS	19	14.3	9.6	-4.0	[-5.9, -2.1]	0.95				
UPA 15 mg QD + TCS	22	13.4	5.3	-8.0	[-9.8, -6.2]	0.90	-4.1	[-6.7, -1.5]	1.31	0.003**
UPA 30 mg QD + TCS	18	11.8	3.9	-8.9	[-10.8, -6.9]	0.98	-4.9	[-7.7, -2.1]	1.38	0.001**
vIGA-AD 3 (Moderate)										
Placebo + TCS	8	11.9	8.5	-2.6	[-5.5, 0.2]	1.38				
UPA 15 mg QD + TCS	8	12.8	3.9	-7.3	[-10.2, -4.4]	1.43	-4.7	[-8.8, -0.6]	1.98	0.026*
UPA 30 mg QD + TCS	12	8.6	3.8	-6.4	[-8.8, -3.9]	1.17	-3.7	[-7.5, -0.0]	1.82	0.050*
vIGA-AD 4 (Severe)										
Placebo + TCS	11	16.0	10.5	-5.2	[-7.9, -2.6]	1.29				
UPA 15 mg QD + TCS	14	13.8	6.1	-8.5	[-10.9, -6.2]	1.15	-3.3	[-6.8, 0.3]	1.74	0.071
UPA 30 mg QD + TCS	6	18.2	4.3	-12.1	[-15.7, -8.5]	1.77	-6.9	[-11.4, -2.4]	2.19	0.004**

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	6	14.0	8.5	-5.0	[-8.7, -1.3]	1.80				
UPA 15 mg QD + TCS	13	14.0	6.4	-7.2	[-9.8, -4.7]	1.22	-2.2	[-6.7, 2.3]	2.18	0.320
UPA 30 mg QD + TCS	10	12.8	4.4	-8.8	[-11.7, -5.9]	1.40	-3.8	[-8.5, 0.9]	2.28	0.109
Japan										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									
China										
Placebo + TCS	2	13.5	8.5	-5.0	[-10.2, 0.2]	0.66				
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo + TCS	11	14.5	10.5	-3.1	[-5.6, -0.5]	1.24				
UPA 15 mg QD + TCS	9	12.6	3.8	-9.0	[-11.8, -6.2]	1.38	-5.9	[-9.7, -2.1]	1.86	0.003**
UPA 30 mg QD + TCS	8	10.5	3.4	-9.2	[-12.2, -6.2]	1.45	-6.1	[-10.1, -2.1]	1.94	0.004**
Adolescent										
Placebo + TCS	19	14.3	9.6	-3.9	[-5.8, -2.0]	0.94				
UPA 15 mg QD + TCS	22	13.4	5.3	-7.9	[-9.7, -6.2]	0.89	-4.0	[-6.6, -1.4]	1.29	0.003**
UPA 30 mg QD + TCS	18	11.8	3.9	-8.9	[-10.9, -7.0]	0.97	-5.0	[-7.7, -2.3]	1.36	0.001**
Adult										
Placebo + TCS	0									
UPA 15 mg QD + TCS	0									
UPA 30 mg QD + TCS	0									

Note: CDLQI = Children's Dermatology Life Quality Index; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　7.3.1

表 2.7.3.6-48.　第 1 ピリオドの来院時別の DLQI スコアの 0 又は 1 を達成した被験者の割合（NRI，LOCF，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 4													
	ALL												
		UPA 30 MG QD	42	21	(50.0)	21	(50.0)	0		47.6	45.8	(30.4, 61.1)	<0.001***
		UPA 15 MG QD	42	8	(19.0)	33	(78.6)	1	(2.4)	16.6	15.8	(3.4, 28.2)	0.013*
		UPA 7.5 MG QD	42	9	(21.4)	33	(78.6)	0		19.0	18.8	(5.8, 31.8)	0.005**
		PLACEBO	41	1	(2.4)	36	(87.8)	4	(9.8)				
	US/PR/CANADA												
		UPA 30 MG QD	29	14	(48.3)	15	(51.7)	0		48.3		(30.1, 66.5)	<0.001***
		UPA 15 MG QD	29	4	(13.8)	24	(82.8)	1	(3.4)	13.8		(1.2, 26.3)	0.112
		UPA 7.5 MG QD	29	7	(24.1)	22	(75.9)	0		24.1		(8.6, 39.7)	0.010**
		PLACEBO	29	0		26	(89.7)	3	(10.3)				
	EU/AUS												
		UPA 30 MG QD	10	4	(40.0)	6	(60.0)	0		40.0		(9.6, 70.4)	0.087
		UPA 15 MG QD	10	3	(30.0)	7	(70.0)	0		30.0		(1.6, 58.4)	0.211
		UPA 7.5 MG QD	11	2	(18.2)	9	(81.8)	0		18.2		(-4.6, 41.0)	0.476
		PLACEBO	10	0		9	(90.0)	1	(10.0)				
	JAPAN												
		UPA 30 MG QD	3	3	(100)	0		0		50.0		(-19.3, 100.0)	0.400
		UPA 15 MG QD	3	1	(33.3)	2	(66.7)	0		-16.7		(-100.0, 70.8)	1.000
		UPA 7.5 MG QD	2	0		2	(100)	0		-50.0		(-100.0, 19.3)	1.000
		PLACEBO	2	1	(50.0)	1	(50.0)	0					
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.127											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.020*											

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 16													
	ALL												
		UPA 30 MG QD	42	18	(42.9)	22	(52.4)	2	(4.8)	40.4	39.7	(24.2, 55.3)	<0.001***
		UPA 15 MG QD	42	5	(11.9)	33	(78.6)	4	(9.5)	9.5	9.0	(-1.9, 19.9)	0.106
		UPA 7.5 MG QD	42	6	(14.3)	28	(66.7)	8	(19.0)	11.8	11.6	(0.3, 23.0)	0.044*
		PLACEBO	41	1	(2.4)	25	(61.0)	15	(36.6)				
	US/PR/CANADA												
		UPA 30 MG QD	29	12	(41.4)	17	(58.6)	0		41.4		(23.5, 59.3)	<0.001***
		UPA 15 MG QD	29	3	(10.3)	25	(86.2)	1	(3.4)	10.3		(-0.7, 21.4)	0.237
		UPA 7.5 MG QD	29	4	(13.8)	22	(75.9)	3	(10.3)	13.8		(1.2, 26.3)	0.112
		PLACEBO	29	0		22	(75.9)	7	(24.1)				
	EU/AUS												
		UPA 30 MG QD	10	5	(50.0)	3	(30.0)	2	(20.0)	50.0		(19.0, 81.0)	0.033*
		UPA 15 MG QD	10	2	(20.0)	5	(50.0)	3	(30.0)	20.0		(-4.8, 44.8)	0.474
		UPA 7.5 MG QD	11	2	(18.2)	4	(36.4)	5	(45.5)	18.2		(-4.6, 41.0)	0.476
		PLACEBO	10	0		2	(20.0)	8	(80.0)				
	JAPAN												
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	0		-16.7		(-100.0, 70.8)	1.000
		UPA 15 MG QD	3	0		3	(100)	0		-50.0		(-100.0, 19.3)	0.400
		UPA 7.5 MG QD	2	0		2	(100)	0		-50.0		(-100.0, 19.3)	1.000
		PLACEBO	2	1	(50.0)	1	(50.0)	0					
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.017*											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.030*											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.050*											

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	21	(50.0)	21	(50.0)	47.3	45.7	(30.3, 61.1)	<0.001***
		UPA 15 MG QD	41	8	(19.5)	33	(80.5)	16.8	16.0	(3.2, 28.8)	0.014*
		UPA 7.5 MG QD	42	9	(21.4)	33	(78.6)	18.7	18.5	(5.5, 31.6)	0.005**
		PLACEBO	37	1	(2.7)	36	(97.3)				
	US/PR/CANADA										
		UPA 30 MG QD	29	14	(48.3)	15	(51.7)	48.3		(30.1, 66.5)	<0.001***
		UPA 15 MG QD	28	4	(14.3)	24	(85.7)	14.3		(1.3, 27.2)	0.112
		UPA 7.5 MG QD	29	7	(24.1)	22	(75.9)	24.1		(8.6, 39.7)	0.011*
		PLACEBO	26	0		26	(100)				
	EU/AUS										
		UPA 30 MG QD	10	4	(40.0)	6	(60.0)	40.0		(9.6, 70.4)	0.087
		UPA 15 MG QD	10	3	(30.0)	7	(70.0)	30.0		(1.6, 58.4)	0.211
		UPA 7.5 MG QD	11	2	(18.2)	9	(81.8)	18.2		(-4.6, 41.0)	0.479
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	3	(100)	0		50.0		(-19.3, 100.0)	0.400
		UPA 15 MG QD	3	1	(33.3)	2	(66.7)	-16.7		(-100.0, 70.8)	1.000
		UPA 7.5 MG QD	2	0		2	(100)	-50.0		(-100.0, 19.3)	1.000
		PLACEBO	2	1	(50.0)	1	(50.0)				

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = NA
UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.137
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.023*

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	42	18	(42.9)	24	(57.1)	40.2	39.5	(23.9, 55.1)	<0.001***
		UPA 15 MG QD	41	5	(12.2)	36	(87.8)	9.5	9.0	(-2.2, 20.2)	0.117
		UPA 7.5 MG QD	42	6	(14.3)	36	(85.7)	11.6	11.4	(-0.0, 22.8)	0.050*
		PLACEBO	37	1	(2.7)	36	(97.3)				
	US/PR/CANADA										
		UPA 30 MG QD	29	12	(41.4)	17	(58.6)	41.4		(23.5, 59.3)	<0.001***
		UPA 15 MG QD	28	3	(10.7)	25	(89.3)	10.7		(-0.7, 22.2)	0.237
		UPA 7.5 MG QD	29	4	(13.8)	25	(86.2)	13.8		(1.2, 26.3)	0.113
		PLACEBO	26	0		26	(100)				
	EU/AUS										
		UPA 30 MG QD	10	5	(50.0)	5	(50.0)	50.0		(19.0, 81.0)	0.033*
		UPA 15 MG QD	10	2	(20.0)	8	(80.0)	20.0		(-4.8, 44.8)	0.474
		UPA 7.5 MG QD	11	2	(18.2)	9	(81.8)	18.2		(-4.6, 41.0)	0.479
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	-16.7		(-100.0, 70.8)	1.000
		UPA 15 MG QD	3	0		3	(100)	-50.0		(-100.0, 19.3)	0.400
		UPA 7.5 MG QD	2	0		2	(100)	-50.0		(-100.0, 19.3)	1.000
		PLACEBO	2	1	(50.0)	1	(50.0)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.021*									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.034*									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.057									

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]

NA = NOT APPLICABLE.
[A]: ACROSS THE STRATA, 95% CI FOR ADJUSTED DIFFERENCE WAS CALCULATED ACCORDING TO THE COCHRAN-MANTEL-HAENSZEL TEST FOR THE COMPARISON OF TWO TREATMENT GROUPS. WITHIN EACH STRATUM, 95% CI FOR DIFFERENCE WAS CALCULATED BASED ON NORMAL APPROXIMATION TO THE BINOMIAL DISTRIBUTION.
[B]: ACROSS THE STRATA, P-VALUE WAS CALCULATED FROM THE COCHRAN-MANTEL-HAENSZEL TEST ADJUSTED FOR STRATA. WITHIN EACH STRATUM, P-VALUE WAS CALCULATED BASED ON CHI-SQUARE TEST (OR FISHER'S EXACT TEST IF >= 25% OF THE CELLS HAVE EXPECTED CELL COUNT < 5).
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2　1.13.2

表 2.7.3.6-49.　第 1 ピリオドの来院時別の DLQI スコアのベースラインからの変化量（LOCF，OC，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	13.7	3.8	-9.9	0.99	-7.9	(-10.3, -5.4)	1.24	<0.001***
		UPA 15 MG QD	40	13.6	6.4	-7.3	1.00	-5.3	(-7.7, -2.8)	1.25	<0.001***
		UPA 7.5 MG QD	42	11.3	6.1	-6.8	1.03	-4.8	(-7.2, -2.3)	1.25	<0.001***
		PLACEBO	37	13.5	11.7	-2.0	1.05				
	US/PR/CANADA										
		UPA 30 MG QD	29	14.8	4.4	-9.8	1.01	-8.0	(-10.9, -5.1)	1.47	<0.001***
		UPA 15 MG QD	27	14.9	7.0	-7.2	1.05	-5.5	(-8.4, -2.5)	1.49	<0.001***
		UPA 7.5 MG QD	29	11.2	5.2	-7.7	1.03	-5.9	(-8.9, -3.0)	1.49	<0.001***
		PLACEBO	26	14.8	12.5	-1.8	1.07				
	EU/AUS										
		UPA 30 MG QD	10	12.5	3.0	-9.2	1.99	-8.6	(-14.5, -2.7)	2.89	0.005**
		UPA 15 MG QD	10	11.2	5.7	-6.0	2.00	-5.4	(-11.3, 0.5)	2.90	0.070
		UPA 7.5 MG QD	11	12.4	9.0	-3.2	1.90	-2.5	(-8.3, 3.2)	2.83	0.376
		PLACEBO	9	12.1	11.4	-0.6	2.10				
	JAPAN										
		UPA 30 MG QD	3	7.0	0.7	-6.3	0.85	-2.2	(-6.1, 1.8)	1.53	0.217
		UPA 15 MG QD	3	9.3	3.0	-4.2	0.98	-0.0	(-4.7, 4.6)	1.81	0.986
		UPA 7.5 MG QD	2	7.0	3.0	-4.0	1.04	0.2	(-4.0, 4.4)	1.64	0.917
		PLACEBO	2	3.5	2.5	-4.2	1.27				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.752

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	42	13.7	4.8	-8.3	1.14	-7.8	(-10.6, -5.0)	1.43	<0.001***
		UPA 15 MG QD	40	13.6	7.8	-5.2	1.16	-4.8	(-7.6, -1.9)	1.45	0.001**
		UPA 7.5 MG QD	42	11.3	8.0	-4.0	1.20	-3.5	(-6.4, -0.7)	1.44	0.016*
		PLACEBO	37	13.5	12.5	-0.5	1.22				
	US/PR/CANADA										
		UPA 30 MG QD	29	14.8	5.1	-9.2	1.18	-8.8	(-12.2, -5.4)	1.71	<0.001***
		UPA 15 MG QD	27	14.9	7.6	-6.8	1.22	-6.4	(-9.8, -2.9)	1.74	<0.001***
		UPA 7.5 MG QD	29	11.2	7.2	-5.4	1.20	-5.0	(-8.4, -1.5)	1.74	0.005**
		PLACEBO	26	14.8	14.0	-0.4	1.25				
	EU/AUS										
		UPA 30 MG QD	10	12.5	4.4	-7.8	2.21	-6.5	(-13.0, -0.0)	3.20	0.049*
		UPA 15 MG QD	10	11.2	7.8	-3.9	2.21	-2.6	(-9.1, 3.9)	3.21	0.418
		UPA 7.5 MG QD	11	12.4	10.4	-1.8	2.10	-0.5	(-6.9, 5.9)	3.13	0.871
		PLACEBO	9	12.1	10.8	-1.3	2.32				
	JAPAN										
		UPA 30 MG QD	3	7.0	3.0	-4.0	1.53	-0.0	(-7.1, 7.1)	2.75	0.994
		UPA 15 MG QD	3	9.3	9.7	2.0	1.76	6.0	(-2.4, 14.4)	3.27	0.127
		UPA 7.5 MG QD	2	7.0	5.5	-1.5	1.87	2.5	(-5.1, 10.1)	2.96	0.440
		PLACEBO	2	3.5	2.0	-4.0	2.29				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.528

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	13.7	3.8	-9.9	0.99	-7.9	(-10.3, -5.4)	1.24	<0.001***
		UPA 15 MG QD	40	13.6	6.4	-7.3	1.00	-5.3	(-7.7, -2.8)	1.25	<0.001***
		UPA 7.5 MG QD	42	11.3	6.1	-6.8	1.03	-4.8	(-7.2, -2.3)	1.25	<0.001***
		PLACEBO	37	13.5	11.7	-2.0	1.05				
	US/PR/CANADA										
		UPA 30 MG QD	29	14.8	4.4	-9.8	1.01	-8.0	(-10.9, -5.1)	1.47	<0.001***
		UPA 15 MG QD	27	14.9	7.0	-7.2	1.05	-5.5	(-8.4, -2.5)	1.49	<0.001***
		UPA 7.5 MG QD	29	11.2	5.2	-7.7	1.03	-5.9	(-8.9, -3.0)	1.49	<0.001***
		PLACEBO	26	14.8	12.5	-1.8	1.07				
	EU/AUS										
		UPA 30 MG QD	10	12.5	3.0	-9.2	1.99	-8.6	(-14.5, -2.7)	2.89	0.005**
		UPA 15 MG QD	10	11.2	5.7	-6.0	2.00	-5.4	(-11.3, 0.5)	2.90	0.070
		UPA 7.5 MG QD	11	12.4	9.0	-3.2	1.90	-2.5	(-8.3, 3.2)	2.83	0.376
		PLACEBO	9	12.1	11.4	-0.6	2.10				
	JAPAN										
		UPA 30 MG QD	3	7.0	0.7	-6.3	0.85	-2.2	(-6.1, 1.8)	1.53	0.217
		UPA 15 MG QD	3	9.3	3.0	-4.2	0.98	-0.0	(-4.7, 4.6)	1.81	0.986
		UPA 7.5 MG QD	2	7.0	3.0	-4.0	1.04	0.2	(-4.0, 4.4)	1.64	0.917
		PLACEBO	2	3.5	2.5	-4.2	1.27				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.752

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 16											
	ALL										
		UPA 30 MG QD	40	13.4	4.5	-8.6	1.11	-7.8	(-10.8, -4.8)	1.51	<0.001***
		UPA 15 MG QD	37	13.5	7.2	-6.0	1.14	-5.2	(-8.2, -2.2)	1.54	<0.001***
		UPA 7.5 MG QD	34	10.7	6.1	-5.7	1.24	-4.9	(-8.0, -1.7)	1.58	0.003**
		PLACEBO	26	14.2	12.8	-0.8	1.34				
	US/PR/CANADA										
		UPA 30 MG QD	29	14.8	5.1	-9.2	1.18	-8.4	(-12.0, -4.8)	1.79	<0.001***
		UPA 15 MG QD	27	14.9	7.6	-6.8	1.22	-6.0	(-9.6, -2.4)	1.82	0.001**
		UPA 7.5 MG QD	26	11.1	6.7	-5.8	1.27	-5.0	(-8.7, -1.3)	1.87	0.009**
		PLACEBO	22	15.0	13.7	-0.8	1.35				
	EU/AUS										
		UPA 30 MG QD	8	10.6	2.5	-8.3	1.65	-10.7	(-18.8, -2.7)	3.81	0.011*
		UPA 15 MG QD	7	10.0	4.3	-6.4	1.77	-8.9	(-17.0, -0.7)	3.89	0.035*
		UPA 7.5 MG QD	6	10.3	4.2	-6.6	1.91	-9.0	(-17.3, -0.8)	3.94	0.034*
		PLACEBO	2	16.0	14.0	2.4	3.43				
	JAPAN										
		UPA 30 MG QD	3	7.0	3.0	-4.0	1.53	-0.0	(-7.1, 7.1)	2.75	0.994
		UPA 15 MG QD	3	9.3	9.7	2.0	1.76	6.0	(-2.4, 14.4)	3.27	0.127
		UPA 7.5 MG QD	2	7.0	5.5	-1.5	1.87	2.5	(-5.1, 10.1)	2.96	0.440
		PLACEBO	2	3.5	2.0	-4.0	2.29				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.679

[A] ACROSS THE STRATA, P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, AND TREATMENT IN THE MODEL.
WITHIN EACH STRATUM, P-VALUES WERE CALCULATED FROM ANCOVA WITH BASELINE VALUE AND THE TREATMENT IN THE MODEL.
@ P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, TREATMENT, INTERACTION OF STRATUM AND TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.
Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.13.1

表 2.7.3.6-50.　二重盲検投与期の来院時別の SCORAD スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-045 試験

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 2										
All										
Placebo	262	66.032	60.027	-7.68	[-10.66, -4.69]	1.520				
UPA 15 mg QD	274	68.288	38.112	-43.05	[-45.99, -40.12]	1.495	-35.38	[-39.10, -31.66]	1.895	<0.001***
UPA 30 mg QD	268	67.185	31.925	-51.96	[-54.90, -49.02]	1.497	-44.28	[-48.02, -40.55]	1.902	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	148	59.948	53.878	-9.67	[-13.30, -6.05]	1.845				
UPA 15 mg QD	149	62.085	33.261	-45.64	[-49.25, -42.03]	1.838	-35.97	[-41.10, -30.84]	2.608	<0.001***
UPA 30 mg QD	147	60.499	27.608	-54.17	[-57.80, -50.53]	1.848	-44.49	[-49.62, -39.36]	2.610	<0.001***
vIGA-AD 4 (Severe)										
Placebo	114	73.930	68.009	-7.31	[-11.21, -3.41]	1.983				
UPA 15 mg QD	125	75.682	43.893	-41.91	[-45.63, -38.19]	1.893	-34.60	[-39.99, -29.20]	2.744	<0.001***
UPA 30 mg QD	121	75.308	37.169	-51.43	[-55.21, -47.65]	1.921	-44.12	[-49.55, -38.69]	2.762	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	120	64.075	57.045	-10.50	[-14.47, -6.52]	2.022				
UPA 15 mg QD	125	66.888	38.677	-42.37	[-46.27, -38.47]	1.983	-31.88	[-37.46, -26.30]	2.838	<0.001***
UPA 30 mg QD	121	65.081	30.365	-53.97	[-57.92, -50.01]	2.010	-43.47	[-49.08, -37.87]	2.850	<0.001***
Japan										
Placebo	11	70.655	72.709	1.89	[-9.99, 13.76]	5.870				
UPA 15 mg QD	15	63.907	35.200	-44.66	[-54.78, -34.54]	5.000	-46.55	[-62.25, -30.84]	7.763	<0.001***
UPA 30 mg QD	16	67.462	36.825	-45.96	[-55.72, -36.20]	4.823	-47.84	[-63.17, -32.51]	7.575	<0.001***
China										
Placebo	14	64.193	57.171	-10.23	[-22.01, 1.55]	5.836				
UPA 15 mg QD	14	66.644	31.194	-53.28	[-64.92, -41.64]	5.763	-43.05	[-59.54, -26.55]	8.166	<0.001***
UPA 30 mg QD	17	70.671	32.573	-52.42	[-63.08, -41.75]	5.281	-42.19	[-58.27, -26.11]	7.967	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 2 (Cont.)										
Other										
Placebo	117	67.824	62.235	-7.48	[-11.51, -3.46]	2.045				
UPA 15 mg QD	120	70.486	38.693	-44.59	[-48.57, -40.62]	2.019	-37.11	[-42.77, -31.45]	2.878	<0.001***
UPA 30 mg QD	114	68.859	32.795	-52.54	[-56.61, -48.47]	2.068	-45.06	[-50.78, -39.34]	2.908	<0.001***
Adolescent										
Placebo	38	65.792	63.733	-2.93	[-9.78, 3.92]	3.460				
UPA 15 mg QD	41	70.006	40.760	-40.97	[-47.56, -34.39]	3.326	-38.04	[-47.59, -28.50]	4.820	<0.001***
UPA 30 mg QD	42	68.592	30.874	-56.12	[-62.61, -49.64]	3.276	-53.19	[-62.64, -43.75]	4.770	<0.001***
Adult										
Placebo	224	66.073	59.398	-9.46	[-12.36, -6.56]	1.477				
UPA 15 mg QD	233	67.986	37.645	-44.61	[-47.45, -41.77]	1.448	-35.15	[-39.21, -31.08]	2.070	<0.001***
UPA 30 mg QD	226	66.924	32.120	-52.24	[-55.12, -49.36]	1.468	-42.78	[-46.87, -38.69]	2.083	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 16										
All										
Placebo	125	64.428	40.735	-32.68	[-37.26, -28.11]	2.329				
UPA 15 mg QD	239	68.272	21.728	-65.71	[-69.20, -62.23]	1.777	-33.03	[-38.44, -27.61]	2.758	<0.001***
UPA 30 mg QD	253	67.369	17.723	-73.07	[-76.47, -69.68]	1.729	-40.39	[-45.75, -35.03]	2.732	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	82	60.429	38.942	-33.07	[-38.38, -27.76]	2.701				
UPA 15 mg QD	135	62.326	18.950	-68.00	[-72.19, -63.81]	2.132	-34.93	[-41.70, -28.16]	3.443	<0.001***
UPA 30 mg QD	133	60.473	14.745	-75.53	[-79.75, -71.31]	2.145	-42.46	[-49.24, -35.68]	3.448	<0.001***
vIGA-AD 4 (Severe)										
Placebo	43	72.053	44.152	-36.00	[-43.53, -28.48]	3.824				
UPA 15 mg QD	104	75.989	25.335	-64.62	[-69.62, -59.61]	2.542	-28.61	[-37.66, -19.57]	4.595	<0.001***
UPA 30 mg QD	120	75.012	21.023	-72.36	[-77.06, -67.65]	2.390	-36.36	[-45.23, -27.48]	4.510	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	61	62.213	40.111	-32.36	[-38.78, -25.94]	3.260				
UPA 15 mg QD	107	67.408	22.732	-64.73	[-69.67, -59.79]	2.510	-32.37	[-40.48, -24.26]	4.122	<0.001***
UPA 30 mg QD	115	65.335	15.691	-76.81	[-81.59, -72.03]	2.427	-44.45	[-52.44, -36.45]	4.064	<0.001***
Japan										
Placebo	1	41.700	23.400	-34.10	[-80.60, 12.41]	22.628				
UPA 15 mg QD	13	62.746	24.208	-59.84	[-72.76, -46.91]	6.288	-25.74	[-73.84, 22.37]	23.403	0.282
UPA 30 mg QD	14	69.586	28.243	-59.87	[-72.30, -47.43]	6.048	-25.77	[-73.99, 22.45]	23.481	0.282
China										
Placebo	7	65.157	39.957	-38.35	[-57.97, -18.73]	9.671				
UPA 15 mg QD	14	66.644	20.363	-69.95	[-84.06, -55.85]	6.938	-31.60	[-55.71, -7.49]	11.882	0.012*
UPA 30 mg QD	16	70.931	20.313	-70.72	[-83.97, -57.47]	6.524	-32.37	[-56.14, -8.60]	11.722	0.009**

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference --- Compared to Placebo --- LS Mean	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 16 (Cont.)										
Other										
Placebo	56	67.155	41.821	-34.96	[-41.36, -28.57]	3.248				
UPA 15 mg QD	105	70.053	20.581	-69.38	[-74.12, -64.64]	2.408	-34.41	[-42.38, -26.45]	4.046	<0.001***
UPA 30 mg QD	108	68.719	18.139	-73.04	[-77.73, -68.36]	2.379	-38.08	[-46.00, -30.15]	4.026	<0.001***
Adolescent										
Placebo	17	62.094	41.112	-30.99	[-42.03, -19.96]	5.566				
UPA 15 mg QD	37	70.450	25.569	-63.38	[-71.18, -55.58]	3.931	-32.39	[-45.95, -18.82]	6.842	<0.001***
UPA 30 mg QD	40	68.327	16.725	-77.29	[-84.81, -69.77]	3.786	-46.29	[-59.65, -32.93]	6.736	<0.001***
Adult										
Placebo	108	64.795	40.675	-34.15	[-38.90, -29.40]	2.418				
UPA 15 mg QD	202	67.873	21.025	-67.48	[-71.01, -63.96]	1.796	-33.33	[-39.25, -27.41]	3.014	<0.001***
UPA 30 mg QD	213	67.189	17.910	-73.31	[-76.75, -69.86]	1.753	-39.16	[-45.03, -33.29]	2.987	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Objective SCORAD										
Week 2										
All										
Placebo	271	51.831	47.345	-7.32	[-10.50, -4.14]	1.622				
UPA 15 mg QD	275	54.298	31.704	-40.26	[-43.43, -37.08]	1.617	-32.94	[-36.95, -28.92]	2.047	<0.001***
UPA 30 mg QD	278	53.031	27.009	-48.15	[-51.29, -45.01]	1.600	-40.83	[-44.83, -36.84]	2.036	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	152	46.247	41.866	-9.12	[-13.09, -5.16]	2.019				
UPA 15 mg QD	150	48.645	27.233	-42.97	[-46.97, -38.98]	2.032	-33.85	[-39.49, -28.21]	2.871	<0.001***
UPA 30 mg QD	151	46.919	23.246	-49.95	[-53.92, -45.97]	2.022	-40.82	[-46.43, -35.21]	2.855	<0.001***
vIGA-AD 4 (Severe)										
Placebo	119	58.964	54.343	-7.39	[-11.45, -3.34]	2.063				
UPA 15 mg QD	125	61.082	37.069	-39.12	[-43.07, -35.17]	2.009	-31.73	[-37.40, -26.06]	2.883	<0.001***
UPA 30 mg QD	127	60.298	31.482	-48.27	[-52.19, -44.35]	1.992	-40.88	[-46.52, -35.24]	2.868	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Objective SCORAD										
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	122	50.360	45.437	-9.39	[-13.64, -5.13]	2.164				
UPA 15 mg QD	126	52.731	32.046	-39.05	[-43.25, -34.86]	2.132	-29.67	[-35.65, -23.68]	3.042	<0.001***
UPA 30 mg QD	127	50.704	26.153	-48.86	[-53.03, -44.69]	2.119	-39.47	[-45.42, -33.52]	3.027	<0.001***
Japan										
Placebo	12	54.350	57.892	5.45	[-5.65, 16.55]	5.489				
UPA 15 mg QD	15	51.440	27.800	-46.34	[-56.26, -36.42]	4.908	-51.79	[-66.70, -36.88]	7.376	<0.001***
UPA 30 mg QD	16	53.900	30.888	-43.81	[-53.41, -34.20]	4.751	-49.26	[-63.91, -34.60]	7.248	<0.001***
China										
Placebo	14	49.979	44.743	-9.17	[-23.00, 4.67]	6.853				
UPA 15 mg QD	14	52.144	23.623	-55.38	[-69.07, -41.70]	6.776	-46.22	[-65.61, -26.83]	9.601	<0.001***
UPA 30 mg QD	17	55.612	26.632	-49.63	[-62.16, -37.11]	6.203	-40.46	[-59.33, -21.60]	9.344	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Objective SCORAD										
Week 2 (Cont.)										
Other										
Placebo	123	53.257	48.504	-8.52	[-12.81, -4.23]	2.179				
UPA 15 mg QD	120	56.553	32.776	-41.50	[-45.83, -37.16]	2.203	-32.97	[-39.08, -26.87]	3.107	<0.001***
UPA 30 mg QD	118	55.046	27.459	-49.80	[-54.16, -45.44]	2.218	-41.28	[-47.39, -35.16]	3.110	<0.001***
Adolescent										
Placebo	39	52.733	50.771	-3.84	[-11.03, 3.35]	3.632				
UPA 15 mg QD	41	56.469	34.639	-37.56	[-44.58, -30.54]	3.546	-33.72	[-43.81, -23.64]	5.094	<0.001***
UPA 30 mg QD	42	54.307	26.112	-53.12	[-60.04, -46.21]	3.491	-49.29	[-59.26, -39.31]	5.038	<0.001***
Adult										
Placebo	232	51.680	46.769	-8.90	[-12.01, -5.79]	1.585				
UPA 15 mg QD	234	53.918	31.190	-42.08	[-45.18, -38.98]	1.578	-33.18	[-37.57, -28.78]	2.239	<0.001***
UPA 30 mg QD	236	52.804	27.169	-48.36	[-51.44, -45.27]	1.570	-39.45	[-43.83, -35.07]	2.231	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Objective SCORAD										
Week 16										
All										
Placebo	132	50.317	31.440	-33.27	[-37.99, -28.55]	2.404				
UPA 15 mg QD	245	54.401	17.451	-65.25	[-68.89, -61.62]	1.851	-31.98	[-37.58, -26.39]	2.850	<0.001***
UPA 30 mg QD	259	53.126	14.348	-72.26	[-75.79, -68.72]	1.800	-38.99	[-44.53, -33.45]	2.820	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	88	46.658	29.290	-34.79	[-40.33, -29.24]	2.820				
UPA 15 mg QD	138	48.927	14.879	-67.46	[-71.93, -62.99]	2.271	-32.67	[-39.80, -25.54]	3.625	<0.001***
UPA 30 mg QD	137	46.830	11.956	-74.55	[-79.03, -70.08]	2.275	-39.76	[-46.88, -32.64]	3.621	<0.001***
vIGA-AD 4 (Severe)										
Placebo	44	57.634	35.740	-34.59	[-42.27, -26.92]	3.898				
UPA 15 mg QD	107	61.461	20.768	-64.51	[-69.57, -59.46]	2.569	-29.92	[-39.12, -20.72]	4.674	<0.001***
UPA 30 mg QD	122	60.196	17.033	-71.90	[-76.66, -67.14]	2.419	-37.31	[-46.34, -28.28]	4.588	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Objective SCORAD										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	62	47.850	31.172	-31.35	[-38.16, -24.55]	3.458				
UPA 15 mg QD	110	53.141	18.367	-63.75	[-68.94, -58.56]	2.637	-32.40	[-40.97, -23.82]	4.359	<0.001***
UPA 30 mg QD	119	50.887	13.283	-74.73	[-79.72, -69.74]	2.536	-43.38	[-51.81, -34.94]	4.286	<0.001***
Japan										
Placebo	1	30.700	16.400	-37.98	[-86.53, 10.57]	23.619				
UPA 15 mg QD	13	50.054	18.900	-61.46	[-74.56, -48.36]	6.366	-23.48	[-73.61, 26.66]	24.380	0.345
UPA 30 mg QD	14	55.371	22.743	-59.65	[-72.28, -47.03]	6.134	-21.67	[-71.97, 28.63]	24.483	0.384
China										
Placebo	7	50.729	29.814	-41.05	[-61.40, -20.69]	10.030				
UPA 15 mg QD	14	52.144	14.934	-72.24	[-86.83, -57.65]	7.175	-31.19	[-56.18, -6.20]	12.308	0.016*
UPA 30 mg QD	16	55.869	15.125	-71.58	[-85.31, -57.86]	6.758	-30.53	[-55.21, -5.86]	12.162	0.017*

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Objective SCORAD										
Week 16 (Cont.)										
Other										
Placebo	62	53.053	32.134	-36.92	[-43.35, -30.49]	3.269				
UPA 15 mg QD	108	56.500	16.670	-69.00	[-73.92, -64.07]	2.500	-32.08	[-40.19, -23.96]	4.121	<0.001***
UPA 30 mg QD	110	54.863	14.317	-73.24	[-78.12, -68.37]	2.477	-36.32	[-44.39, -28.25]	4.101	<0.001***
Adolescent										
Placebo	18	48.950	32.744	-31.71	[-43.04, -20.38]	5.712				
UPA 15 mg QD	38	56.254	21.199	-61.87	[-69.83, -53.92]	4.006	-30.17	[-44.07, -16.26]	7.008	<0.001***
UPA 30 mg QD	40	54.027	13.275	-77.14	[-84.88, -69.39]	3.902	-45.43	[-59.15, -31.71]	6.915	<0.001***
Adult										
Placebo	114	50.532	31.234	-34.80	[-39.70, -29.90]	2.495				
UPA 15 mg QD	207	54.061	16.763	-67.34	[-71.02, -63.66]	1.874	-32.55	[-38.68, -26.41]	3.124	<0.001***
UPA 30 mg QD	219	52.961	14.543	-72.40	[-75.98, -68.82]	1.823	-37.61	[-43.68, -31.53]	3.091	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Itch										
Week 2										
All										
Placebo	264	7.7	6.9	-5.91	[-10.72, -1.10]	2.451				
UPA 15 mg QD	274	7.7	3.5	-53.88	[-58.60, -49.16]	2.405	-47.97	[-53.92, -42.03]	3.028	<0.001***
UPA 30 mg QD	274	7.8	2.7	-63.87	[-68.57, -59.16]	2.398	-57.96	[-63.91, -52.02]	3.029	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	148	7.5	6.7	-5.99	[-12.04, 0.07]	3.083				
UPA 15 mg QD	149	7.5	3.4	-55.06	[-61.08, -49.03]	3.067	-49.07	[-57.61, -40.52]	4.348	<0.001***
UPA 30 mg QD	148	7.6	2.5	-64.68	[-70.73, -58.63]	3.077	-58.70	[-67.26, -50.13]	4.356	<0.001***
vIGA-AD 4 (Severe)										
Placebo	116	7.9	7.2	-6.90	[-12.70, -1.10]	2.949				
UPA 15 mg QD	125	7.8	3.7	-53.41	[-59.00, -47.83]	2.841	-46.52	[-54.57, -38.46]	4.095	<0.001***
UPA 30 mg QD	126	8.0	2.9	-63.94	[-69.50, -58.37]	2.829	-57.04	[-65.08, -49.00]	4.087	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Itch										
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	121	7.5	6.6	-7.94	[-15.00, -0.89]	3.587				
UPA 15 mg QD	125	7.8	3.8	-51.47	[-58.40, -44.55]	3.523	-43.53	[-53.42, -33.65]	5.026	<0.001***
UPA 30 mg QD	122	7.9	2.5	-67.23	[-74.23, -60.22]	3.562	-59.28	[-69.25, -49.32]	5.067	<0.001***
Japan										
Placebo	11	8.6	8.2	-1.13	[-18.36, 16.10]	8.513				
UPA 15 mg QD	15	7.6	3.9	-46.25	[-60.58, -31.93]	7.075	-45.12	[-67.79, -22.45]	11.202	<0.001***
UPA 30 mg QD	16	7.7	3.3	-55.34	[-69.17, -41.51]	6.832	-54.21	[-76.48, -31.94]	11.002	<0.001***
China										
Placebo	14	7.1	6.9	-1.70	[-18.12, 14.72]	8.133				
UPA 15 mg QD	14	8.0	4.6	-42.48	[-58.42, -26.54]	7.891	-40.78	[-63.85, -17.72]	11.422	0.001**
UPA 30 mg QD	17	8.1	3.3	-59.45	[-73.95, -44.95]	7.179	-57.75	[-79.90, -35.59]	10.974	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Itch										
Week 2 (Cont.)										
Other										
Placebo	118	7.8	7.1	-6.23	[-11.90, -0.57]	2.882				
UPA 15 mg QD	120	7.5	3.1	-59.82	[-65.42, -54.23]	2.845	-53.59	[-61.56, -45.61]	4.055	<0.001***
UPA 30 mg QD	119	7.6	2.8	-62.93	[-68.55, -57.31]	2.859	-56.70	[-64.68, -48.71]	4.060	<0.001***
Adolescent										
Placebo	38	6.9	6.7	-2.69	[-14.06, 8.68]	5.742				
UPA 15 mg QD	41	7.5	3.4	-54.51	[-65.16, -43.86]	5.377	-51.82	[-67.37, -36.27]	7.851	<0.001***
UPA 30 mg QD	42	8.0	2.8	-61.91	[-72.58, -51.25]	5.387	-59.22	[-75.11, -43.34]	8.023	<0.001***
Adult										
Placebo	226	7.8	7.0	-7.25	[-11.85, -2.64]	2.347				
UPA 15 mg QD	233	7.7	3.5	-54.28	[-58.81, -49.75]	2.307	-47.03	[-53.49, -40.57]	3.292	<0.001***
UPA 30 mg QD	232	7.7	2.7	-64.57	[-69.11, -60.03]	2.312	-57.33	[-63.80, -50.86]	3.294	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Itch										
Week 16										
All										
Placebo	125	7.6	5.1	-27.77	[-34.50, -21.04]	3.428				
UPA 15 mg QD	239	7.6	2.5	-64.56	[-69.87, -59.25]	2.703	-36.79	[-44.74, -28.84]	4.048	<0.001***
UPA 30 mg QD	255	7.8	2.0	-73.01	[-78.19, -67.82]	2.641	-45.24	[-53.12, -37.36]	4.014	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	82	7.5	5.2	-24.99	[-33.10, -16.87]	4.129				
UPA 15 mg QD	135	7.4	2.5	-66.04	[-72.71, -59.37]	3.392	-41.06	[-51.56, -30.55]	5.344	<0.001***
UPA 30 mg QD	134	7.6	1.9	-72.72	[-79.41, -66.02]	3.405	-47.73	[-58.25, -37.21]	5.352	<0.001***
vIGA-AD 4 (Severe)										
Placebo	43	7.9	4.8	-34.59	[-44.92, -24.27]	5.247				
UPA 15 mg QD	104	7.9	2.6	-63.89	[-70.84, -56.94]	3.531	-29.29	[-41.74, -16.85]	6.325	<0.001***
UPA 30 mg QD	121	8.0	2.1	-74.17	[-80.70, -67.65]	3.314	-39.58	[-51.80, -27.37]	6.206	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Itch										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	61	7.7	5.1	-27.11	[-36.63, -17.58]	4.843				
UPA 15 mg QD	107	7.7	2.5	-64.36	[-72.03, -56.70]	3.895	-37.26	[-49.48, -25.03]	6.214	<0.001***
UPA 30 mg QD	115	8.0	1.6	-77.95	[-85.44, -70.45]	3.808	-50.84	[-62.97, -38.71]	6.167	<0.001***
Japan										
Placebo	1	8.0	6.0	-9.55	[-90.31, 71.21]	39.196				
UPA 15 mg QD	13	7.7	3.2	-60.23	[-82.77, -37.68]	10.947	-50.68	[-134.52, 33.16]	40.708	0.225
UPA 30 mg QD	14	7.8	3.0	-58.18	[-79.89, -36.47]	10.541	-48.63	[-132.24, 34.98]	40.594	0.242
China										
Placebo	7	7.4	5.3	-31.64	[-56.79, -6.49]	12.414				
UPA 15 mg QD	14	8.0	3.4	-57.28	[-75.79, -38.76]	9.102	-25.63	[-56.94, 5.67]	15.445	0.106
UPA 30 mg QD	16	8.1	2.4	-70.91	[-88.16, -53.66]	8.487	-39.27	[-69.89, -8.65]	15.110	0.013*

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Itch										
Week 16 (Cont.)										
Other										
Placebo	56	7.6	5.0	-30.59	[-39.61, -21.57]	4.582				
UPA 15 mg QD	105	7.5	2.4	-67.07	[-73.85, -60.29]	3.443	-36.48	[-47.77, -25.20]	5.733	<0.001***
UPA 30 mg QD	110	7.6	2.1	-70.93	[-77.58, -64.28]	3.378	-40.34	[-51.54, -29.13]	5.693	<0.001***
Adolescent										
Placebo	17	6.9	4.2	-34.33	[-52.16, -16.50]	8.994				
UPA 15 mg QD	37	7.6	2.9	-63.44	[-76.30, -50.58]	6.472	-29.11	[-51.08, -7.15]	11.075	0.010**
UPA 30 mg QD	40	8.1	2.0	-72.61	[-85.19, -60.02]	6.336	-38.28	[-60.31, -16.25]	11.110	0.001**
Adult										
Placebo	108	7.8	5.2	-27.51	[-34.31, -20.72]	3.459				
UPA 15 mg QD	202	7.6	2.5	-65.33	[-70.55, -60.10]	2.660	-37.81	[-46.39, -29.24]	4.365	<0.001***
UPA 30 mg QD	215	7.8	2.0	-73.43	[-78.53, -68.33]	2.597	-45.92	[-54.41, -37.42]	4.326	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Sleep										
Week 2										
All										
Placebo	260	6.6	5.8	-2.23	[-9.79, 5.32]	3.849				
UPA 15 mg QD	273	6.3	3.0	-46.75	[-54.14, -39.36]	3.764	-44.52	[-53.96, -35.08]	4.808	<0.001***
UPA 30 mg QD	273	6.4	2.2	-64.60	[-71.96, -57.23]	3.753	-62.36	[-71.80, -52.93]	4.806	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	147	6.3	5.2	-5.73	[-16.17, 4.70]	5.309				
UPA 15 mg QD	149	6.0	2.8	-43.55	[-53.90, -33.20]	5.266	-37.82	[-52.52, -23.12]	7.480	<0.001***
UPA 30 mg QD	147	6.0	1.9	-65.86	[-76.27, -55.45]	5.296	-60.13	[-74.87, -45.39]	7.501	<0.001***
vIGA-AD 4 (Severe)										
Placebo	113	7.0	6.6	-0.42	[-8.08, 7.25]	3.897				
UPA 15 mg QD	124	6.8	3.1	-53.57	[-60.90, -46.25]	3.723	-53.16	[-63.76, -42.55]	5.391	<0.001***
UPA 30 mg QD	126	7.0	2.5	-66.36	[-73.63, -59.10]	3.693	-65.95	[-76.50, -55.39]	5.369	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Sleep										
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	119	6.5	5.3	-16.50	[-24.18, -8.83]	3.902				
UPA 15 mg QD	125	6.4	3.0	-50.97	[-58.47, -43.46]	3.816	-34.46	[-45.20, -23.73]	5.459	<0.001***
UPA 30 mg QD	122	6.4	1.8	-72.07	[-79.65, -64.49]	3.854	-55.57	[-66.35, -44.78]	5.485	<0.001***
Japan										
Placebo	11	7.0	6.8	30.54	[-13.62, 74.70]	21.820				
UPA 15 mg QD	15	4.9	3.5	-33.11	[-70.65, 4.43]	18.543	-63.65	[-122.63, -4.68]	29.153	0.035*
UPA 30 mg QD	16	5.9	2.6	-50.42	[-86.25, -14.59]	17.687	-80.96	[-137.67, -24.24]	28.008	0.006**
China										
Placebo	14	7.1	5.5	-20.99	[-39.76, -2.21]	9.295				
UPA 15 mg QD	14	6.5	3.0	-48.86	[-67.66, -30.05]	9.311	-27.87	[-54.50, -1.24]	13.183	0.041*
UPA 30 mg QD	17	7.0	2.6	-58.04	[-75.07, -41.01]	8.430	-37.05	[-62.37, -11.73]	12.534	0.005**

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Sleep										
Week 2 (Cont.)										
Other										
Placebo	116	6.6	6.3	8.50	[-3.33, 20.32]	6.014				
UPA 15 mg QD	119	6.5	2.8	-46.61	[-58.27, -34.96]	5.926	-55.11	[-71.71, -38.50]	8.443	<0.001***
UPA 30 mg QD	118	6.5	2.5	-62.81	[-74.52, -51.10]	5.956	-71.31	[-87.95, -54.66]	8.464	<0.001***
Adolescent										
Placebo	38	5.9	5.8	16.71	[-5.65, 39.06]	11.288				
UPA 15 mg QD	41	6.0	2.7	-45.43	[-66.94, -23.92]	10.860	-62.14	[-93.15, -31.13]	15.658	<0.001***
UPA 30 mg QD	42	6.3	2.0	-67.20	[-88.46, -45.94]	10.735	-83.91	[-114.78, -53.03]	15.588	<0.001***
Adult										
Placebo	222	6.7	5.8	-7.28	[-14.20, -0.35]	3.527				
UPA 15 mg QD	232	6.4	3.0	-48.63	[-55.40, -41.86]	3.448	-41.35	[-51.04, -31.66]	4.933	<0.001***
UPA 30 mg QD	231	6.5	2.2	-65.67	[-72.45, -58.89]	3.454	-58.39	[-68.08, -48.70]	4.937	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Sleep										
Week 16										
All										
Placebo	125	6.3	3.9	-22.31	[-31.74, -12.88]	4.803				
UPA 15 mg QD	239	6.4	1.6	-70.70	[-78.15, -63.25]	3.796	-48.39	[-59.40, -37.38]	5.608	<0.001***
UPA 30 mg QD	254	6.4	1.4	-72.74	[-80.03, -65.45]	3.713	-50.43	[-61.35, -39.51]	5.563	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	82	6.1	3.9	-16.90	[-29.30, -4.51]	6.304				
UPA 15 mg QD	135	5.9	1.5	-70.78	[-80.92, -60.64]	5.158	-53.88	[-69.89, -37.86]	8.147	<0.001***
UPA 30 mg QD	133	6.0	1.1	-74.87	[-85.07, -64.66]	5.191	-57.96	[-74.02, -41.90]	8.167	<0.001***
vIGA-AD 4 (Severe)										
Placebo	43	6.6	3.8	-36.83	[-48.37, -25.29]	5.861				
UPA 15 mg QD	104	6.9	1.6	-73.93	[-81.66, -66.20]	3.926	-37.10	[-50.99, -23.22]	7.054	<0.001***
UPA 30 mg QD	121	6.9	1.8	-73.59	[-80.83, -66.34]	3.679	-36.76	[-50.38, -23.13]	6.921	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Sleep										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	61	6.4	3.8	-31.79	[-43.36, -20.23]	5.878				
UPA 15 mg QD	107	6.4	1.7	-66.51	[-75.74, -57.29]	4.687	-34.72	[-49.51, -19.93]	7.518	<0.001***
UPA 30 mg QD	114	6.4	1.0	-82.09	[-91.11, -73.07]	4.584	-50.30	[-64.96, -35.63]	7.454	<0.001***
Japan										
Placebo	1	3.0	1.0	-61.36	[-172.28, 49.56]	53.825				
UPA 15 mg QD	13	5.0	2.2	-70.74	[-104.69, -36.80]	16.132	-9.39	[-124.66, 105.89]	55.920	0.868
UPA 30 mg QD	14	6.4	2.5	-53.33	[-85.69, -20.96]	15.398	8.03	[-107.45, 123.52]	56.104	0.887
China										
Placebo	7	7.0	4.9	-33.78	[-64.51, -3.05]	15.176				
UPA 15 mg QD	14	6.5	2.0	-65.98	[-89.41, -42.54]	11.498	-32.20	[-70.85, 6.45]	19.056	0.100
UPA 30 mg QD	16	7.0	2.8	-64.14	[-85.84, -42.43]	10.659	-30.36	[-67.94, 7.23]	18.537	0.110

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Sleep										
Week 16 (Cont.)										
Other										
Placebo	56	6.1	3.9	-15.48	[-29.67, -1.29]	7.212				
UPA 15 mg QD	105	6.5	1.3	-77.62	[-88.44, -66.80]	5.497	-62.14	[-79.98, -44.29]	9.069	<0.001***
UPA 30 mg QD	110	6.3	1.5	-70.04	[-80.67, -59.40]	5.404	-54.55	[-72.29, -36.82]	9.010	<0.001***
Adolescent										
Placebo	17	5.9	3.5	-19.71	[-45.44, 6.02]	13.012				
UPA 15 mg QD	37	6.2	1.5	-71.90	[-92.93, -50.86]	10.615	-52.19	[-85.41, -18.97]	16.789	0.002**
UPA 30 mg QD	40	6.3	1.5	-75.61	[-96.20, -55.01]	10.388	-55.90	[-88.87, -22.93]	16.660	0.001**
Adult										
Placebo	108	6.3	3.9	-25.71	[-34.84, -16.58]	4.649				
UPA 15 mg QD	202	6.4	1.6	-72.28	[-79.15, -65.41]	3.498	-46.57	[-58.00, -35.15]	5.818	<0.001***
UPA 30 mg QD	214	6.4	1.4	-73.89	[-80.59, -67.18]	3.411	-48.18	[-59.50, -36.85]	5.766	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　8.4.1

表 2.7.3.6-51. 二重盲検投与期の来院時別の SCORAD 50 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo	281	7 (2.5) [0.7, 4.3]	0					
UPA 15 mg QD	281	112 (39.9) [34.1, 45.6]	0	37.4	37.4	[31.4, 43.3]	<0.001***	0.792
UPA 30 mg QD	285	152 (53.3) [47.5, 59.1]	0	50.8	50.9	[44.8, 56.9]	<0.001***	0.506
vIGA-AD 3 (Moderate)								
Placebo	156	5 (3.2) [0.4, 6.0]	0					
UPA 15 mg QD	154	67 (43.5) [35.7, 51.3]	0	40.3		[32.0, 48.6]	<0.001***	
UPA 30 mg QD	154	86 (55.8) [48.0, 63.7]	0	52.6		[44.3, 61.0]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	125	2 (1.6) [0.0, 3.8]	0					
UPA 15 mg QD	127	45 (35.4) [27.1, 43.8]	0	33.8		[25.2, 42.4]	<0.001***	
UPA 30 mg QD	131	66 (50.4) [41.8, 58.9]	0	48.8		[39.9, 57.6]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo	128	5 (3.9) [0.5, 7.3]	0					
UPA 15 mg QD	128	47 (36.7) [28.4, 45.1]	0	32.8		[23.8, 41.8]	<0.001***	
UPA 30 mg QD	129	72 (55.8) [47.2, 64.4]	0	51.9		[42.7, 61.1]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	15	6 (40.0) [15.2, 64.8]	0	40.0		[15.2, 64.8]	0.002**	
UPA 30 mg QD	16	7 (43.8) [19.4, 68.1]	0	43.8		[19.4, 68.1]	<0.001***	
China								
Placebo	14	0	0					
UPA 15 mg QD	14	8 (57.1) [31.2, 83.1]	0	57.1		[31.2, 83.1]	<0.001***	
UPA 30 mg QD	17	11 (64.7) [42.0, 87.4]	0	64.7		[42.0, 87.4]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo	125	2 (1.6) [0.0, 3.8]	0					
UPA 15 mg QD	124	51 (41.1) [32.5, 49.8]	0	39.5		[30.6, 48.5]	<0.001***	
UPA 30 mg QD	123	62 (50.4) [41.6, 59.2]	0	48.8		[39.7, 57.9]	<0.001***	
Adolescent								
Placebo	40	0	0					
UPA 15 mg QD	42	15 (35.7) [21.2, 50.2]	0	35.7		[21.2, 50.2]	<0.001***	
UPA 30 mg QD	42	26 (61.9) [47.2, 76.6]	0	61.9		[47.2, 76.6]	<0.001***	
Adult								
Placebo	241	7 (2.9) [0.8, 5.0]	0					
UPA 15 mg QD	239	97 (40.6) [34.4, 46.8]	0	37.7		[31.1, 44.3]	<0.001***	
UPA 30 mg QD	243	126 (51.9) [45.6, 58.1]	0	48.9		[42.3, 55.6]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	281	42 (14.9) [10.7, 19.1]	4					
UPA 15 mg QD	281	186 (66.0) [60.5, 71.6]	1	51.1	51.1	[44.3, 58.0]	<0.001***	0.194
UPA 30 mg QD	285	219 (76.7) [71.8, 81.7]	2	61.8	61.8	[55.4, 68.2]	<0.001***	0.102
vIGA-AD 3 (Moderate)								
Placebo	156	28 (17.8) [11.8, 23.9]	3					
UPA 15 mg QD	154	106 (68.8) [61.5, 76.1]	0	51.0		[41.5, 60.5]	<0.001***	
UPA 30 mg QD	154	117 (75.8) [69.0, 82.6]	1	58.0		[48.9, 67.1]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	125	14 (11.3) [5.7, 16.9]	1					
UPA 15 mg QD	127	80 (62.7) [54.2, 71.1]	1	51.3		[41.2, 61.5]	<0.001***	
UPA 30 mg QD	131	102 (77.8) [70.7, 85.0]	1	66.5		[57.5, 75.6]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	128	19 (15.1) [8.8, 21.3]	1					
UPA 15 mg QD	128	82 (64.1) [55.8, 72.4]	0	49.0		[38.6, 59.4]	<0.001***	
UPA 30 mg QD	129	101 (78.3) [71.2, 85.4]	0	63.2		[53.8, 72.7]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	15	9 (60.0) [35.2, 84.8]	0	60.0		[35.2, 84.8]	<0.001***	
UPA 30 mg QD	16	10 (62.5) [38.8, 86.2]	0	62.5		[38.8, 86.2]	<0.001***	
China								
Placebo	14	2 (14.3) [0.0, 32.6]	0					
UPA 15 mg QD	14	11 (78.6) [57.1, 100.0]	0	64.3		[36.0, 92.5]	<0.001***	
UPA 30 mg QD	17	12 (70.6) [48.9, 92.2]	0	56.3		[27.9, 84.7]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	125	21 (16.5) [9.9, 23.1]	3					
UPA 15 mg QD	124	84 (67.4) [59.1, 75.7]	1	50.9		[40.3, 61.4]	<0.001***	
UPA 30 mg QD	123	96 (77.8) [70.4, 85.2]	2	61.3		[51.4, 71.2]	<0.001***	
Adolescent								
Placebo	40	4 (10.7) [0.8, 20.5]	1					
UPA 15 mg QD	42	28 (66.7) [52.4, 80.9]	0	56.0		[38.7, 73.3]	<0.001***	
UPA 30 mg QD	42	36 (85.7) [75.1, 96.3]	0	75.0		[60.6, 89.5]	<0.001***	
Adult								
Placebo	241	38 (15.6) [11.0, 20.2]	3					
UPA 15 mg QD	239	158 (65.9) [59.9, 72.0]	1	50.3		[42.7, 57.9]	<0.001***	
UPA 30 mg QD	243	183 (75.2) [69.7, 80.6]	2	59.6		[52.4, 66.7]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　8.1.1

表 2.7.3.6-52.　二重盲検投与期の来院時別の SCORAD 75 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo	281	0	0					
UPA 15 mg QD	281	24 (8.5) [5.3, 11.8]	0	8.5	8.6	[5.3, 11.8]	<0.001***	NA
UPA 30 mg QD	285	44 (15.4) [11.2, 19.6]	0	15.4	15.5	[11.3, 19.6]	<0.001***	NA
vIGA-AD 3 (Moderate)								
Placebo	156	0	0					
UPA 15 mg QD	154	13 (8.4) [4.1, 12.8]	0	8.4		[4.1, 12.8]	<0.001***	
UPA 30 mg QD	154	25 (16.2) [10.4, 22.1]	0	16.2		[10.4, 22.1]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	125	0	0					
UPA 15 mg QD	127	11 (8.7) [3.8, 13.6]	0	8.7		[3.8, 13.6]	0.001**	
UPA 30 mg QD	131	19 (14.5) [8.5, 20.5]	0	14.5		[8.5, 20.5]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo	128	0	0					
UPA 15 mg QD	128	7 (5.5) [1.5, 9.4]	0	5.5		[1.5, 9.4]	0.007**	
UPA 30 mg QD	129	21 (16.3) [9.9, 22.6]	0	16.3		[9.9, 22.6]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	15	1 (6.7) [0.0, 19.3]	0	6.7		[-6.0, 19.3]	0.301	
UPA 30 mg QD	16	0	0	0.0			NA	
China								
Placebo	14	0	0					
UPA 15 mg QD	14	2 (14.3) [0.0, 32.6]	0	14.3		[-4.0, 32.6]	0.127	
UPA 30 mg QD	17	3 (17.6) [0.0, 35.8]	0	17.6		[-0.5, 35.8]	0.056	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo	125	0	0					
UPA 15 mg QD	124	14 (11.3) [5.7, 16.9]	0	11.3		[5.7, 16.9]	<0.001***	
UPA 30 mg QD	123	20 (16.3) [9.7, 22.8]	0	16.3		[9.7, 22.8]	<0.001***	
Adolescent								
Placebo	40	0	0					
UPA 15 mg QD	42	2 (4.8) [0.0, 11.2]	0	4.8		[-1.7, 11.2]	0.147	
UPA 30 mg QD	42	7 (16.7) [5.4, 27.9]	0	16.7		[5.4, 27.9]	0.004**	
Adult								
Placebo	241	0	0					
UPA 15 mg QD	239	22 (9.2) [5.5, 12.9]	0	9.2		[5.5, 12.9]	<0.001***	
UPA 30 mg QD	243	37 (15.2) [10.7, 19.7]	0	15.2		[10.7, 19.7]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	281	11 (4.0) [1.7, 6.3]	4					
UPA 15 mg QD	281	107 (38.1) [32.4, 43.8]	1	34.1	34.2	[28.1, 40.3]	<0.001***	0.520
UPA 30 mg QD	285	140 (49.1) [43.3, 54.9]	2	45.1	45.1	[38.8, 51.3]	<0.001***	0.404
vIGA-AD 3 (Moderate)								
Placebo	156	5 (3.3) [0.4, 6.2]	3					
UPA 15 mg QD	154	62 (40.3) [32.5, 48.0]	0	36.9		[28.7, 45.2]	<0.001***	
UPA 30 mg QD	154	73 (47.6) [39.7, 55.5]	1	44.3		[35.9, 52.7]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	125	6 (4.8) [1.1, 8.5]	1					
UPA 15 mg QD	127	45 (35.5) [27.2, 43.8]	1	30.7		[21.6, 39.9]	<0.001***	
UPA 30 mg QD	131	67 (50.9) [42.3, 59.5]	1	46.1		[36.7, 55.4]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	128	5 (4.0) [0.6, 7.4]	1					
UPA 15 mg QD	128	43 (33.6) [25.4, 41.8]	0	29.6		[20.8, 38.5]	<0.001***	
UPA 30 mg QD	129	71 (55.0) [46.5, 63.6]	0	51.1		[41.8, 60.3]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	15	4 (26.7) [4.3, 49.0]	0	26.7		[4.3, 49.0]	0.020*	
UPA 30 mg QD	16	4 (25.0) [3.8, 46.2]	0	25.0		[3.8, 46.2]	0.021*	
China								
Placebo	14	1 (7.1) [0.0, 20.6]	0					
UPA 15 mg QD	14	7 (50.0) [23.8, 76.2]	0	42.9		[13.4, 72.3]	0.004**	
UPA 30 mg QD	17	7 (41.2) [17.8, 64.6]	0	34.0		[7.0, 61.0]	0.014*	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	125	5 (4.1) [0.6, 7.6]	3					
UPA 15 mg QD	124	53 (42.8) [34.1, 51.5]	1		38.7	[29.3, 48.1]	<0.001***	
UPA 30 mg QD	123	58 (47.1) [38.2, 56.0]	2		43.0	[33.5, 52.6]	<0.001***	
Adolescent								
Placebo	40	0 (<0.1) [-1.2, 1.4]	1					
UPA 15 mg QD	42	13 (31.0) [17.0, 44.9]	0		30.9	[16.8, 44.9]	<0.001***	
UPA 30 mg QD	42	25 (59.5) [44.7, 74.4]	0		59.4	[44.5, 74.3]	<0.001***	
Adult								
Placebo	241	11 (4.6) [1.9, 7.3]	3					
UPA 15 mg QD	239	94 (39.4) [33.2, 45.6]	1		34.8	[28.0, 41.5]	<0.001***	
UPA 30 mg QD	243	115 (47.3) [41.0, 53.6]	2		42.7	[35.8, 49.5]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　8.2.1

表 2.7.3.6-53.　二重盲検投与期の来院時別の SCORAD 90 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo	281	0	0					
UPA 15 mg QD	281	2 (0.7) [0.0, 1.7]	0	0.7	0.7	[-0.3, 1.7]	0.154	NA
UPA 30 mg QD	285	9 (3.2) [1.1, 5.2]	0	3.2	3.2	[1.2, 5.2]	0.002**	NA
vIGA-AD 3 (Moderate)								
Placebo	156	0	0					
UPA 15 mg QD	154	2 (1.3) [0.0, 3.1]	0	1.3		[-0.5, 3.1]	0.155	
UPA 30 mg QD	154	8 (5.2) [1.7, 8.7]	0	5.2		[1.7, 8.7]	0.004**	
vIGA-AD 4 (Severe)								
Placebo	125	0	0					
UPA 15 mg QD	127	0	0	0.0			NA	
UPA 30 mg QD	131	1 (0.8) [0.0, 2.3]	0	0.8		[-0.7, 2.3]	0.315	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo	128	0	0					
UPA 15 mg QD	128	1 (0.8) [0.0, 2.3]	0	0.8		[-0.7, 2.3]	0.315	
UPA 30 mg QD	129	5 (3.9) [0.5, 7.2]	0	3.9		[0.5, 7.2]	0.023*	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	15	1 (6.7) [0.0, 19.3]	0	6.7		[-6.0, 19.3]	0.301	
UPA 30 mg QD	16	0	0	0.0			NA	
China								
Placebo	14	0	0					
UPA 15 mg QD	14	0	0	0.0			NA	
UPA 30 mg QD	17	1 (5.9) [0.0, 17.1]	0	5.9		[-5.3, 17.1]	0.303	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo	125	0	0					
UPA 15 mg QD	124	0	0	0.0			NA	
UPA 30 mg QD	123	3 (2.4) [0.0, 5.2]	0	2.4		[-0.3, 5.2]	0.080	
Adolescent								
Placebo	40	0	0					
UPA 15 mg QD	42	0	0	0.0			NA	
UPA 30 mg QD	42	2 (4.8) [0.0, 11.2]	0	4.8		[-1.7, 11.2]	0.147	
Adult								
Placebo	241	0	0					
UPA 15 mg QD	239	2 (0.8) [0.0, 2.0]	0	0.8		[-0.3, 2.0]	0.156	
UPA 30 mg QD	243	7 (2.9) [0.8, 5.0]	0	2.9		[0.8, 5.0]	0.007**	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	281	2 (0.7) [0.0, 1.8]	4					
UPA 15 mg QD	281	51 (18.2) [13.7, 22.7]	1	17.4	17.5	[12.8, 22.1]	<0.001***	0.439
UPA 30 mg QD	285	81 (28.5) [23.2, 33.7]	2	27.7	27.7	[22.4, 33.0]	<0.001***	0.406
vIGA-AD 3 (Moderate)								
Placebo	156	0 (<0.1) [0.0, 0.5]	3					
UPA 15 mg QD	154	28 (18.2) [12.1, 24.3]	0	18.1		[12.0, 24.2]	<0.001***	
UPA 30 mg QD	154	46 (29.9) [22.7, 37.1]	1	29.8		[22.6, 37.1]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	125	2 (1.6) [0.0, 3.8]	1					
UPA 15 mg QD	127	23 (18.2) [11.5, 24.9]	1	16.6		[9.5, 23.7]	<0.001***	
UPA 30 mg QD	131	35 (26.8) [19.2, 34.4]	1	25.2		[17.3, 33.1]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	128	0	1					
UPA 15 mg QD	128	21 (16.4) [10.0, 22.8]	0	16.4		[10.0, 22.8]	<0.001***	
UPA 30 mg QD	129	45 (34.9) [26.7, 43.1]	0	34.9		[26.7, 43.1]	<0.001***	
Japan								
Placebo	14	0	0					
UPA 15 mg QD	15	0	0	0.0			NA	
UPA 30 mg QD	16	2 (12.5) [0.0, 28.7]	0	12.5		[-3.7, 28.7]	0.131	
China								
Placebo	14	0	0					
UPA 15 mg QD	14	3 (21.4) [0.0, 42.9]	0	21.4		[-0.1, 42.9]	0.051	
UPA 30 mg QD	17	6 (35.3) [12.6, 58.0]	0	35.3		[12.6, 58.0]	0.002**	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	125	2 (1.7) [0.0, 3.9]	3					
UPA 15 mg QD	124	27 (21.9) [14.6, 29.1]	1	20.2		[12.6, 27.8]	<0.001***	
UPA 30 mg QD	123	28 (22.8) [15.4, 30.3]	2	21.2		[13.4, 29.0]	<0.001***	
Adolescent								
Placebo	40	0	1					
UPA 15 mg QD	42	6 (14.3) [3.7, 24.9]	0	14.3		[3.7, 24.9]	0.008**	
UPA 30 mg QD	42	14 (33.3) [19.1, 47.6]	0	33.3		[19.1, 47.6]	<0.001***	
Adult								
Placebo	241	2 (0.9) [0.0, 2.0]	3					
UPA 15 mg QD	239	45 (18.9) [13.9, 23.8]	1	18.0		[12.9, 23.1]	<0.001***	
UPA 30 mg QD	243	67 (27.6) [22.0, 33.2]	2	26.8		[21.0, 32.5]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　8.3.1

表 2.7.3.6-54. 二重盲検投与期の来院時別の SCORAD スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-047 試験

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 2										
All										
Placebo + TCS	290	68.095	55.913	-17.00	[-19.84, -14.16]	1.448				
UPA 15 mg QD + TCS	293	66.280	36.940	-43.66	[-46.49, -40.83]	1.441	-26.66	[-30.12, -23.20]	1.764	<0.001***
UPA 30 mg QD + TCS	288	67.365	33.338	-50.14	[-52.99, -47.28]	1.455	-33.13	[-36.61, -29.66]	1.769	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	134	60.231	50.576	-16.21	[-19.77, -12.66]	1.807				
UPA 15 mg QD + TCS	136	59.220	31.014	-47.20	[-50.72, -43.67]	1.794	-30.98	[-35.99, -25.98]	2.547	<0.001***
UPA 30 mg QD + TCS	135	61.221	27.668	-54.22	[-57.76, -50.67]	1.802	-38.00	[-43.02, -32.99]	2.553	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	156	74.850	60.497	-19.15	[-22.52, -15.78]	1.715				
UPA 15 mg QD + TCS	157	72.397	42.073	-41.91	[-45.27, -38.55]	1.709	-22.76	[-27.53, -18.00]	2.425	<0.001***
UPA 30 mg QD + TCS	153	72.786	38.340	-47.62	[-51.02, -44.22]	1.731	-28.47	[-33.26, -23.68]	2.438	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	105	66.529	50.842	-22.88	[-27.26, -18.51]	2.224				
UPA 15 mg QD + TCS	106	67.166	37.386	-44.88	[-49.24, -40.52]	2.214	-22.00	[-28.17, -15.82]	3.138	<0.001***
UPA 30 mg QD + TCS	102	66.221	32.784	-50.65	[-55.10, -46.20]	2.260	-27.77	[-34.01, -21.53]	3.171	<0.001***
Japan										
Placebo + TCS	18	68.108	54.908	-20.36	[-28.95, -11.77]	4.271				
UPA 15 mg QD + TCS	16	66.170	38.479	-42.10	[-51.25, -32.96]	4.548	-21.75	[-34.28, -9.21]	6.232	0.001**
UPA 30 mg QD + TCS	17	73.993	41.392	-47.25	[-56.23, -38.26]	4.471	-26.89	[-39.35, -14.43]	6.197	<0.001***
China										
Placebo + TCS	17	75.665	68.753	-8.81	[-18.85, 1.23]	4.988				
UPA 15 mg QD + TCS	17	68.304	34.102	-47.89	[-57.63, -38.14]	4.842	-39.08	[-53.18, -24.98]	7.007	<0.001***
UPA 30 mg QD + TCS	16	64.803	39.079	-41.82	[-52.07, -31.58]	5.089	-33.02	[-47.72, -18.31]	7.306	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean	Within Group: [95% CI]	Within Group: SE	Between Groups Difference: LS Mean	Between Groups Difference: [95% CI]	Between Groups Difference: SE	Between Groups Difference: P-value
Overall SCORAD Score										
Week 2 (Cont.)										
Other										
Placebo + TCS	150	68.331	58.128	-14.71	[-17.99, -11.43]	1.669				
UPA 15 mg QD + TCS	154	65.459	36.786	-43.62	[-46.86, -40.39]	1.648	-28.91	[-33.53, -24.29]	2.350	<0.001***
UPA 30 mg QD + TCS	153	67.659	32.212	-52.59	[-55.83, -49.34]	1.650	-37.87	[-42.48, -33.27]	2.345	<0.001***
Adolescent										
Placebo + TCS	37	69.714	57.348	-18.56	[-25.72, -11.40]	3.612				
UPA 15 mg QD + TCS	38	66.498	39.512	-40.80	[-47.83, -33.77]	3.549	-22.24	[-32.30, -12.18]	5.074	<0.001***
UPA 30 mg QD + TCS	36	66.944	35.414	-47.58	[-54.81, -40.35]	3.649	-29.02	[-39.21, -18.84]	5.139	<0.001***
Adult										
Placebo + TCS	253	67.858	55.703	-17.66	[-20.28, -15.04]	1.336				
UPA 15 mg QD + TCS	255	66.248	36.556	-44.80	[-47.41, -42.19]	1.331	-27.14	[-30.84, -23.43]	1.887	<0.001***
UPA 30 mg QD + TCS	252	67.425	33.041	-51.32	[-53.95, -48.70]	1.338	-33.66	[-37.37, -29.95]	1.890	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 16										
All										
Placebo + TCS	202	66.812	42.996	-33.62	[-37.34, -29.89]	1.898				
UPA 15 mg QD + TCS	274	66.229	25.112	-61.20	[-64.53, -57.86]	1.699	-27.58	[-32.16, -23.01]	2.331	<0.001***
UPA 30 mg QD + TCS	270	67.607	19.465	-70.95	[-74.32, -67.59]	1.714	-37.34	[-41.93, -32.75]	2.338	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	103	59.787	39.210	-33.23	[-38.22, -28.23]	2.542				
UPA 15 mg QD + TCS	129	59.390	20.562	-65.07	[-69.58, -60.56]	2.293	-31.85	[-38.58, -25.12]	3.423	<0.001***
UPA 30 mg QD + TCS	133	61.657	14.477	-75.70	[-80.15, -71.24]	2.267	-42.47	[-49.17, -35.77]	3.407	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	99	74.121	46.935	-35.71	[-40.41, -31.01]	2.391				
UPA 15 mg QD + TCS	145	72.314	29.160	-59.11	[-63.09, -55.13]	2.024	-23.39	[-29.56, -17.23]	3.135	<0.001***
UPA 30 mg QD + TCS	137	73.382	24.308	-67.71	[-71.79, -63.63]	2.076	-32.00	[-38.22, -25.77]	3.167	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	65.600	39.691	-37.73	[-43.39, -32.06]	2.879				
UPA 15 mg QD + TCS	104	66.682	22.279	-66.27	[-71.32, -61.21]	2.568	-28.54	[-36.13, -20.94]	3.859	<0.001***
UPA 30 mg QD + TCS	97	66.423	19.482	-71.01	[-76.24, -65.78]	2.657	-33.29	[-41.00, -25.58]	3.918	<0.001***
Japan										
Placebo + TCS	11	63.785	36.596	-39.72	[-49.46, -29.98]	4.825				
UPA 15 mg QD + TCS	15	64.648	23.124	-62.95	[-71.40, -54.50]	4.174	-23.23	[-36.01, -10.44]	6.322	0.001**
UPA 30 mg QD + TCS	16	73.978	22.195	-72.61	[-80.87, -64.34]	4.084	-32.89	[-45.81, -19.96]	6.402	<0.001***
China										
Placebo + TCS	17	75.665	53.224	-29.48	[-42.47, -16.50]	6.446				
UPA 15 mg QD + TCS	14	68.647	22.440	-66.32	[-80.13, -52.51]	6.858	-36.84	[-55.86, -17.81]	9.449	<0.001***
UPA 30 mg QD + TCS	16	64.803	24.319	-65.18	[-78.48, -51.87]	6.604	-35.69	[-54.55, -16.83]	9.368	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Overall SCORAD Score										
Week 16 (Cont.)										
Other										
Placebo + TCS	94	66.596	44.708	-31.90	[-36.99, -26.82]	2.585				
UPA 15 mg QD + TCS	141	65.824	27.678	-57.91	[-62.13, -53.68]	2.150	-26.00	[-32.61, -19.39]	3.363	<0.001***
UPA 30 mg QD + TCS	141	68.016	18.592	-73.13	[-77.35, -68.90]	2.149	-41.22	[-47.83, -34.61]	3.362	<0.001***
Adolescent										
Placebo + TCS	27	67.861	44.267	-33.73	[-42.71, -24.74]	4.526				
UPA 15 mg QD + TCS	35	67.206	27.455	-58.08	[-66.05, -50.11]	4.013	-24.35	[-36.36, -12.34]	6.051	<0.001***
UPA 30 mg QD + TCS	33	66.036	19.444	-71.53	[-79.75, -63.31]	4.139	-37.81	[-49.99, -25.62]	6.138	<0.001***
Adult										
Placebo + TCS	175	66.650	42.800	-34.51	[-38.26, -30.77]	1.907				
UPA 15 mg QD + TCS	239	66.086	24.769	-62.41	[-65.68, -59.15]	1.664	-27.90	[-32.87, -22.93]	2.531	<0.001***
UPA 30 mg QD + TCS	237	67.825	19.468	-71.76	[-75.04, -68.48]	1.671	-37.25	[-42.23, -32.27]	2.536	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Objective SCORAD										
Week 2										
All										
Placebo + TCS	295	53.760	45.275	-14.93	[-17.98, -11.88]	1.554				
UPA 15 mg QD + TCS	297	52.590	31.081	-40.53	[-43.57, -37.49]	1.549	-25.60	[-29.34, -21.86]	1.904	<0.001***
UPA 30 mg QD + TCS	291	52.961	27.955	-47.03	[-50.10, -43.96]	1.565	-32.10	[-35.85, -28.34]	1.913	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	137	46.901	40.344	-14.11	[-17.98, -10.24]	1.969				
UPA 15 mg QD + TCS	140	46.271	25.697	-43.99	[-47.82, -40.17]	1.948	-29.89	[-35.33, -24.44]	2.769	<0.001***
UPA 30 mg QD + TCS	137	47.662	22.365	-52.23	[-56.10, -48.36]	1.969	-38.12	[-43.60, -32.65]	2.785	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	158	59.708	49.551	-16.63	[-20.24, -13.01]	1.837				
UPA 15 mg QD + TCS	157	58.225	35.882	-38.40	[-42.02, -34.78]	1.841	-21.78	[-26.89, -16.66]	2.602	<0.001***
UPA 30 mg QD + TCS	154	57.675	32.929	-43.01	[-46.67, -39.36]	1.861	-26.39	[-31.53, -21.24]	2.618	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Objective SCORAD										
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	106	52.528	41.583	-19.86	[-24.47, -15.25]	2.342				
UPA 15 mg QD + TCS	107	53.703	31.516	-42.27	[-46.87, -37.68]	2.335	-22.41	[-28.92, -15.91]	3.307	<0.001***
UPA 30 mg QD + TCS	103	51.514	27.570	-46.68	[-51.36, -42.00]	2.380	-26.82	[-33.39, -20.25]	3.339	<0.001***
Japan										
Placebo + TCS	18	52.663	42.297	-20.01	[-30.29, -9.74]	5.111				
UPA 15 mg QD + TCS	16	52.358	32.541	-38.41	[-49.32, -27.51]	5.424	-18.40	[-33.35, -3.45]	7.434	0.017*
UPA 30 mg QD + TCS	17	58.758	33.451	-46.22	[-56.97, -35.47]	5.347	-26.21	[-41.17, -11.24]	7.443	0.001**
China										
Placebo + TCS	17	58.782	55.224	-5.66	[-15.86, 4.54]	5.068				
UPA 15 mg QD + TCS	17	54.421	27.985	-46.39	[-56.36, -36.42]	4.953	-40.73	[-55.01, -26.45]	7.096	<0.001***
UPA 30 mg QD + TCS	16	50.615	31.641	-39.49	[-49.98, -29.00]	5.213	-33.83	[-48.77, -18.89]	7.424	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean	Within Group: [95% CI]	Within Group: SE	Between Groups Difference: LS Mean	Between Groups Difference: [95% CI]	Between Groups Difference: SE	Between Groups Difference: P-value
Objective SCORAD										
Week 2 (Cont.)										
Other										
Placebo + TCS	154	54.182	47.066	-12.77	[-16.41, -9.13]	1.851				
UPA 15 mg QD + TCS	157	51.657	30.971	-39.70	[-43.31, -36.10]	1.834	-26.93	[-32.06, -21.80]	2.611	<0.001***
UPA 30 mg QD + TCS	155	53.529	27.228	-49.16	[-52.78, -45.54]	1.842	-36.39	[-41.52, -31.26]	2.609	<0.001***
Adolescent										
Placebo + TCS	39	55.526	46.517	-16.82	[-24.42, -9.21]	3.839				
UPA 15 mg QD + TCS	39	53.604	34.353	-36.06	[-43.67, -28.45]	3.840	-19.24	[-30.01, -8.47]	5.436	0.001**
UPA 30 mg QD + TCS	37	55.340	30.619	-45.10	[-52.91, -37.29]	3.940	-28.28	[-39.17, -17.39]	5.497	<0.001***
Adult										
Placebo + TCS	256	53.491	45.086	-15.24	[-18.08, -12.39]	1.449				
UPA 15 mg QD + TCS	258	52.437	30.586	-41.64	[-44.48, -38.81]	1.442	-26.41	[-30.42, -22.39]	2.045	<0.001***
UPA 30 mg QD + TCS	254	52.614	27.567	-47.85	[-50.70, -45.00]	1.454	-32.61	[-36.64, -28.58]	2.053	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Objective SCORAD										
Week 16										
All										
Placebo + TCS	208	52.654	33.952	-34.00	[-37.94, -30.06]	2.006				
UPA 15 mg QD + TCS	276	52.626	20.377	-60.45	[-64.00, -56.89]	1.813	-26.45	[-31.31, -21.58]	2.477	<0.001***
UPA 30 mg QD + TCS	277	53.181	15.729	-70.34	[-73.90, -66.77]	1.815	-36.34	[-41.20, -31.47]	2.477	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	106	46.571	30.092	-34.30	[-39.63, -28.97]	2.713				
UPA 15 mg QD + TCS	131	46.436	16.305	-64.30	[-69.14, -59.45]	2.462	-29.99	[-37.20, -22.79]	3.663	<0.001***
UPA 30 mg QD + TCS	135	47.988	11.491	-74.93	[-79.72, -70.14]	2.434	-40.63	[-47.80, -33.46]	3.646	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	102	58.976	37.963	-34.86	[-39.82, -29.90]	2.523				
UPA 15 mg QD + TCS	145	58.218	24.057	-57.95	[-62.19, -53.71]	2.157	-23.09	[-29.61, -16.56]	3.320	<0.001***
UPA 30 mg QD + TCS	142	58.117	19.757	-66.80	[-71.09, -62.52]	2.180	-31.94	[-38.50, -25.39]	3.335	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Objective SCORAD										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	83	51.627	32.480	-36.01	[-41.94, -30.07]	3.017				
UPA 15 mg QD + TCS	104	53.394	18.222	-65.63	[-71.01, -60.24]	2.736	-29.62	[-37.64, -21.60]	4.074	<0.001***
UPA 30 mg QD + TCS	99	51.601	15.650	-69.72	[-75.24, -64.20]	2.803	-33.71	[-41.82, -25.61]	4.117	<0.001***
Japan										
Placebo + TCS	11	49.331	27.415	-40.93	[-53.40, -28.47]	6.176				
UPA 15 mg QD + TCS	15	51.115	18.724	-62.23	[-73.35, -51.11]	5.480	-21.30	[-37.91, -4.69]	8.208	0.013*
UPA 30 mg QD + TCS	16	59.040	18.445	-70.67	[-81.60, -59.75]	5.387	-29.74	[-46.48, -13.00]	8.290	0.001**
China										
Placebo + TCS	17	58.782	42.106	-28.31	[-42.12, -14.49]	6.857				
UPA 15 mg QD + TCS	14	54.219	15.869	-69.77	[-84.58, -54.97]	7.354	-41.47	[-61.73, -21.20]	10.064	<0.001***
UPA 30 mg QD + TCS	16	50.615	20.006	-63.20	[-77.42, -48.97]	7.061	-34.89	[-54.94, -14.84]	9.957	0.001**

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
Objective SCORAD										
Week 16 (Cont.)										
Other										
Placebo + TCS	97	52.837	34.523	-33.55	[-38.92, -28.19]	2.729				
UPA 15 mg QD + TCS	143	52.070	22.560	-56.33	[-60.82, -51.84]	2.282	-22.78	[-29.77, -15.78]	3.558	<0.001***
UPA 30 mg QD + TCS	146	53.890	15.015	-72.62	[-77.06, -68.18]	2.260	-39.07	[-46.03, -32.10]	3.543	<0.001***
Adolescent										
Placebo + TCS	30	53.922	33.883	-36.65	[-45.93, -27.38]	4.676				
UPA 15 mg QD + TCS	35	54.178	22.513	-56.95	[-65.60, -48.31]	4.357	-20.30	[-32.98, -7.62]	6.390	0.002**
UPA 30 mg QD + TCS	35	55.308	15.362	-73.49	[-82.15, -64.82]	4.366	-36.83	[-49.53, -24.14]	6.398	<0.001***
Adult										
Placebo + TCS	178	52.441	33.963	-34.18	[-38.17, -30.20]	2.031				
UPA 15 mg QD + TCS	241	52.401	20.067	-61.45	[-64.94, -57.96]	1.776	-27.27	[-32.57, -21.97]	2.698	<0.001***
UPA 30 mg QD + TCS	242	52.873	15.782	-70.51	[-73.99, -67.02]	1.775	-36.32	[-41.62, -31.03]	2.697	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Itch										
Week 2										
All										
Placebo + TCS	292	7.8	5.9	-21.88	[-26.16, -17.61]	2.180				
UPA 15 mg QD + TCS	294	7.5	3.3	-54.40	[-58.68, -50.11]	2.183	-32.51	[-37.70, -27.33]	2.640	<0.001***
UPA 30 mg QD + TCS	288	7.8	2.8	-61.33	[-65.64, -57.03]	2.195	-39.45	[-44.65, -34.25]	2.649	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	134	7.4	5.7	-20.76	[-26.36, -15.15]	2.853				
UPA 15 mg QD + TCS	137	7.4	3.2	-54.14	[-59.69, -48.60]	2.818	-33.39	[-41.27, -25.51]	4.010	<0.001***
UPA 30 mg QD + TCS	135	7.4	2.7	-61.82	[-67.40, -56.23]	2.841	-41.06	[-48.97, -33.15]	4.026	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	158	8.2	6.0	-26.01	[-30.80, -21.23]	2.436				
UPA 15 mg QD + TCS	157	7.6	3.3	-56.51	[-61.33, -51.69]	2.451	-30.50	[-37.32, -23.68]	3.471	<0.001***
UPA 30 mg QD + TCS	153	8.1	2.9	-63.91	[-68.76, -59.05]	2.471	-37.89	[-44.70, -31.08]	3.465	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Itch										
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	106	7.8	5.3	-29.54	[-35.82, -23.26]	3.192				
UPA 15 mg QD + TCS	106	7.4	3.3	-54.88	[-61.17, -48.59]	3.197	-25.34	[-34.25, -16.44]	4.526	<0.001***
UPA 30 mg QD + TCS	102	7.8	2.8	-63.51	[-69.92, -57.09]	3.258	-33.97	[-42.93, -25.00]	4.557	<0.001***
Japan										
Placebo + TCS	18	7.9	6.6	-19.13	[-33.41, -4.85]	7.099				
UPA 15 mg QD + TCS	16	7.9	3.2	-61.42	[-76.56, -46.27]	7.529	-42.29	[-63.10, -21.48]	10.348	<0.001***
UPA 30 mg QD + TCS	17	8.2	3.2	-60.45	[-75.20, -45.70]	7.333	-41.32	[-61.84, -20.80]	10.203	<0.001***
China										
Placebo + TCS	17	8.7	7.0	-14.78	[-33.50, 3.94]	9.291				
UPA 15 mg QD + TCS	17	7.5	3.6	-51.46	[-70.01, -32.92]	9.201	-36.68	[-63.36, -10.01]	13.243	0.008**
UPA 30 mg QD + TCS	16	7.7	3.9	-52.29	[-71.30, -33.27]	9.435	-37.51	[-64.41, -10.61]	13.352	0.007**

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Itch										
Week 2 (Cont.)										
Other										
Placebo + TCS	151	7.7	6.1	-20.39	[-25.29, -15.50]	2.490				
UPA 15 mg QD + TCS	155	7.6	3.2	-56.26	[-61.09, -51.43]	2.459	-35.86	[-42.74, -28.98]	3.501	<0.001***
UPA 30 mg QD + TCS	153	7.7	2.7	-63.97	[-68.83, -59.11]	2.474	-43.58	[-50.47, -36.68]	3.510	<0.001***
Adolescent										
Placebo + TCS	37	7.4	5.9	-18.84	[-29.61, -8.07]	5.434				
UPA 15 mg QD + TCS	38	7.2	3.1	-54.77	[-65.38, -44.16]	5.352	-35.93	[-51.03, -20.82]	7.621	<0.001***
UPA 30 mg QD + TCS	36	6.8	2.9	-53.71	[-64.67, -42.75]	5.530	-34.87	[-50.28, -19.45]	7.779	<0.001***
Adult										
Placebo + TCS	255	7.9	5.9	-23.96	[-27.86, -20.06]	1.986				
UPA 15 mg QD + TCS	256	7.6	3.3	-55.85	[-59.75, -51.95]	1.985	-31.89	[-37.41, -26.37]	2.811	<0.001***
UPA 30 mg QD + TCS	252	7.9	2.8	-64.25	[-68.17, -60.32]	1.998	-40.29	[-45.81, -34.76]	2.815	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Itch										
Week 16										
All										
Placebo + TCS	202	7.8	5.1	-30.15	[-37.09, -23.20]	3.537				
UPA 15 mg QD + TCS	274	7.5	2.9	-56.45	[-62.58, -50.33]	3.120	-26.30	[-35.03, -17.58]	4.443	<0.001***
UPA 30 mg QD + TCS	271	7.8	2.1	-70.31	[-76.46, -64.16]	3.134	-40.17	[-48.90, -31.43]	4.451	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	103	7.3	5.1	-26.90	[-33.58, -20.21]	3.399				
UPA 15 mg QD + TCS	129	7.4	2.7	-62.46	[-68.50, -56.42]	3.073	-35.56	[-44.57, -26.55]	4.582	<0.001***
UPA 30 mg QD + TCS	133	7.4	1.7	-74.64	[-80.61, -68.67]	3.037	-47.74	[-56.71, -38.78]	4.558	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	99	8.2	5.0	-36.68	[-48.14, -25.22]	5.828				
UPA 15 mg QD + TCS	145	7.6	3.1	-53.20	[-62.71, -43.68]	4.839	-16.51	[-31.42, -1.61]	7.582	0.030*
UPA 30 mg QD + TCS	138	8.1	2.5	-69.15	[-78.89, -59.41]	4.952	-32.47	[-47.50, -17.43]	7.645	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Itch										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	7.8	4.5	-37.81	[-45.23, -30.39]	3.770				
UPA 15 mg QD + TCS	104	7.3	2.6	-64.26	[-70.93, -57.58]	3.390	-26.45	[-36.44, -16.45]	5.078	<0.001***
UPA 30 mg QD + TCS	97	7.9	2.2	-71.37	[-78.25, -64.48]	3.499	-33.55	[-43.67, -23.44]	5.138	<0.001***
Japan										
Placebo + TCS	11	7.5	5.1	-25.53	[-43.32, -7.75]	8.809				
UPA 15 mg QD + TCS	15	7.8	2.7	-64.55	[-79.91, -49.19]	7.592	-39.02	[-62.48, -15.55]	11.615	0.002**
UPA 30 mg QD + TCS	16	8.1	1.9	-76.58	[-91.47, -61.69]	7.362	-51.04	[-74.30, -27.79]	11.514	<0.001***
China										
Placebo + TCS	17	8.7	6.1	-24.28	[-92.49, 43.93]	33.787				
UPA 15 mg QD + TCS	14	7.6	3.8	-3.22	[-78.08, 71.64]	37.106	21.06	[-80.24, 122.37]	50.205	0.677
UPA 30 mg QD + TCS	16	7.7	2.2	-75.24	[-145.48, -5.00]	34.789	-50.96	[-148.92, 47.00]	48.526	0.300

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Itch										
Week 16 (Cont.)										
Other										
Placebo + TCS	94	7.6	5.3	-27.39	[-34.04, -20.74]	3.381				
UPA 15 mg QD + TCS	141	7.6	3.0	-58.87	[-64.41, -53.33]	2.818	-31.48	[-40.13, -22.83]	4.401	<0.001***
UPA 30 mg QD + TCS	142	7.7	2.1	-71.43	[-76.96, -65.91]	2.811	-44.04	[-52.69, -35.40]	4.397	<0.001***
Adolescent										
Placebo + TCS	27	7.5	5.3	-24.06	[-38.34, -9.78]	7.193				
UPA 15 mg QD + TCS	35	7.3	3.3	-53.61	[-66.22, -40.99]	6.354	-29.54	[-48.57, -10.52]	9.584	0.003**
UPA 30 mg QD + TCS	33	6.7	2.2	-63.25	[-76.31, -50.20]	6.574	-39.19	[-58.60, -19.79]	9.777	<0.001***
Adult										
Placebo + TCS	175	7.8	5.0	-32.62	[-39.91, -25.32]	3.716				
UPA 15 mg QD + TCS	239	7.5	2.8	-58.36	[-64.65, -52.08]	3.202	-25.75	[-35.38, -16.11]	4.907	<0.001***
UPA 30 mg QD + TCS	238	7.9	2.1	-73.15	[-79.45, -66.85]	3.208	-40.53	[-50.17, -30.89]	4.909	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Sleep										
Week 2										
All										
Placebo + TCS	289	6.5	4.7	-18.75	[-26.33, -11.17]	3.862				
UPA 15 mg QD + TCS	292	6.2	2.7	-51.15	[-58.72, -43.59]	3.857	-32.41	[-41.69, -23.12]	4.732	<0.001***
UPA 30 mg QD + TCS	286	6.7	2.5	-49.83	[-57.46, -42.20]	3.889	-31.08	[-40.41, -21.76]	4.753	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	131	6.0	4.4	-18.95	[-28.73, -9.16]	4.977				
UPA 15 mg QD + TCS	135	5.8	2.4	-53.34	[-62.98, -43.70]	4.901	-34.39	[-48.12, -20.66]	6.985	<0.001***
UPA 30 mg QD + TCS	134	6.1	2.4	-50.30	[-59.98, -40.62]	4.923	-31.35	[-45.11, -17.59]	7.000	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	158	7.0	4.9	-24.52	[-33.47, -15.56]	4.556				
UPA 15 mg QD + TCS	157	6.5	2.8	-55.13	[-64.14, -46.12]	4.584	-30.62	[-43.32, -17.91]	6.466	<0.001***
UPA 30 mg QD + TCS	152	7.1	2.6	-55.47	[-64.61, -46.34]	4.649	-30.96	[-43.74, -18.17]	6.507	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Sleep										
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	106	6.2	4.0	-30.29	[-42.19, -18.39]	6.050				
UPA 15 mg QD + TCS	105	6.1	2.7	-53.15	[-65.10, -41.19]	6.075	-22.86	[-39.72, -6.00]	8.569	0.008**
UPA 30 mg QD + TCS	100	6.9	2.4	-60.13	[-72.40, -47.86]	6.235	-29.84	[-46.94, -12.73]	8.693	0.001**
Japan										
Placebo + TCS	18	7.5	6.0	-13.47	[-40.67, 13.73]	13.521				
UPA 15 mg QD + TCS	16	5.9	2.8	-55.25	[-84.07, -26.42]	14.328	-41.77	[-81.72, -1.83]	19.864	0.041*
UPA 30 mg QD + TCS	17	7.1	4.7	-20.64	[-48.45, 7.16]	13.815	-7.17	[-45.93, 31.58]	19.255	0.711
China										
Placebo + TCS	16	8.7	6.4	-18.63	[-39.82, 2.56]	10.515				
UPA 15 mg QD + TCS	16	6.8	2.6	-66.59	[-86.88, -46.30]	10.063	-47.96	[-77.77, -18.14]	14.797	0.002**
UPA 30 mg QD + TCS	16	6.5	3.6	-46.84	[-67.26, -26.41]	10.132	-28.21	[-58.37, 1.96]	14.970	0.066

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Sleep										
Week 2 (Cont.)										
Other										
Placebo + TCS	149	6.4	4.8	-17.64	[-26.36, -8.91]	4.441				
UPA 15 mg QD + TCS	155	6.2	2.7	-52.78	[-61.35, -44.21]	4.362	-35.14	[-47.38, -22.91]	6.225	<0.001***
UPA 30 mg QD + TCS	153	6.5	2.3	-53.18	[-61.79, -44.56]	4.386	-35.54	[-47.81, -23.28]	6.241	<0.001***
Adolescent										
Placebo + TCS	37	6.4	4.5	-5.38	[-35.33, 24.57]	15.107				
UPA 15 mg QD + TCS	38	5.5	2.1	-54.51	[-83.97, -25.05]	14.859	-49.13	[-91.21, -7.06]	21.223	0.023*
UPA 30 mg QD + TCS	35	5.1	2.6	-30.53	[-61.34, 0.28]	15.539	-25.15	[-68.26, 17.95]	21.742	0.250
Adult										
Placebo + TCS	252	6.6	4.7	-24.10	[-30.25, -17.94]	3.135				
UPA 15 mg QD + TCS	254	6.3	2.7	-54.12	[-60.26, -47.97]	3.128	-30.02	[-38.71, -21.33]	4.428	<0.001***
UPA 30 mg QD + TCS	251	6.9	2.5	-56.64	[-62.82, -50.46]	3.147	-32.54	[-41.27, -23.82]	4.443	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Sleep										
Week 16										
All										
Placebo + TCS	198	6.6	3.8	-30.38	[-40.00, -20.76]	4.903				
UPA 15 mg QD + TCS	273	6.1	1.8	-61.61	[-70.18, -53.04]	4.366	-31.23	[-42.98, -19.48]	5.986	<0.001***
UPA 30 mg QD + TCS	268	6.8	1.6	-66.33	[-74.97, -57.68]	4.405	-35.95	[-47.74, -24.16]	6.006	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	100	6.0	3.7	-26.51	[-37.98, -15.04]	5.835				
UPA 15 mg QD + TCS	128	5.7	1.7	-66.49	[-76.78, -56.19]	5.233	-39.98	[-55.39, -24.57]	7.836	<0.001***
UPA 30 mg QD + TCS	132	6.2	1.1	-74.45	[-84.62, -64.28]	5.171	-47.94	[-63.28, -32.61]	7.798	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	98	7.2	3.9	-40.82	[-54.36, -27.28]	6.885				
UPA 15 mg QD + TCS	145	6.5	2.0	-63.57	[-74.83, -52.32]	5.723	-22.75	[-40.38, -5.13]	8.961	0.012*
UPA 30 mg QD + TCS	136	7.3	2.0	-64.56	[-76.16, -52.96]	5.899	-23.74	[-41.55, -5.92]	9.060	0.009**

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
SCORAD Sleep										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	78	6.6	3.1	-48.25	[-56.87, -39.64]	4.375				
UPA 15 mg QD + TCS	104	5.9	1.5	-72.72	[-80.33, -65.12]	3.863	-24.47	[-35.97, -12.97]	5.840	<0.001***
UPA 30 mg QD + TCS	96	6.8	1.4	-76.73	[-84.64, -68.82]	4.015	-28.48	[-40.17, -16.79]	5.933	<0.001***
Japan										
Placebo + TCS	11	7.0	4.1	-40.57	[-62.29, -18.84]	10.740				
UPA 15 mg QD + TCS	15	5.7	1.7	-70.08	[-89.21, -50.95]	9.458	-29.51	[-58.70, -0.32]	14.435	0.048*
UPA 30 mg QD + TCS	16	6.9	1.8	-72.41	[-90.53, -54.29]	8.952	-31.84	[-60.07, -3.62]	13.953	0.028*
China										
Placebo + TCS	17	8.2	5.0	-33.01	[-102.41, 36.40]	34.429				
UPA 15 mg QD + TCS	14	6.8	2.8	-0.75	[-77.36, 75.86]	38.000	32.26	[-71.16, 135.67]	51.299	0.533
UPA 30 mg QD + TCS	16	6.5	2.1	-71.25	[-142.74, 0.25]	35.465	-38.24	[-138.01, 61.53]	49.498	0.444

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
SCORAD Sleep										
Week 16 (Cont.)										
Other										
Placebo + TCS	92	6.2	4.2	-22.69	[-35.61, -9.77]	6.573				
UPA 15 mg QD + TCS	140	6.2	2.0	-63.41	[-74.19, -52.63]	5.483	-40.72	[-57.54, -23.89]	8.558	<0.001***
UPA 30 mg QD + TCS	140	6.7	1.6	-64.65	[-75.44, -53.86]	5.487	-41.96	[-58.80, -25.12]	8.565	<0.001***
Adolescent										
Placebo + TCS	27	6.7	4.9	-19.18	[-38.27, -0.10]	9.595				
UPA 15 mg QD + TCS	35	5.7	1.6	-63.42	[-80.15, -46.69]	8.397	-44.24	[-69.66, -18.82]	12.771	0.001**
UPA 30 mg QD + TCS	31	5.2	1.7	-60.06	[-77.94, -42.19]	8.974	-40.88	[-67.28, -14.48]	13.262	0.003**
Adult										
Placebo + TCS	171	6.6	3.7	-35.63	[-45.45, -25.81]	5.000				
UPA 15 mg QD + TCS	238	6.2	1.9	-64.56	[-73.00, -56.12]	4.298	-28.93	[-41.88, -15.99]	6.592	<0.001***
UPA 30 mg QD + TCS	237	7.0	1.5	-71.41	[-79.87, -62.95]	4.309	-35.78	[-48.75, -22.82]	6.602	<0.001***

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　8.4.1

表 2.7.3.6-55.　二重盲検投与期の来院時別の SCORAD 50 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo + TCS	304	29 (9.5) [6.2, 12.8]	0					
UPA 15 mg QD + TCS	300	121 (40.3) [34.8, 45.9]	0	30.8	30.7	[24.3, 37.1]	<0.001***	0.500
UPA 30 mg QD + TCS	297	150 (50.5) [44.8, 56.2]	0	41.0	40.9	[34.4, 47.5]	<0.001***	0.631
vIGA-AD 3 (Moderate)								
Placebo + TCS	141	14 (9.9) [5.0, 14.9]	0					
UPA 15 mg QD + TCS	143	69 (48.3) [40.1, 56.4]	0	38.3		[28.8, 47.9]	<0.001***	
UPA 30 mg QD + TCS	140	80 (57.1) [48.9, 65.3]	0	47.2		[37.6, 56.8]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo + TCS	163	15 (9.2) [4.8, 13.6]	0					
UPA 15 mg QD + TCS	157	52 (33.1) [25.8, 40.5]	0	23.9		[15.3, 32.5]	<0.001***	
UPA 30 mg QD + TCS	157	70 (44.6) [36.8, 52.4]	0	35.4		[26.4, 44.3]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	108	14 (13.0) [6.6, 19.3]	0					
UPA 15 mg QD + TCS	108	49 (45.4) [36.0, 54.8]	0	32.4		[21.1, 43.7]	<0.001***	
UPA 30 mg QD + TCS	106	50 (47.2) [37.7, 56.7]	0	34.2		[22.8, 45.6]	<0.001***	
Japan								
Placebo + TCS	18	2 (11.1) [0.0, 25.6]	0					
UPA 15 mg QD + TCS	16	5 (31.3) [8.5, 54.0]	0	20.1		[-6.8, 47.1]	0.143	
UPA 30 mg QD + TCS	17	7 (41.2) [17.8, 64.6]	0	30.1		[2.5, 57.6]	0.032*	
China								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	17	7 (41.2) [17.8, 64.6]	0	41.2		[17.8, 64.6]	0.001**	
UPA 30 mg QD + TCS	16	7 (43.8) [19.4, 68.1]	0	43.8		[19.4, 68.1]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo + TCS	160	13 (8.1) [3.9, 12.4]	0					
UPA 15 mg QD + TCS	159	60 (37.7) [30.2, 45.3]	0	29.6		[21.0, 38.3]	<0.001***	
UPA 30 mg QD + TCS	158	86 (54.4) [46.7, 62.2]	0	46.3		[37.5, 55.2]	<0.001***	
Adolescent								
Placebo + TCS	40	5 (12.5) [2.3, 22.7]	0					
UPA 15 mg QD + TCS	39	14 (35.9) [20.8, 51.0]	0	23.4		[5.2, 41.6]	0.012*	
UPA 30 mg QD + TCS	37	18 (48.6) [32.5, 64.8]	0	36.1		[17.1, 55.2]	<0.001***	
Adult								
Placebo + TCS	264	24 (9.1) [5.6, 12.6]	0					
UPA 15 mg QD + TCS	261	107 (41.0) [35.0, 47.0]	0	31.9		[25.0, 38.8]	<0.001***	
UPA 30 mg QD + TCS	260	132 (50.8) [44.7, 56.8]	0	41.7		[34.7, 48.7]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	304	67 (22.0) [17.3, 26.6]	2					
UPA 15 mg QD + TCS	300	195 (65.0) [59.6, 70.5]	3	43.1	43.1	[35.9, 50.2]	<0.001***	0.968
UPA 30 mg QD + TCS	297	222 (74.9) [69.9, 79.8]	2	52.9	52.9	[46.1, 59.6]	<0.001***	0.370
vIGA-AD 3 (Moderate)								
Placebo + TCS	141	33 (23.2) [16.2, 30.3]	2					
UPA 15 mg QD + TCS	143	94 (65.7) [58.0, 73.5]	1	42.5		[32.0, 53.0]	<0.001***	
UPA 30 mg QD + TCS	140	115 (82.1) [75.8, 88.5]	0	58.9		[49.4, 68.4]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo + TCS	163	34 (20.9) [14.6, 27.1]	0					
UPA 15 mg QD + TCS	157	101 (64.4) [56.9, 72.0]	2	43.6		[33.8, 53.3]	<0.001***	
UPA 30 mg QD + TCS	157	107 (68.4) [61.1, 75.8]	2	47.6		[37.9, 57.2]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	108	33 (30.3) [21.5, 39.1]	2					
UPA 15 mg QD + TCS	108	80 (74.1) [65.8, 82.3]	1	43.8		[31.7, 55.8]	<0.001***	
UPA 30 mg QD + TCS	106	78 (73.2) [64.7, 81.7]	1	42.9		[30.7, 55.1]	<0.001***	
Japan								
Placebo + TCS	18	4 (22.2) [3.0, 41.4]	0					
UPA 15 mg QD + TCS	16	14 (87.5) [71.3, 100.0]	0	65.3		[40.1, 90.4]	<0.001***	
UPA 30 mg QD + TCS	17	14 (82.4) [64.2, 100.0]	0	60.1		[33.7, 86.5]	<0.001***	
China								
Placebo + TCS	18	5 (27.8) [7.1, 48.5]	0					
UPA 15 mg QD + TCS	17	12 (70.6) [48.9, 92.2]	0	42.8		[12.9, 72.8]	0.005**	
UPA 30 mg QD + TCS	16	12 (75.0) [53.8, 96.2]	0	47.2		[17.6, 76.9]	0.002**	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo + TCS	160	25 (15.6) [10.0, 21.3]	0					
UPA 15 mg QD + TCS	159	89 (56.1) [48.3, 63.8]	2	40.4		[30.8, 50.0]	<0.001***	
UPA 30 mg QD + TCS	158	119 (75.2) [68.5, 82.0]	1	59.6		[50.8, 68.4]	<0.001***	
Adolescent								
Placebo + TCS	40	8 (20.0) [7.6, 32.4]	0					
UPA 15 mg QD + TCS	39	23 (59.0) [43.5, 74.4]	0	39.0		[19.2, 58.8]	<0.001***	
UPA 30 mg QD + TCS	37	26 (70.3) [55.5, 85.0]	0	50.3		[31.0, 69.5]	<0.001***	
Adult								
Placebo + TCS	264	59 (22.2) [17.2, 27.3]	2					
UPA 15 mg QD + TCS	261	172 (66.0) [60.2, 71.7]	3	43.7		[36.0, 51.4]	<0.001***	
UPA 30 mg QD + TCS	260	196 (75.6) [70.3, 80.8]	2	53.3		[46.0, 60.6]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　8.1.1

表 2.7.3.6-56.　　二重盲検投与期の来院時別の SCORAD 75 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo + TCS	304	3 (1.0) [0.0, 2.1]	0					
UPA 15 mg QD + TCS	300	17 (5.7) [3.1, 8.3]	0	4.7	4.7	[1.9, 7.5]	0.001**	0.424
UPA 30 mg QD + TCS	297	42 (14.1) [10.2, 18.1]	0	13.2	13.1	[9.1, 17.2]	<0.001***	0.781
vIGA-AD 3 (Moderate)								
Placebo + TCS	141	1 (0.7) [0.0, 2.1]	0					
UPA 15 mg QD + TCS	143	10 (7.0) [2.8, 11.2]	0	6.3		[1.9, 10.7]	0.005**	
UPA 30 mg QD + TCS	140	21 (15.0) [9.1, 20.9]	0	14.3		[8.2, 20.4]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo + TCS	163	2 (1.2) [0.0, 2.9]	0					
UPA 15 mg QD + TCS	157	7 (4.5) [1.2, 7.7]	0	3.2		[-0.4, 6.9]	0.082	
UPA 30 mg QD + TCS	157	21 (13.4) [8.1, 18.7]	0	12.1		[6.6, 17.7]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	108	3 (2.8) [0.0, 5.9]	0					
UPA 15 mg QD + TCS	108	8 (7.4) [2.5, 12.3]	0	4.6		[-1.2, 10.5]	0.120	
UPA 30 mg QD + TCS	106	19 (17.9) [10.6, 25.2]	0	15.1		[7.2, 23.1]	<0.001***	
Japan								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	16	0	0	0.0			NA	
UPA 30 mg QD + TCS	17	0	0	0.0			NA	
China								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	17	1 (5.9) [0.0, 17.1]	0	5.9		[-5.3, 17.1]	0.303	
UPA 30 mg QD + TCS	16	1 (6.3) [0.0, 18.1]	0	6.3		[-5.6, 18.1]	0.302	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo + TCS	160	0	0					
UPA 15 mg QD + TCS	159	8 (5.0) [1.6, 8.4]	0	5.0		[1.6, 8.4]	0.004**	
UPA 30 mg QD + TCS	158	22 (13.9) [8.5, 19.3]	0	13.9		[8.5, 19.3]	<0.001***	
Adolescent								
Placebo + TCS	40	0	0					
UPA 15 mg QD + TCS	39	2 (5.1) [0.0, 12.1]	0	5.1		[-1.8, 12.1]	0.147	
UPA 30 mg QD + TCS	37	4 (10.8) [0.8, 20.8]	0	10.8		[0.8, 20.8]	0.034*	
Adult								
Placebo + TCS	264	3 (1.1) [0.0, 2.4]	0					
UPA 15 mg QD + TCS	261	15 (5.7) [2.9, 8.6]	0	4.6		[1.5, 7.7]	0.004**	
UPA 30 mg QD + TCS	260	38 (14.6) [10.3, 18.9]	0	13.5		[9.0, 18.0]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	304	21 (6.9) [4.1, 9.8]	2					
UPA 15 mg QD + TCS	300	89 (29.6) [24.4, 34.8]	3	22.7	22.6	[16.7, 28.5]	<0.001***	0.485
UPA 30 mg QD + TCS	297	142 (48.0) [42.3, 53.7]	2	41.0	41.0	[34.7, 47.3]	<0.001***	0.518
vIGA-AD 3 (Moderate)								
Placebo + TCS	141	11 (7.9) [3.4, 12.3]	2					
UPA 15 mg QD + TCS	143	51 (35.4) [27.5, 43.2]	1	27.5		[18.4, 36.5]	<0.001***	
UPA 30 mg QD + TCS	140	79 (56.4) [48.2, 64.6]	0	48.6		[39.2, 57.9]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo + TCS	163	10 (6.1) [2.5, 9.8]	0					
UPA 15 mg QD + TCS	157	38 (24.4) [17.6, 31.1]	2	18.2		[10.5, 25.9]	<0.001***	
UPA 30 mg QD + TCS	157	63 (40.4) [32.7, 48.1]	2	34.3		[25.7, 42.8]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	108	10 (9.4) [3.8, 14.9]	2					
UPA 15 mg QD + TCS	108	40 (36.6) [27.5, 45.8]	1	27.3		[16.6, 38.0]	<0.001***	
UPA 30 mg QD + TCS	106	49 (46.3) [36.8, 55.8]	1	37.0		[26.0, 48.0]	<0.001***	
Japan								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	16	5 (31.3) [8.5, 54.0]	0	31.3		[8.5, 54.0]	0.007**	
UPA 30 mg QD + TCS	17	8 (47.1) [23.3, 70.8]	0	47.1		[23.3, 70.8]	<0.001***	
China								
Placebo + TCS	18	1 (5.6) [0.0, 16.1]	0					
UPA 15 mg QD + TCS	17	6 (35.3) [12.6, 58.0]	0	29.7		[4.7, 54.8]	0.020*	
UPA 30 mg QD + TCS	16	5 (31.3) [8.5, 54.0]	0	25.7		[0.6, 50.8]	0.044*	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo + TCS	160	10 (6.3) [2.5, 10.0]	0					
UPA 15 mg QD + TCS	159	38 (24.0) [17.4, 30.7]	2	17.8		[10.1, 25.4]	<0.001***	
UPA 30 mg QD + TCS	158	80 (50.8) [43.0, 58.7]	1	44.6		[35.9, 53.3]	<0.001***	
Adolescent								
Placebo + TCS	40	2 (5.0) [0.0, 11.8]	0					
UPA 15 mg QD + TCS	39	7 (17.9) [5.9, 30.0]	0	12.9		[-0.9, 26.8]	0.066	
UPA 30 mg QD + TCS	37	19 (51.4) [35.2, 67.5]	0	46.4		[28.9, 63.8]	<0.001***	
Adult								
Placebo + TCS	264	19 (7.2) [4.1, 10.4]	2					
UPA 15 mg QD + TCS	261	82 (31.3) [25.7, 37.0]	3	24.1		[17.6, 30.6]	<0.001***	
UPA 30 mg QD + TCS	260	123 (47.5) [41.4, 53.6]	2	40.2		[33.4, 47.1]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　8.2.1

表 2.7.3.6-57.　二重盲検投与期の来院時別の SCORAD 90 を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2								
All								
Placebo + TCS	304	1 (0.3) [0.0, 1.0]	0					
UPA 15 mg QD + TCS	300	1 (0.3) [0.0, 1.0]	0	0.0	0.0	[-0.9, 0.9]	0.994	0.160
UPA 30 mg QD + TCS	297	10 (3.4) [1.3, 5.4]	0	3.0	3.0	[0.9, 5.2]	0.006**	0.519
vIGA-AD 3 (Moderate)								
Placebo + TCS	141	0	0					
UPA 15 mg QD + TCS	143	1 (0.7) [0.0, 2.1]	0	0.7		[-0.7, 2.1]	0.316	
UPA 30 mg QD + TCS	140	6 (4.3) [0.9, 7.6]	0	4.3		[0.9, 7.6]	0.012*	
vIGA-AD 4 (Severe)								
Placebo + TCS	163	1 (0.6) [0.0, 1.8]	0					
UPA 15 mg QD + TCS	157	0	0	-0.6		[-1.8, 0.6]	0.316	
UPA 30 mg QD + TCS	157	4 (2.5) [0.1, 5.0]	0	1.9		[-0.8, 4.7]	0.167	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	108	1 (0.9) [0.0, 2.7]	0					
UPA 15 mg QD + TCS	108	0	0	-0.9		[-2.7, 0.9]	0.315	
UPA 30 mg QD + TCS	106	4 (3.8) [0.1, 7.4]	0	2.8		[-1.2, 6.9]	0.168	
Japan								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	16	0	0	0.0			NA	
UPA 30 mg QD + TCS	17	0	0	0.0			NA	
China								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	17	0	0	0.0			NA	
UPA 30 mg QD + TCS	16	0	0	0.0			NA	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 2 (Cont.)								
Other								
Placebo + TCS	160	0	0					
UPA 15 mg QD + TCS	159	1 (0.6) [0.0, 1.9]	0	0.6		[-0.6, 1.9]	0.316	
UPA 30 mg QD + TCS	158	6 (3.8) [0.8, 6.8]	0	3.8		[0.8, 6.8]	0.013*	
Adolescent								
Placebo + TCS	40	0	0					
UPA 15 mg QD + TCS	39	0	0	0.0			NA	
UPA 30 mg QD + TCS	37	1 (2.7) [0.0, 7.9]	0	2.7		[-2.5, 7.9]	0.311	
Adult								
Placebo + TCS	264	1 (0.4) [0.0, 1.1]	0					
UPA 15 mg QD + TCS	261	1 (0.4) [0.0, 1.1]	0	0.0		[-1.0, 1.1]	0.994	
UPA 30 mg QD + TCS	260	9 (3.5) [1.2, 5.7]	0	3.1		[0.7, 5.4]	0.010**	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	304	4 (1.3) [0.0, 2.6]	2					
UPA 15 mg QD + TCS	300	42 (14.1) [10.1, 18.0]	3	12.8	12.7	[8.6, 16.8]	<0.001***	0.875
UPA 30 mg QD + TCS	297	71 (23.9) [19.1, 28.8]	2	22.6	22.6	[17.6, 27.5]	<0.001***	0.843
vIGA-AD 3 (Moderate)								
Placebo + TCS	141	2 (1.4) [0.0, 3.4]	2					
UPA 15 mg QD + TCS	143	27 (19.0) [12.5, 25.4]	1	17.6		[10.8, 24.3]	<0.001***	
UPA 30 mg QD + TCS	140	42 (30.0) [22.4, 37.6]	0	28.6		[20.7, 36.4]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo + TCS	163	2 (1.2) [0.0, 2.9]	0					
UPA 15 mg QD + TCS	157	15 (9.6) [5.0, 14.2]	2	8.4		[3.5, 13.3]	0.001**	
UPA 30 mg QD + TCS	157	29 (18.5) [12.4, 24.6]	2	17.3		[11.0, 23.6]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	108	1 (0.9) [0.0, 2.7]	2					
UPA 15 mg QD + TCS	108	21 (19.6) [12.1, 27.1]	1	18.6		[10.9, 26.4]	<0.001***	
UPA 30 mg QD + TCS	106	28 (26.4) [18.0, 34.8]	1	25.5		[16.9, 34.1]	<0.001***	
Japan								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	16	0	0	0.0			NA	
UPA 30 mg QD + TCS	17	2 (11.8) [0.0, 27.1]	0	11.8		[-3.6, 27.1]	0.132	
China								
Placebo + TCS	18	0	0					
UPA 15 mg QD + TCS	17	2 (11.8) [0.0, 27.1]	0	11.8		[-3.6, 27.1]	0.132	
UPA 30 mg QD + TCS	16	4 (25.0) [3.8, 46.2]	0	25.0		[3.8, 46.2]	0.021*	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo + TCS	160	3 (1.9) [0.0, 4.0]	0					
UPA 15 mg QD + TCS	159	19 (12.0) [6.9, 17.1]	2	10.1		[4.6, 15.6]	<0.001***	
UPA 30 mg QD + TCS	158	37 (23.4) [16.8, 30.0]	1	21.6		[14.6, 28.5]	<0.001***	
Adolescent								
Placebo + TCS	40	0	0					
UPA 15 mg QD + TCS	39	3 (7.7) [0.0, 16.1]	0	7.7		[-0.7, 16.1]	0.071	
UPA 30 mg QD + TCS	37	9 (24.3) [10.5, 38.1]	0	24.3		[10.5, 38.1]	0.001**	
Adult								
Placebo + TCS	264	4 (1.5) [0.0, 3.0]	2					
UPA 15 mg QD + TCS	261	39 (15.0) [10.7, 19.4]	3	13.5		[8.9, 18.1]	<0.001***	
UPA 30 mg QD + TCS	260	62 (23.9) [18.7, 29.1]	2	22.4		[17.0, 27.7]	<0.001***	

Note: SCORAD = Scoring Atopic Dermatitis; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　8.3.1

表 2.7.3.6-58. 第 1 ピリオドの来院時別の SCORAD スコアのベースラインからの変化率（%）（LOCF，OC，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 2											
	ALL										
		UPA 30 MG QD	40	62.3	32.7	-46.5	4.43	-44.8	(-55.8, -33.7)	5.57	<0.001***
		UPA 15 MG QD	35	65.9	39.7	-39.2	4.63	-37.5	(-48.8, -26.1)	5.76	<0.001***
		UPA 7.5 MG QD	39	64.0	47.2	-26.1	4.44	-24.4	(-35.5, -13.4)	5.61	<0.001***
		PLACEBO	30	62.9	61.6	-1.7	4.83				
	US/PR/CANADA										
		UPA 30 MG QD	29	62.4	31.5	-49.0	4.01	-48.5	(-60.7, -36.2)	6.19	<0.001***
		UPA 15 MG QD	25	66.3	40.1	-40.3	4.32	-39.7	(-52.4, -27.1)	6.38	<0.001***
		UPA 7.5 MG QD	27	63.4	46.2	-28.2	4.15	-27.7	(-40.1, -15.2)	6.28	<0.001***
		PLACEBO	21	65.4	65.2	-0.6	4.70				
	EU/AUS										
		UPA 30 MG QD	9	61.8	37.1	-39.5	9.09	-30.5	(-59.5, -1.5)	14.18	0.040*
		UPA 15 MG QD	8	60.7	35.6	-39.6	9.65	-30.5	(-60.0, -1.0)	14.44	0.043*
		UPA 7.5 MG QD	10	66.7	51.5	-23.0	8.92	-14.0	(-43.7, 15.8)	14.55	0.344
		PLACEBO	7	53.4	49.2	-9.1	10.82				
	JAPAN										
		UPA 30 MG QD	2	62.1	30.4	-64.1	18.53	-66.8	(-150.4, 16.9)	26.28	0.085
		UPA 15 MG QD	2	81.1	51.2	-9.4	21.76	-12.1	(-97.7, 73.6)	26.91	0.685
		UPA 7.5 MG QD	2	58.1	39.8	-41.2	20.09	-43.8	(-132.2, 44.6)	27.78	0.213
		PLACEBO	2	70.7	67.5	2.6	17.82				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.925

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 4											
	ALL										
		UPA 30 MG QD	40	62.3	25.7	-58.7	4.81	-51.0	(-62.7, -39.3)	5.91	<0.001***
		UPA 15 MG QD	36	65.7	33.5	-49.3	4.96	-41.6	(-53.5, -29.6)	6.05	<0.001***
		UPA 7.5 MG QD	39	64.0	41.4	-35.3	4.82	-27.6	(-39.3, -15.8)	5.93	<0.001***
		PLACEBO	33	64.2	58.9	-7.7	5.08				
	US/PR/CANADA										
		UPA 30 MG QD	29	62.4	25.6	-59.0	4.18	-49.6	(-62.0, -37.1)	6.29	<0.001***
		UPA 15 MG QD	25	66.3	33.0	-51.3	4.50	-41.9	(-54.7, -29.0)	6.47	<0.001***
		UPA 7.5 MG QD	27	63.4	41.2	-34.8	4.32	-25.4	(-38.0, -12.7)	6.38	<0.001***
		PLACEBO	23	66.0	59.1	-9.5	4.68				
	EU/AUS										
		UPA 30 MG QD	9	61.8	28.6	-53.3	11.10	-48.5	(-81.7, -15.2)	16.29	0.006**
		UPA 15 MG QD	9	60.4	33.4	-43.2	11.12	-38.3	(-71.4, -5.2)	16.23	0.025*
		UPA 7.5 MG QD	10	66.7	43.6	-37.2	10.76	-32.3	(-65.6, 1.0)	16.33	0.057
		PLACEBO	8	57.7	55.1	-4.9	11.93				
	JAPAN										
		UPA 30 MG QD	2	62.1	13.5	-89.5	11.58	-97.6	(-149.9, -45.4)	16.42	0.010**
		UPA 15 MG QD	2	81.1	39.8	-26.3	13.59	-34.4	(-87.9, 19.1)	16.81	0.133
		UPA 7.5 MG QD	2	58.1	33.4	-52.0	12.55	-60.2	(-115.4, -4.9)	17.35	0.040*
		PLACEBO	2	70.7	72.1	8.1	11.13				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.901

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF WEEK 8											
	ALL										
		UPA 30 MG QD	40	62.3	21.0	-65.3	5.52	-58.3	(-71.7, -44.9)	6.78	<0.001***
		UPA 15 MG QD	36	65.7	35.5	-44.1	5.69	-37.1	(-50.8, -23.4)	6.94	<0.001***
		UPA 7.5 MG QD	39	64.0	41.0	-35.4	5.53	-28.4	(-41.9, -15.0)	6.81	<0.001***
		PLACEBO	33	64.2	59.0	-7.0	5.84				
	US/PR/CANADA										
		UPA 30 MG QD	29	62.4	20.1	-67.8	5.09	-57.8	(-73.0, -42.5)	7.67	<0.001***
		UPA 15 MG QD	25	66.3	35.8	-45.6	5.48	-35.5	(-51.2, -19.9)	7.89	<0.001***
		UPA 7.5 MG QD	27	63.4	41.3	-35.3	5.26	-25.3	(-40.7, -9.9)	7.77	0.002**
		PLACEBO	23	66.0	59.0	-10.0	5.71				
	EU/AUS										
		UPA 30 MG QD	9	61.8	25.7	-58.6	11.50	-52.2	(-86.6, -17.7)	16.88	0.004**
		UPA 15 MG QD	9	60.4	33.7	-42.1	11.53	-35.6	(-70.0, -1.3)	16.82	0.042*
		UPA 7.5 MG QD	10	66.7	41.5	-41.1	11.15	-34.7	(-69.2, -0.2)	16.92	0.049*
		PLACEBO	8	57.7	53.9	-6.4	12.37				
	JAPAN										
		UPA 30 MG QD	2	62.1	13.1	-90.6	14.78	-109.3	(-176.1, -42.6)	20.96	0.014*
		UPA 15 MG QD	2	81.1	39.4	-26.1	17.36	-44.9	(-113.2, 23.4)	21.46	0.128
		UPA 7.5 MG QD	2	58.1	34.7	-50.2	16.02	-69.0	(-139.5, 1.5)	22.15	0.053
		PLACEBO	2	70.7	79.4	18.8	14.21				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.864

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 12											
	ALL										
		UPA 30 MG QD	40	62.3	21.8	-62.4	5.45	-50.6	(-63.8, -37.4)	6.68	<0.001***
		UPA 15 MG QD	36	65.7	33.9	-46.5	5.61	-34.7	(-48.2, -21.2)	6.84	<0.001***
		UPA 7.5 MG QD	39	64.0	45.1	-27.8	5.46	-16.0	(-29.3, -2.7)	6.71	0.018*
		PLACEBO	33	64.2	55.8	-11.8	5.75				
	US/PR/CANADA										
		UPA 30 MG QD	29	62.4	19.8	-67.9	5.24	-49.0	(-64.7, -33.4)	7.89	<0.001***
		UPA 15 MG QD	25	66.3	31.6	-53.0	5.64	-34.0	(-50.2, -17.9)	8.13	<0.001***
		UPA 7.5 MG QD	27	63.4	46.5	-26.7	5.42	-7.8	(-23.7, 8.1)	8.00	0.332
		PLACEBO	23	66.0	54.6	-18.9	5.88				
	EU/AUS										
		UPA 30 MG QD	9	61.8	29.6	-52.4	9.92	-47.5	(-77.2, -17.8)	14.56	0.003**
		UPA 15 MG QD	9	60.4	35.0	-40.9	9.94	-36.0	(-65.6, -6.4)	14.50	0.019*
		UPA 7.5 MG QD	10	66.7	44.5	-34.6	9.62	-29.7	(-59.5, 0.0)	14.59	0.050*
		PLACEBO	8	57.7	54.9	-4.9	10.66				
	JAPAN										
		UPA 30 MG QD	2	62.1	16.4	-79.5	18.07	-88.2	(-169.8, -6.6)	25.63	0.041*
		UPA 15 MG QD	2	81.1	57.1	-14.3	21.22	-23.0	(-106.5, 60.5)	26.24	0.446
		UPA 7.5 MG QD	2	58.1	28.7	-59.0	19.60	-67.6	(-153.8, 18.6)	27.09	0.088
		PLACEBO	2	70.7	73.5	8.7	17.37				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.444

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	40	62.3	22.3	-60.4	5.65	-48.0	(-61.7, -34.3)	6.93	<0.001***
		UPA 15 MG QD	36	65.7	33.4	-46.9	5.82	-34.5	(-48.5, -20.5)	7.10	<0.001***
		UPA 7.5 MG QD	39	64.0	42.8	-32.5	5.66	-20.2	(-33.9, -6.4)	6.96	0.004**
		PLACEBO	33	64.2	54.4	-12.4	5.97				
	US/PR/CANADA										
		UPA 30 MG QD	29	62.4	19.7	-68.2	5.30	-51.5	(-67.4, -35.7)	7.98	<0.001***
		UPA 15 MG QD	25	66.3	30.6	-55.0	5.71	-38.3	(-54.6, -22.0)	8.22	<0.001***
		UPA 7.5 MG QD	27	63.4	40.7	-38.2	5.48	-21.5	(-37.5, -5.4)	8.09	0.009**
		PLACEBO	23	66.0	55.5	-16.7	5.94				
	EU/AUS										
		UPA 30 MG QD	9	61.8	31.7	-45.2	10.64	-36.6	(-68.4, -4.7)	15.61	0.026*
		UPA 15 MG QD	9	60.4	34.1	-43.0	10.66	-34.3	(-66.0, -2.6)	15.55	0.035*
		UPA 7.5 MG QD	10	66.7	48.7	-24.4	10.31	-15.8	(-47.7, 16.1)	15.65	0.321
		PLACEBO	8	57.7	54.0	-8.7	11.43				
	JAPAN										
		UPA 30 MG QD	2	62.1	17.2	-74.7	20.00	-38.7	(-129.0, 51.6)	28.37	0.266
		UPA 15 MG QD	2	81.1	64.9	-8.7	23.49	27.3	(-65.1, 119.8)	29.04	0.416
		UPA 7.5 MG QD	2	58.1	41.2	-35.8	21.68	0.3	(-95.1, 95.7)	29.98	0.993
		PLACEBO	2	70.7	43.9	-36.1	19.23				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.622

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 2											
	ALL										
		UPA 30 MG QD	40	62.3	32.7	-46.5	4.43	-44.8	(-55.8, -33.7)	5.57	<0.001***
		UPA 15 MG QD	35	65.9	39.7	-39.2	4.63	-37.5	(-48.8, -26.1)	5.76	<0.001***
		UPA 7.5 MG QD	39	64.0	47.2	-26.1	4.44	-24.4	(-35.5, -13.4)	5.61	<0.001***
		PLACEBO	30	62.9	61.6	-1.7	4.83				
	US/PR/CANADA										
		UPA 30 MG QD	29	62.4	31.5	-49.0	4.01	-48.5	(-60.7, -36.2)	6.19	<0.001***
		UPA 15 MG QD	25	66.3	40.1	-40.3	4.32	-39.7	(-52.4, -27.1)	6.38	<0.001***
		UPA 7.5 MG QD	27	63.4	46.2	-28.2	4.15	-27.7	(-40.1, -15.2)	6.28	<0.001***
		PLACEBO	21	65.4	65.2	-0.6	4.70				
	EU/AUS										
		UPA 30 MG QD	9	61.8	37.1	-39.5	9.09	-30.5	(-59.5, -1.5)	14.18	0.040*
		UPA 15 MG QD	8	60.7	35.6	-39.6	9.65	-30.5	(-60.0, -1.0)	14.44	0.043*
		UPA 7.5 MG QD	10	66.7	51.5	-23.0	8.92	-14.0	(-43.7, 15.8)	14.55	0.344
		PLACEBO	7	53.4	49.2	-9.1	10.82				
	JAPAN										
		UPA 30 MG QD	2	62.1	30.4	-64.1	18.53	-66.8	(-150.4, 16.9)	26.28	0.085
		UPA 15 MG QD	2	81.1	51.2	-9.4	21.76	-12.1	(-97.7, 73.6)	26.91	0.685
		UPA 7.5 MG QD	2	58.1	39.8	-41.2	20.09	-43.8	(-132.2, 44.6)	27.78	0.213
		PLACEBO	2	70.7	67.5	2.6	17.82				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.925

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 4											
	ALL										
		UPA 30 MG QD	37	62.6	24.2	-62.2	4.85	-51.9	(-63.9, -39.8)	6.10	<0.001***
		UPA 15 MG QD	35	65.5	33.1	-50.7	4.87	-40.4	(-52.6, -28.2)	6.16	<0.001***
		UPA 7.5 MG QD	38	64.4	41.2	-37.3	4.74	-27.0	(-39.0, -15.0)	6.06	<0.001***
		PLACEBO	27	65.4	58.5	-10.4	5.50				
	US/PR/CANADA										
		UPA 30 MG QD	28	63.3	25.6	-59.9	4.21	-48.7	(-61.5, -35.9)	6.43	<0.001***
		UPA 15 MG QD	24	66.1	32.4	-52.1	4.55	-40.8	(-54.0, -27.7)	6.64	<0.001***
		UPA 7.5 MG QD	26	64.0	40.9	-36.2	4.36	-25.0	(-38.0, -12.1)	6.53	<0.001***
		PLACEBO	21	65.5	57.3	-11.2	4.85				
	EU/AUS										
		UPA 30 MG QD	7	60.3	21.8	-61.8	11.83	-61.2	(-98.7, -23.6)	18.27	0.002**
		UPA 15 MG QD	9	60.4	33.4	-43.6	10.44	-43.0	(-78.8, -7.2)	17.41	0.020*
		UPA 7.5 MG QD	10	66.7	43.6	-36.2	10.01	-35.6	(-70.8, -0.3)	17.15	0.048*
		PLACEBO	5	62.9	62.8	-0.6	13.93				
	JAPAN										
		UPA 30 MG QD	2	62.1	13.5	-88.8	9.46	-81.6	(-153.6, -9.6)	16.73	0.040*
		UPA 15 MG QD	2	81.1	39.8	-28.8	11.10	-21.6	(-89.9, 46.7)	15.87	0.306
		UPA 7.5 MG QD	2	58.1	33.4	-50.6	10.31	-43.4	(-119.2, 32.3)	17.60	0.132
		PLACEBO	1	74.5	61.2	-7.2	13.07				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.932

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 8											
	ALL										
		UPA 30 MG QD	40	62.3	21.0	-65.3	5.42	-55.6	(-69.8, -41.4)	7.20	<0.001***
		UPA 15 MG QD	33	66.0	35.1	-45.0	5.73	-35.3	(-50.1, -20.5)	7.47	<0.001***
		UPA 7.5 MG QD	38	64.2	40.7	-36.2	5.48	-26.5	(-40.8, -12.2)	7.25	<0.001***
		PLACEBO	25	65.0	57.6	-9.7	6.30				
	US/PR/CANADA										
		UPA 30 MG QD	29	62.4	20.1	-67.8	5.12	-52.8	(-69.3, -36.3)	8.30	<0.001***
		UPA 15 MG QD	23	66.4	36.4	-44.5	5.74	-29.5	(-46.6, -12.3)	8.64	<0.001***
		UPA 7.5 MG QD	27	63.4	41.3	-35.3	5.29	-20.3	(-37.0, -3.6)	8.39	0.018*
		PLACEBO	18	66.7	56.3	-15.0	6.49				
	EU/AUS										
		UPA 30 MG QD	9	61.8	25.7	-58.3	10.39	-56.0	(-92.1, -19.9)	17.56	0.004**
		UPA 15 MG QD	8	61.1	30.2	-48.8	11.04	-46.4	(-83.2, -9.7)	17.90	0.015*
		UPA 7.5 MG QD	9	68.0	40.1	-46.4	10.73	-44.0	(-81.6, -6.4)	18.29	0.023*
		PLACEBO	5	56.6	53.7	-2.4	14.25				
	JAPAN										
		UPA 30 MG QD	2	62.1	13.1	-90.6	14.78	-109.3	(-176.1, -42.6)	20.96	0.014*
		UPA 15 MG QD	2	81.1	39.4	-26.1	17.36	-44.9	(-113.2, 23.4)	21.46	0.128
		UPA 7.5 MG QD	2	58.1	34.7	-50.2	16.02	-69.0	(-139.5, 1.5)	22.15	0.053
		PLACEBO	2	70.7	79.4	18.8	14.21				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.653

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 12											
	ALL										
		UPA 30 MG QD	37	61.5	20.3	-64.5	5.50	-45.5	(-59.9, -31.1)	7.28	<0.001***
		UPA 15 MG QD	32	65.7	32.6	-49.1	5.75	-30.1	(-44.9, -15.3)	7.46	<0.001***
		UPA 7.5 MG QD	34	64.2	43.7	-30.7	5.60	-11.7	(-26.4, 2.9)	7.38	0.114
		PLACEBO	24	65.3	52.7	-19.0	6.39				
	US/PR/CANADA										
		UPA 30 MG QD	28	62.5	19.7	-68.1	5.35	-43.7	(-60.4, -27.0)	8.41	<0.001***
		UPA 15 MG QD	24	66.1	31.0	-53.6	5.77	-29.3	(-46.5, -12.1)	8.66	0.001**
		UPA 7.5 MG QD	25	63.6	47.1	-26.4	5.64	-2.0	(-19.1, 15.0)	8.60	0.814
		PLACEBO	19	65.6	50.7	-24.4	6.48				
	EU/AUS										
		UPA 30 MG QD	7	57.3	23.7	-56.9	8.79	-42.4	(-75.6, -9.2)	15.80	0.015*
		UPA 15 MG QD	6	58.8	30.6	-47.1	9.39	-32.6	(-66.5, 1.4)	16.17	0.059
		UPA 7.5 MG QD	7	67.8	35.7	-50.0	9.07	-35.5	(-69.4, -1.6)	16.13	0.041*
		PLACEBO	3	59.7	51.4	-14.5	13.21				
	JAPAN										
		UPA 30 MG QD	2	62.1	16.4	-79.5	18.07	-88.2	(-169.8, -6.6)	25.63	0.041*
		UPA 15 MG QD	2	81.1	57.1	-14.3	21.22	-23.0	(-106.5, 60.5)	26.24	0.446
		UPA 7.5 MG QD	2	58.1	28.7	-59.0	19.60	-67.6	(-153.8, 18.6)	27.09	0.088
		PLACEBO	2	70.7	73.5	8.7	17.37				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.180

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 16											
	ALL										
		UPA 30 MG QD	37	61.7	20.6	-62.2	5.88	-44.4	(-60.4, -28.4)	8.07	<0.001***
		UPA 15 MG QD	30	66.5	30.5	-52.8	6.20	-35.0	(-51.5, -18.4)	8.37	<0.001***
		UPA 7.5 MG QD	32	62.9	40.3	-35.2	6.13	-17.4	(-33.7, -1.0)	8.26	0.038*
		PLACEBO	21	66.8	52.8	-17.8	7.28				
	US/PR/CANADA										
		UPA 30 MG QD	29	62.4	19.7	-68.2	5.25	-49.1	(-65.9, -32.2)	8.48	<0.001***
		UPA 15 MG QD	22	66.4	28.6	-58.3	6.02	-39.2	(-57.0, -21.4)	8.95	<0.001***
		UPA 7.5 MG QD	25	63.6	40.8	-38.9	5.63	-19.7	(-37.1, -2.4)	8.72	0.026*
		PLACEBO	18	65.8	53.6	-19.1	6.65				
	EU/AUS										
		UPA 30 MG QD	6	58.0	25.9	-53.1	12.60	-50.1	(-126.7, 26.5)	35.45	0.181
		UPA 15 MG QD	6	61.8	26.0	-56.3	12.39	-53.3	(-127.7, 21.1)	34.44	0.146
		UPA 7.5 MG QD	5	60.9	37.4	-39.3	13.56	-36.3	(-112.1, 39.6)	35.10	0.321
		PLACEBO	1	75.8	56.7	-3.0	32.33				
	JAPAN										
		UPA 30 MG QD	2	62.1	17.2	-74.7	20.00	-38.7	(-129.0, 51.6)	28.37	0.266
		UPA 15 MG QD	2	81.1	64.9	-8.7	23.49	27.3	(-65.1, 119.8)	29.04	0.416
		UPA 7.5 MG QD	2	58.1	41.2	-35.8	21.68	0.3	(-95.1, 95.7)	29.98	0.993
		PLACEBO	2	70.7	43.9	-36.1	19.23				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.467

[A] ACROSS THE STRATA, P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, AND TREATMENT IN THE MODEL.
WITHIN EACH STRATUM, P-VALUES WERE CALCULATED FROM ANCOVA WITH BASELINE VALUE AND THE TREATMENT IN THE MODEL.
@ P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, TREATMENT, INTERACTION OF STRATUM AND TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.
Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.8.1

表 2.7.3.6-59.　第 1 ピリオドの来院時別の SCORAD 50 を達成した被験者の割合（NRI，LOCF，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 2													
	ALL												
		UPA 30 MG QD	42	19	(45.2)	22	(52.4)	1	(2.4)	40.4	40.3	(23.9, 56.7)	<0.001***
		UPA 15 MG QD	42	12	(28.6)	29	(69.0)	1	(2.4)	23.7	23.9	(8.8, 39 1)	0.002**
		UPA 7.5 MG QD	42	8	(19.0)	32	(76.2)	2	(4.8)	14.2	14.2	(0.7, 27.6)	0.039*
		PLACEBO	41	2	(4.9)	33	(80.5)	6	(14.6)				
	US/PR/CANADA												
		UPA 30 MG QD	29	14	(48.3)	15	(51.7)	0		44.8		(25.5, 64.2)	<0.001***
		UPA 15 MG QD	29	9	(31.0)	20	(69.0)	0		27.6		(9.5, 45.7)	0.005**
		UPA 7.5 MG QD	29	6	(20.7)	21	(72.4)	2	(6.9)	17.2		(1.1, 33.4)	0.102
		PLACEBO	29	1	(3.4)	24	(82.8)	4	(13.8)				
	EU/AUS												
		UPA 30 MG QD	10	4	(40.0)	6	(60.0)	0		30.0		(-5.6, 65.6)	0.303
		UPA 15 MG QD	10	3	(30.0)	6	(60.0)	1	(10.0)	20.0		(-13.9, 53.9)	0.582
		UPA 7.5 MG QD	11	1	(9.1)	10	(90.9)	0		-0.9		(-26.1, 24.3)	1.000
		PLACEBO	10	1	(10.0)	7	(70.0)	2	(20.0)				
	JAPAN												
		UPA 30 MG QD	3	1	(33.3)	1	(33.3)	1	(33.3)	33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	1	(50.0)	1	(50.0)	0		50.0		(-19.3, 100.0)	1.000
		PLACEBO	2	0		2	(100)	0					

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.625
UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.468
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.377

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 4													
	ALL												
		UPA 30 MG QD	42	30	(71.4)	9	(21.4)	3	(7.1)	71.4	70.4	(57.1, 83.8)	<0.001***
		UPA 15 MG QD	42	18	(42.9)	22	(52.4)	2	(4.8)	42.9	42.3	(27.2, 57.4)	<0.001***
		UPA 7.5 MG QD	42	14	(33.3)	25	(59.5)	3	(7.1)	33.3	32.8	(18.5, 47.1)	<0.001***
		PLACEBO	41	0		30	(73.2)	11	(26.8)				
	US/PR/CANADA												
		UPA 30 MG QD	29	23	(79.3)	5	(17.2)	1	(3.4)	79.3		(64.6, 94.1)	<0.001***
		UPA 15 MG QD	29	13	(44.8)	14	(48.3)	2	(6.9)	44.8		(26.7, 62.9)	<0.001***
		UPA 7.5 MG QD	29	9	(31.0)	17	(58.6)	3	(10.3)	31.0		(14.2, 47.9)	0.002**
		PLACEBO	29	0		24	(82.8)	5	(17.2)				
	EU/AUS												
		UPA 30 MG QD	10	5	(50.0)	3	(30.0)	2	(20.0)	50.0		(19.0, 81.0)	0.033*
		UPA 15 MG QD	10	4	(40.0)	6	(60.0)	0		40.0		(9.6, 70.4)	0.087
		UPA 7.5 MG QD	11	4	(36.4)	7	(63.6)	0		36.4		(7.9, 64.8)	0.090
		PLACEBO	10	0		5	(50.0)	5	(50.0)				
	JAPAN												
		UPA 30 MG QD	3	2	(66.7)	1	(33.3)	0		66.7		(13.3, 100.0)	0.400
		UPA 15 MG QD	3	1	(33.3)	2	(66.7)	0		33.3		(-20.0, 86.7)	1.000
		UPA 7.5 MG QD	2	1	(50.0)	1	(50.0)	0		50.0		(-19.3, 100.0)	1.000
		PLACEBO	2	0		1	(50.0)	1	(50.0)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA											

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 8													
	ALL												
		UPA 30 MG QD	42	32	(76.2)	10	(23.8)	0		68.9	68.4	(54.0, 82.8)	<0.001***
		UPA 15 MG QD	42	18	(42.9)	21	(50.0)	3	(7.1)	35.5	35.3	(18.5, 52.2)	<0.001***
		UPA 7.5 MG QD	42	14	(33.3)	25	(59.5)	3	(7.1)	26.0	25.7	(9.6, 41.7)	0.002**
		PLACEBO	41	3	(7.3)	26	(63.4)	12	(29.3)				
	US/PR/CANADA												
		UPA 30 MG QD	29	25	(86.2)	4	(13.8)	0		75.9		(59.1, 92.6)	<0.001***
		UPA 15 MG QD	29	12	(41.4)	15	(51.7)	2	(6.9)	31.0		(10.0, 52.1)	0.007**
		UPA 7.5 MG QD	29	8	(27.6)	19	(65.5)	2	(6.9)	17.2		(-2.4, 36.9)	0.094
		PLACEBO	29	3	(10.3)	18	(62.1)	8	(27.6)				
	EU/AUS												
		UPA 30 MG QD	10	5	(50.0)	5	(50.0)	0		50.0		(19.0, 81.0)	0.033*
		UPA 15 MG QD	10	5	(50.0)	4	(40.0)	1	(10.0)	50.0		(19.0, 81.0)	0.033*
		UPA 7.5 MG QD	11	5	(45.5)	5	(45.5)	1	(9.1)	45.5		(16.0, 74.9)	0.035*
		PLACEBO	10	0		6	(60.0)	4	(40.0)				
	JAPAN												
		UPA 30 MG QD	3	2	(66.7)	1	(33.3)	0		66.7		(13.3, 100.0)	0.400
		UPA 15 MG QD	3	1	(33.3)	2	(66.7)	0		33.3		(-20.0, 86.7)	1.000
		UPA 7.5 MG QD	2	1	(50.0)	1	(50.0)	0		50.0		(-19.3, 100.0)	1.000
		PLACEBO	2	0		2	(100)	0					
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.861											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.477											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.321											

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 12													
	ALL												
		UPA 30 MG QD	42	30	(71.4)	10	(23.8)	2	(4.8)	61.7	61.2	(45.8, 76.6)	<0.001***
		UPA 15 MG QD	42	18	(42.9)	20	(47.6)	4	(9.5)	33.1	33.4	(16.4, 50.4)	<0.001***
		UPA 7.5 MG QD	42	9	(21.4)	26	(61.9)	7	(16.7)	11.7	11.5	(-3.3, 26.3)	0.129
		PLACEBO	41	4	(9.8)	24	(58.5)	13	(31.7)				
	US/PR/CANADA												
		UPA 30 MG QD	29	24	(82.8)	5	(17.2)	0		69.0		(50.4, 87.6)	<0.001***
		UPA 15 MG QD	29	15	(51.7)	12	(41.4)	2	(6.9)	37.9		(15.8, 60.0)	0.002**
		UPA 7.5 MG QD	29	4	(13.8)	21	(72.4)	4	(13.8)	0.0		(-17.7, 17.7)	1.000
		PLACEBO	29	4	(13.8)	18	(62.1)	7	(24.1)				
	EU/AUS												
		UPA 30 MG QD	10	4	(40.0)	4	(40.0)	2	(20.0)	40.0		(9.6, 70.4)	0.087
		UPA 15 MG QD	10	3	(30.0)	5	(50.0)	2	(20.0)	30.0		(1.6, 58.4)	0.211
		UPA 7.5 MG QD	11	4	(36.4)	4	(36.4)	3	(27.3)	36.4		(7.9, 64.8)	0.090
		PLACEBO	10	0		4	(40.0)	6	(60.0)				
	JAPAN												
		UPA 30 MG QD	3	2	(66.7)	1	(33.3)	0		66.7		(13.3, 100.0)	0.400
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	1	(50.0)	1	(50.0)	0		50.0		(-19.3, 100.0)	1.000
		PLACEBO	2	0		2	(100)	0					
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.825											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.434											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.124											

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 16													
	ALL												
		UPA 30 MG QD	42	26	(61.9)	13	(31.0)	3	(7.1)	54.6	54.5	(39.0, 69.9)	<0.001***
		UPA 15 MG QD	42	18	(42.9)	16	(38.1)	8	(19.0)	35.5	35.8	(19.1, 52.5)	<0.001***
		UPA 7.5 MG QD	42	12	(28.6)	21	(50.0)	9	(21.4)	21.3	21.2	(5.7, 36.8)	0.008**
		PLACEBO	41	3	(7.3)	21	(51.2)	17	(41.5)				
	US/PR/CANADA												
		UPA 30 MG QD	29	22	(75.9)	7	(24.1)	0		65.5		(46.4, 84.6)	<0.001***
		UPA 15 MG QD	29	14	(48.3)	11	(37.9)	4	(13.8)	37.9		(16.6, 59.2)	0.002**
		UPA 7.5 MG QD	29	10	(34.5)	15	(51.7)	4	(13.8)	24.1		(3.6, 44.7)	0.028*
		PLACEBO	29	3	(10.3)	17	(58.6)	9	(31.0)				
	EU/AUS												
		UPA 30 MG QD	10	3	(30.0)	4	(40.0)	3	(30.0)	30.0		(1.6, 58.4)	0.211
		UPA 15 MG QD	10	4	(40.0)	3	(30.0)	3	(30.0)	40.0		(9.6, 70.4)	0.087
		UPA 7.5 MG QD	11	2	(18.2)	4	(36.4)	5	(45.5)	18.2		(-4.6, 41.0)	0.476
		PLACEBO	10	0		2	(20.0)	8	(80.0)				
	JAPAN												
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	0		33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		2	(66.7)	1	(33.3)				NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.897											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.383											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.494											

IMPUTATION / VISIT / STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF										
WEEK 2										
ALL										
	UPA 30 MG QD	41	19	(46.3)	22	(53.7)	40.6	40.4	(23.3, 57.5)	<0.001***
	UPA 15 MG QD	41	12	(29.3)	29	(70.7)	23.6	23.7	(7.9, 39.5)	0.003**
	UPA 7.5 MG QD	40	8	(20.0)	32	(80.0)	14.3	14.5	(-0.2, 29.1)	0.053
	PLACEBO	35	2	(5.7)	33	(94.3)				
US/PR/CANADA										
	UPA 30 MG QD	29	14	(48.3)	15	(51.7)	44.3		(24.5, 64.0)	<0.001***
	UPA 15 MG QD	29	9	(31.0)	20	(69.0)	27.0		(8.5, 45.5)	0.014*
	UPA 7.5 MG QD	27	6	(22.2)	21	(77.8)	18.2		(0.8, 35.7)	0.101
	PLACEBO	25	1	(4.0)	24	(96.0)				
EU/AUS										
	UPA 30 MG QD	10	4	(40.0)	6	(60.0)	27.5		(-10.5, 65.5)	0.314
	UPA 15 MG QD	9	3	(33.3)	6	(66.7)	20.8		(-17.6, 59.2)	0.576
	UPA 7.5 MG QD	11	1	(9.1)	10	(90.9)	-3.4		(-31.9, 25.1)	1.000
	PLACEBO	8	1	(12.5)	7	(87.5)				
JAPAN										
	UPA 30 MG QD	2	1	(50.0)	1	(50.0)	50.0		(-19.3, 100.0)	1.000
	UPA 15 MG QD	3	0		3	(100)				NA
	UPA 7.5 MG QD	2	1	(50.0)	1	(50.0)	50.0		(-19.3, 100.0)	1.000
	PLACEBO	2	0		2	(100)				

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.565
UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.495
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.317

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	30	(71.4)	12	(28.6)	68.8	68.2	(54.1, 82.4)	<0.001***
		UPA 15 MG QD	42	18	(42.9)	24	(57.1)	40.2	39.9	(24.0, 55.7)	<0.001***
		UPA 7.5 MG QD	40	14	(35.0)	26	(65.0)	32.4	31.8	(16.1, 47.5)	<0.001***
		PLACEBO	38	1	(2.6)	37	(97.4)				
	US/PR/CANADA										
		UPA 30 MG QD	29	23	(79.3)	6	(20.7)	79.3		(64.6, 94.1)	<0.001***
		UPA 15 MG QD	29	13	(44.8)	16	(55.2)	44.8		(26.7, 62.9)	<0.001***
		UPA 7.5 MG QD	27	9	(33.3)	18	(66.7)	33.3		(15.6, 51.1)	0.002**
		PLACEBO	27	0		27	(100)				
	EU/AUS										
		UPA 30 MG QD	10	5	(50.0)	5	(50.0)	38.9		(1.7, 76.1)	0.141
		UPA 15 MG QD	10	4	(40.0)	6	(60.0)	28.9		(-7.8, 65.5)	0.303
		UPA 7.5 MG QD	11	4	(36.4)	7	(63.6)	25.3		(-9.8, 60.3)	0.319
		PLACEBO	9	1	(11.1)	8	(88.9)				
	JAPAN										
		UPA 30 MG QD	3	2	(66.7)	1	(33.3)	66.7		(13.3, 100.0)	0.400
		UPA 15 MG QD	3	1	(33.3)	2	(66.7)	33.3		(-20.0, 86.7)	1.000
		UPA 7.5 MG QD	2	1	(50.0)	1	(50.0)	50.0		(-19.3, 100.0)	1.000
		PLACEBO	2	0		2	(100)				

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.087
UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.243
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.312

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 8											
	ALL										
		UPA 30 MG QD	42	32	(76.2)	10	(23.8)	65.7	65.6	(50.2, 81.0)	<0.001***
		UPA 15 MG QD	42	18	(42.9)	24	(57.1)	32.3	32.3	(14.5, 50.1)	<0.001***
		UPA 7.5 MG QD	40	14	(35.0)	26	(65.0)	24.5	24.0	(6.5, 41.6)	0.007**
		PLACEBO	38	4	(10.5)	34	(89.5)				
	US/PR/CANADA										
		UPA 30 MG QD	29	25	(86.2)	4	(13.8)	75.1		(57.8, 92.4)	<0.001***
		UPA 15 MG QD	29	12	(41.4)	17	(58.6)	30.3		(8.8, 51.8)	0.011*
		UPA 7.5 MG QD	27	8	(29.6)	19	(70.4)	18.5		(-2.4, 39.4)	0.091
		PLACEBO	27	3	(11.1)	24	(88.9)				
	EU/AUS										
		UPA 30 MG QD	10	5	(50.0)	5	(50.0)	38.9		(1.7, 76.1)	0.141
		UPA 15 MG QD	10	5	(50.0)	5	(50.0)	38.9		(1.7, 76.1)	0.141
		UPA 7.5 MG QD	11	5	(45.5)	6	(54.5)	34.3		(-1.5, 70.2)	0.157
		PLACEBO	9	1	(11.1)	8	(88.9)				
	JAPAN										
		UPA 30 MG QD	3	2	(66.7)	1	(33.3)	66.7		(13.3, 100.0)	0.400
		UPA 15 MG QD	3	1	(33.3)	2	(66.7)	33.3		(-20.0, 86.7)	1.000
		UPA 7.5 MG QD	2	1	(50.0)	1	(50.0)	50.0		(-19.3, 100.0)	1.000
		PLACEBO	2	0		2	(100)				

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.410
UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.897
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.722

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 12											
	ALL										
		UPA 30 MG QD	42	30	(71.4)	12	(28.6)	58.3	58.3	(41.8, 74.7)	<0.001***
		UPA 15 MG QD	42	18	(42.9)	24	(57.1)	29.7	30.2	(12.2, 48.1)	<0.001***
		UPA 7.5 MG QD	40	10	(25.0)	30	(75.0)	11.8	11.5	(-5.3, 28.3)	0.180
		PLACEBO	38	5	(13.2)	33	(86.8)				
	US/PR/CANADA										
		UPA 30 MG QD	29	24	(82.8)	5	(17.2)	67.9		(48.7, 87.1)	<0.001***
		UPA 15 MG QD	29	15	(51.7)	14	(48.3)	36.9		(14.3, 59.5)	0.004**
		UPA 7.5 MG QD	27	5	(18.5)	22	(81.5)	3.7		(-16.2, 23.6)	1.000
		PLACEBO	27	4	(14.8)	23	(85.2)				
	EU/AUS										
		UPA 30 MG QD	10	4	(40.0)	6	(60.0)	28.9		(-7.8, 65.5)	0.303
		UPA 15 MG QD	10	3	(30.0)	7	(70.0)	18.9		(-16.2, 53.9)	0.582
		UPA 7.5 MG QD	11	4	(36.4)	7	(63.6)	25.3		(-9.8, 60.3)	0.319
		PLACEBO	9	1	(11.1)	8	(88.9)				
	JAPAN										
		UPA 30 MG QD	3	2	(66.7)	1	(33.3)	66.7		(13.3, 100.0)	0.400
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	1	(50.0)	1	(50.0)	50.0		(-19.3, 100.0)	1.000
		PLACEBO	2	0		2	(100)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.447									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.680									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.453									

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	42	26	(61.9)	16	(38.1)	48.7	49.0	(32.0, 66.0)	<0.001***
		UPA 15 MG QD	42	18	(42.9)	24	(57.1)	29.7	30.1	(12.0, 48.2)	0.001**
		UPA 7.5 MG QD	40	13	(32.5)	27	(67.5)	19.3	19.7	(2.0, 37.4)	0.030*
		PLACEBO	38	5	(13.2)	33	(86.8)				
	US/PR/CANADA										
		UPA 30 MG QD	29	22	(75.9)	7	(24.1)	61.0		(40.5, 81.6)	<0.001***
		UPA 15 MG QD	29	14	(48.3)	15	(51.7)	33.5		(10.9, 56.1)	0.007**
		UPA 7.5 MG QD	27	11	(40.7)	16	(59.3)	25.9		(3.1, 48.8)	0.033*
		PLACEBO	27	4	(14.8)	23	(85.2)				
	EU/AUS										
		UPA 30 MG QD	10	3	(30.0)	7	(70.0)	18.9		(-16.2, 53.9)	0.582
		UPA 15 MG QD	10	4	(40.0)	6	(60.0)	28.9		(-7.8, 65.5)	0.303
		UPA 7.5 MG QD	11	2	(18.2)	9	(81.8)	7.1		(-23.6, 37.7)	1.000
		PLACEBO	9	1	(11.1)	8	(88.9)				
	JAPAN										
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.468									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.996									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = 0.585									

NA = NOT APPLICABLE.
[A]: ACROSS THE STRATA, 95% CI FOR ADJUSTED DIFFERENCE WAS CALCULATED ACCORDING TO THE COCHRAN-MANTEL-HAENSZEL TEST FOR THE COMPARISON OF TWO TREATMENT GROUPS. WITHIN EACH STRATUM, 95% CI FOR DIFFERENCE WAS CALCULATED BASED ON NORMAL APPROXIMATION TO THE BINOMIAL DISTRIBUTION.
[B]: ACROSS THE STRATA, P-VALUE WAS CALCULATED FROM THE COCHRAN-MANTEL-HAENSZEL TEST ADJUSTED FOR STRATA. WITHIN EACH STRATUM, P-VALUE WAS CALCULATED BASED ON CHI-SQUARE TEST (OR FISHER'S EXACT TEST IF >= 25% OF THE CELLS HAVE EXPECTED CELL COUNT < 5).
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.9

表 2.7.3.6-60.　第 1 ピリオドの来院時別の SCORAD 75 を達成した被験者の割合（NRI，LOCF，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 2													
	ALL												
		UPA 30 MG QD	42	3	(7.1)	38	(90.5)	1	(2.4)	7.1	7.1	(-1.5, 15.6)	0.104
		UPA 15 MG QD	42	1	(2.4)	40	(95.2)	1	(2.4)	2.4	2.3	(-3.5, 8.1)	0.440
		UPA 7.5 MG QD	42	1	(2.4)	39	(92.9)	2	(4.8)	2.4	2.4	(-3.4, 8.1)	0.426
		PLACEBO	41	0		35	(85.4)	6	(14.6)				
	US/PR/CANADA												
		UPA 30 MG QD	29	2	(6.9)	27	(93.1)	0		6.9		(-2.3, 16.1)	0.491
		UPA 15 MG QD	29	1	(3.4)	28	(96.6)	0		3.4		(-3.2, 10.1)	1.000
		UPA 7.5 MG QD	29	1	(3.4)	26	(89.7)	2	(6.9)	3.4		(-3.2, 10.1)	1.000
		PLACEBO	29	0		25	(86.2)	4	(13.8)				
	EU/AUS												
		UPA 30 MG QD	10	1	(10.0)	9	(90.0)	0		10.0		(-8.6, 28.6)	1.000
		UPA 15 MG QD	10	0		9	(90.0)	1	(10.0)				NA
		UPA 7.5 MG QD	11	0		11	(100)	0					NA
		PLACEBO	10	0		8	(80.0)	2	(20.0)				
	JAPAN												
		UPA 30 MG QD	3	0		2	(66.7)	1	(33.3)				NA
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = NA
UPA 15 MG QD VS. PLACEBO: P-VALUE = NA
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 4													
	ALL												
		UPA 30 MG QD	42	8	(19.0)	31	(73.8)	3	(7.1)	19.0	18.1	(6.6, 29 5)	0.002**
		UPA 15 MG QD	42	6	(14.3)	34	(81.0)	2	(4.8)	14.3	14.2	(3.2, 25 2)	0.012*
		UPA 7.5 MG QD	42	5	(11.9)	34	(81.0)	3	(7.1)	11.9	11.6	(1.5, 21.8)	0.024*
		PLACEBO	41	0		30	(73.2)	11	(26.8)				
	US/PR/CANADA												
		UPA 30 MG QD	29	4	(13.8)	24	(82.8)	1	(3.4)	13.8		(1.2, 26 3)	0.112
		UPA 15 MG QD	29	4	(13.8)	23	(79.3)	2	(6.9)	13.8		(1.2, 26 3)	0.112
		UPA 7.5 MG QD	29	3	(10.3)	23	(79.3)	3	(10.3)	10.3		(-0.7, 21.4)	0.237
		PLACEBO	29	0		24	(82.8)	5	(17.2)				
	EU/AUS												
		UPA 30 MG QD	10	2	(20.0)	6	(60.0)	2	(20.0)	20.0		(-4.8, 44.8)	0.474
		UPA 15 MG QD	10	2	(20.0)	8	(80.0)	0		20.0		(-4.8, 44.8)	0.474
		UPA 7.5 MG QD	11	2	(18.2)	9	(81.8)	0		18.2		(-4.6, 41.0)	0.476
		PLACEBO	10	0		5	(50.0)	5	(50.0)				
	JAPAN												
		UPA 30 MG QD	3	2	(66.7)	1	(33.3)	0		66.7		(13.3, 100.0)	0.400
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		1	(50.0)	1	(50.0)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA											

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 8													
	ALL												
		UPA 30 MG QD	42	13	(31.0)	29	(69.0)	0		31.0	30.4	(16.2, 44.6)	<0.001***
		UPA 15 MG QD	42	4	(9.5)	34	(81.0)	4	(9.5)	9.5	9.4	(-0.1, 18.9)	0.052
		UPA 7.5 MG QD	42	4	(9.5)	35	(83.3)	3	(7.1)	9.5	9.3	(0.1, 18 5)	0.048*
		PLACEBO	41	0		29	(70.7)	12	(29.3)				
	US/PR/CANADA												
		UPA 30 MG QD	29	9	(31.0)	20	(69.0)	0		31.0		(14.2, 47.9)	0.002**
		UPA 15 MG QD	29	3	(10.3)	23	(79.3)	3	(10.3)	10.3		(-0.7, 21.4)	0.237
		UPA 7.5 MG QD	29	2	(6.9)	25	(86.2)	2	(6.9)	6.9		(-2.3, 16.1)	0.491
		PLACEBO	29	0		21	(72.4)	8	(27.6)				
	EU/AUS												
		UPA 30 MG QD	10	3	(30.0)	7	(70.0)	0		30.0		(1.6, 58.4)	0.211
		UPA 15 MG QD	10	1	(10.0)	8	(80.0)	1	(10.0)	10.0		(-8.6, 28.6)	1.000
		UPA 7.5 MG QD	11	2	(18.2)	8	(72.7)	1	(9.1)	18.2		(-4.6, 41.0)	0.476
		PLACEBO	10	0		6	(60.0)	4	(40.0)				
	JAPAN												
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	0		33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA											

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 12													
	ALL												
		UPA 30 MG QD	42	12	(28.6)	27	(64.3)	3	(7.1)	26.1	25.8	(11.3, 40.3)	<0.001***
		UPA 15 MG QD	42	7	(16.7)	30	(71.4)	5	(11.9)	14.2	14.3	(1.8, 26.7)	0.025*
		UPA 7.5 MG QD	42	2	(4.8)	33	(78.6)	7	(16.7)	2.3	2.4	(-6.0, 10.8)	0.581
		PLACEBO	41	1	(2.4)	27	(65.9)	13	(31.7)				
	US/PR/CANADA												
		UPA 30 MG QD	29	9	(31.0)	19	(65.5)	1	(3.4)	27.6		(9.5, 45.7)	0.005**
		UPA 15 MG QD	29	5	(17.2)	22	(75.9)	2	(6.9)	13.8		(-1.5, 29.1)	0.194
		UPA 7.5 MG QD	29	2	(6.9)	23	(79.3)	4	(13.8)	3.4		(-7.9, 14.8)	1.000
		PLACEBO	29	1	(3.4)	21	(72.4)	7	(24.1)				
	EU/AUS												
		UPA 30 MG QD	10	2	(20.0)	6	(60.0)	2	(20.0)	20.0		(-4.8, 44.8)	0.474
		UPA 15 MG QD	10	2	(20.0)	5	(50.0)	3	(30.0)	20.0		(-4.8, 44.8)	0.474
		UPA 7.5 MG QD	11	0		8	(72.7)	3	(27.3)				NA
		PLACEBO	10	0		4	(40.0)	6	(60.0)				
	JAPAN												
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	0		33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.872
UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.529
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 16													
	ALL												
		UPA 30 MG QD	42	17	(40.5)	22	(52.4)	3	(7.1)	38.0	37.7	(22.2, 53.3)	<0.001***
		UPA 15 MG QD	42	9	(21.4)	25	(59.5)	8	(19.0)	19.0	19.0	(5.6, 32 5)	0.006**
		UPA 7.5 MG QD	42	2	(4.8)	31	(73.8)	9	(21.4)	2.3	2.4	(-6.0, 10.8)	0.581
		PLACEBO	41	1	(2.4)	23	(56.1)	17	(41.5)				
	US/PR/CANADA												
		UPA 30 MG QD	29	13	(44.8)	16	(55.2)	0		41.4		(22.1, 60.7)	<0.001***
		UPA 15 MG QD	29	7	(24.1)	18	(62.1)	4	(13.8)	20.7		(3.8, 37.6)	0.052
		UPA 7.5 MG QD	29	2	(6.9)	23	(79.3)	4	(13.8)	3.4		(-7.9, 14.8)	1.000
		PLACEBO	29	1	(3.4)	19	(65.5)	9	(31.0)				
	EU/AUS												
		UPA 30 MG QD	10	3	(30.0)	4	(40.0)	3	(30.0)	30.0		(1.6, 58.4)	0.211
		UPA 15 MG QD	10	2	(20.0)	5	(50.0)	3	(30.0)	20.0		(-4.8, 44.8)	0.474
		UPA 7.5 MG QD	11	0		6	(54.5)	5	(45.5)				NA
		PLACEBO	10	0		2	(20.0)	8	(80.0)				
	JAPAN												
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	0		33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		2	(66.7)	1	(33.3)				NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.888
UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.603
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 2											
	ALL										
		UPA 30 MG QD	41	3	(7.3)	38	(92.7)	7.3	7.1	(-1.6, 15.7)	0.111
		UPA 15 MG QD	41	1	(2.4)	40	(97.6)	2.4	2.3	(-3.8, 8.3)	0.469
		UPA 7.5 MG QD	40	1	(2.5)	39	(97.5)	2.5	2.4	(-3.9, 8.7)	0.447
		PLACEBO	35	0		35	(100)				
	US/PR/CANADA										
		UPA 30 MG QD	29	2	(6.9)	27	(93.1)	6.9		(-2.3, 16.1)	0.493
		UPA 15 MG QD	29	1	(3.4)	28	(96.6)	3.4		(-3.2, 10.1)	1.000
		UPA 7.5 MG QD	27	1	(3.7)	26	(96.3)	3.7		(-3.4, 10.8)	1.000
		PLACEBO	25	0		25	(100)				
	EU/AUS										
		UPA 30 MG QD	10	1	(10.0)	9	(90.0)	10.0		(-8.6, 28.6)	1.000
		UPA 15 MG QD	9	0		9	(100)				NA
		UPA 7.5 MG QD	11	0		11	(100)				NA
		PLACEBO	8	0		8	(100)				
	JAPAN										
		UPA 30 MG QD	2	0		2	(100)				NA
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA									

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	8	(19.0)	34	(81.0)	19.0	18.1	(6.6, 29.6)	0.002**
		UPA 15 MG QD	42	6	(14.3)	36	(85.7)	14.3	14.1	(3.1, 25.1)	0.012*
		UPA 7.5 MG QD	40	5	(12.5)	35	(87.5)	12.5	12.1	(1.5, 22.7)	0.025*
		PLACEBO	38	0		38	(100)				
	US/PR/CANADA										
		UPA 30 MG QD	29	4	(13.8)	25	(86.2)	13.8		(1.2, 26.3)	0.112
		UPA 15 MG QD	29	4	(13.8)	25	(86.2)	13.8		(1.2, 26.3)	0.112
		UPA 7.5 MG QD	27	3	(11.1)	24	(88.9)	11.1		(-0.7, 23.0)	0.236
		PLACEBO	27	0		27	(100)				
	EU/AUS										
		UPA 30 MG QD	10	2	(20.0)	8	(80.0)	20.0		(-4.8, 44.8)	0.474
		UPA 15 MG QD	10	2	(20.0)	8	(80.0)	20.0		(-4.8, 44.8)	0.474
		UPA 7.5 MG QD	11	2	(18.2)	9	(81.8)	18.2		(-4.6, 41.0)	0.479
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	2	(66.7)	1	(33.3)	66.7		(13.3, 100.0)	0.400
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = NA
UPA 15 MG QD VS. PLACEBO: P-VALUE = NA
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 8											
	ALL										
		UPA 30 MG QD	42	13	(31.0)	29	(69.0)	31.0	30.4	(16.2, 44.6)	<0.001***
		UPA 15 MG QD	42	5	(11.9)	37	(88.1)	11.9	11.7	(1.4, 22.1)	0.026*
		UPA 7.5 MG QD	40	4	(10.0)	36	(90.0)	10.0	9.6	(-0.0, 19.2)	0.050*
		PLACEBO	38	0		38	(100)				
	US/PR/CANADA										
		UPA 30 MG QD	29	9	(31.0)	20	(69.0)	31.0		(14.2, 47.9)	0.002**
		UPA 15 MG QD	29	4	(13.8)	25	(86.2)	13.8		(1.2, 26.3)	0.112
		UPA 7.5 MG QD	27	2	(7.4)	25	(92.6)	7.4		(-2.5, 17.3)	0.491
		PLACEBO	27	0		27	(100)				
	EU/AUS										
		UPA 30 MG QD	10	3	(30.0)	7	(70.0)	30.0		(1.6, 58.4)	0.211
		UPA 15 MG QD	10	1	(10.0)	9	(90.0)	10.0		(-8.6, 28.6)	1.000
		UPA 7.5 MG QD	11	2	(18.2)	9	(81.8)	18.2		(-4.6, 41.0)	0.479
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = NA
UPA 15 MG QD VS. PLACEBO: P-VALUE = NA
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 12											
	ALL										
		UPA 30 MG QD	42	12	(28.6)	30	(71.4)	25.9	25.6	(11.0, 40.2)	<0.001***
		UPA 15 MG QD	42	7	(16.7)	35	(83.3)	14.0	14.0	(1.4, 26.6)	0.029*
		UPA 7.5 MG QD	40	2	(5.0)	38	(95.0)	2.4	2.5	(-6.4, 11.4)	0.584
		PLACEBO	38	1	(2.6)	37	(97.4)				
	US/PR/CANADA										
		UPA 30 MG QD	29	9	(31.0)	20	(69.0)	27.3		(9.0, 45.6)	0.012*
		UPA 15 MG QD	29	5	(17.2)	24	(82.8)	13.5		(-1.9, 29.0)	0.195
		UPA 7.5 MG QD	27	2	(7.4)	25	(92.6)	3.7		(-8.5, 15.9)	1.000
		PLACEBO	27	1	(3.7)	26	(96.3)				
	EU/AUS										
		UPA 30 MG QD	10	2	(20.0)	8	(80.0)	20.0		(-4.8, 44.8)	0.474
		UPA 15 MG QD	10	2	(20.0)	8	(80.0)	20.0		(-4.8, 44.8)	0.474
		UPA 7.5 MG QD	11	0		11	(100)				NA
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.872
UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.535
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	42	17	(40.5)	25	(59.5)	37.8	37.6	(21.9, 53.2)	<0.001***
		UPA 15 MG QD	42	9	(21.4)	33	(78.6)	18.8	18.8	(5.2, 32.4)	0.007**
		UPA 7.5 MG QD	40	2	(5.0)	38	(95.0)	2.4	2.5	(-6.4, 11.4)	0.584
		PLACEBO	38	1	(2.6)	37	(97.4)				
	US/PR/CANADA										
		UPA 30 MG QD	29	13	(44.8)	16	(55.2)	41.1		(21.7, 60.6)	<0.001***
		UPA 15 MG QD	29	7	(24.1)	22	(75.9)	20.4		(3.3, 37.6)	0.052
		UPA 7.5 MG QD	27	2	(7.4)	25	(92.6)	3.7		(-8.5, 15.9)	1.000
		PLACEBO	27	1	(3.7)	26	(96.3)				
	EU/AUS										
		UPA 30 MG QD	10	3	(30.0)	7	(70.0)	30.0		(1.6, 58.4)	0.211
		UPA 15 MG QD	10	2	(20.0)	8	(80.0)	20.0		(-4.8, 44.8)	0.474
		UPA 7.5 MG QD	11	0		11	(100)				NA
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = 0.889									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = 0.608									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA									

NA = NOT APPLICABLE.
[A]: ACROSS THE STRATA, 95% CI FOR ADJUSTED DIFFERENCE WAS CALCULATED ACCORDING TO THE COCHRAN-MANTEL-HAENSZEL TEST FOR THE COMPARISON OF TWO TREATMENT GROUPS. WITHIN EACH STRATUM, 95% CI FOR DIFFERENCE WAS CALCULATED BASED ON NORMAL APPROXIMATION TO THE BINOMIAL DISTRIBUTION.
[B]: ACROSS THE STRATA, P-VALUE WAS CALCULATED FROM THE COCHRAN-MANTEL-HAENSZEL TEST ADJUSTED FOR STRATA. WITHIN EACH STRATUM, P-VALUE WAS CALCULATED BASED ON CHI-SQUARE TEST (OR FISHER'S EXACT TEST IF >= 25% OF THE CELLS HAVE EXPECTED CELL COUNT < 5).
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.10

表 2.7.3.6-61.　第 1 ピリオドの来院時別の SCORAD 90 を達成した被験者の割合（NRI，LOCF，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 2													
	ALL												
		UPA 30 MG QD	42	1	(2.4)	40	(95.2)	1	(2.4)	2.4	2.3	(-3.5, 8.1)	0.440
		UPA 15 MG QD	42	0		41	(97.6)	1	(2.4)		-0.1	(-3.7, 3.5)	0.962
		UPA 7.5 MG QD	42	1	(2.4)	39	(92.9)	2	(4.8)	2.4	2.4	(-3.4, 8.1)	0.426
		PLACEBO	41	0		35	(85.4)	6	(14.6)				
	US/PR/CANADA												
		UPA 30 MG QD	29	1	(3.4)	28	(96.6)	0		3.4		(-3.2, 10.1)	1.000
		UPA 15 MG QD	29	0		29	(100)	0					NA
		UPA 7.5 MG QD	29	1	(3.4)	26	(89.7)	2	(6.9)	3.4		(-3.2, 10.1)	1.000
		PLACEBO	29	0		25	(86.2)	4	(13.8)				
	EU/AUS												
		UPA 30 MG QD	10	0		10	(100)	0					NA
		UPA 15 MG QD	10	0		9	(90.0)	1	(10.0)				NA
		UPA 7.5 MG QD	11	0		11	(100)	0					NA
		PLACEBO	10	0		8	(80.0)	2	(20.0)				
	JAPAN												
		UPA 30 MG QD	3	0		2	(66.7)	1	(33.3)				NA
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA											

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 4													
	ALL												
		UPA 30 MG QD	42	3	(7.1)	36	(85.7)	3	(7.1)	7.1	7.1	(-1.5, 15.6)	0.104
		UPA 15 MG QD	42	0		40	(95.2)	2	(4.8)		-0.1	(-3.7, 3.5)	0.962
		UPA 7.5 MG QD	42	1	(2.4)	38	(90.5)	3	(7.1)	2.4	2.4	(-3.4, 8.1)	0.426
		PLACEBO	41	0		30	(73.2)	11	(26.8)				
	US/PR/CANADA												
		UPA 30 MG QD	29	2	(6.9)	26	(89.7)	1	(3.4)	6.9		(-2.3, 16.1)	0.491
		UPA 15 MG QD	29	0		27	(93.1)	2	(6.9)				NA
		UPA 7.5 MG QD	29	1	(3.4)	25	(86.2)	3	(10.3)	3.4		(-3.2, 10.1)	1.000
		PLACEBO	29	0		24	(82.8)	5	(17.2)				
	EU/AUS												
		UPA 30 MG QD	10	1	(10.0)	7	(70.0)	2	(20.0)	10.0		(-8.6, 28.6)	1.000
		UPA 15 MG QD	10	0		10	(100)	0					NA
		UPA 7.5 MG QD	11	0		11	(100)	0					NA
		PLACEBO	10	0		5	(50.0)	5	(50.0)				
	JAPAN												
		UPA 30 MG QD	3	0		3	(100)	0					NA
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		1	(50.0)	1	(50.0)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA											

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 8													
	ALL												
		UPA 30 MG QD	42	6	(14.3)	36	(85.7)	0		14.3	14.2	(3.2, 25 2)	0.012*
		UPA 15 MG QD	42	1	(2.4)	37	(88.1)	4	(9.5)	2.4	2.3	(-3.4, 8.0)	0.428
		UPA 7.5 MG QD	42	2	(4.8)	37	(88.1)	3	(7.1)	4.8	4.6	(-2.5, 11.8)	0.206
		PLACEBO	41	0		29	(70.7)	12	(29.3)				
	US/PR/CANADA												
		UPA 30 MG QD	29	4	(13.8)	25	(86.2)	0		13.8		(1.2, 26 3)	0.112
		UPA 15 MG QD	29	0		26	(89.7)	3	(10.3)				NA
		UPA 7.5 MG QD	29	1	(3.4)	26	(89.7)	2	(6.9)	3.4		(-3.2, 10.1)	1.000
		PLACEBO	29	0		21	(72.4)	8	(27.6)				
	EU/AUS												
		UPA 30 MG QD	10	2	(20.0)	8	(80.0)	0		20.0		(-4.8, 44.8)	0.474
		UPA 15 MG QD	10	1	(10.0)	8	(80.0)	1	(10.0)	10.0		(-8.6, 28.6)	1.000
		UPA 7.5 MG QD	11	1	(9.1)	9	(81.8)	1	(9.1)	9.1		(-7.9, 26.1)	1.000
		PLACEBO	10	0		6	(60.0)	4	(40.0)				
	JAPAN												
		UPA 30 MG QD	3	0		3	(100)	0					NA
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = NA
UPA 15 MG QD VS. PLACEBO: P-VALUE = NA
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 12													
	ALL												
		UPA 30 MG QD	42	7	(16.7)	32	(76.2)	3	(7.1)	16.7	16.6	(5.0, 28 2)	0.005**
		UPA 15 MG QD	42	2	(4.8)	35	(83.3)	5	(11.9)	4.8	4.7	(-2.6, 12.0)	0.209
		UPA 7.5 MG QD	42	2	(4.8)	33	(78.6)	7	(16.7)	4.8	4.7	(-2.5, 12.0)	0.202
		PLACEBO	41	0		28	(68.3)	13	(31.7)				
	US/PR/CANADA												
		UPA 30 MG QD	29	6	(20.7)	22	(75.9)	1	(3.4)	20.7		(5.9, 35.4)	0.023*
		UPA 15 MG QD	29	2	(6.9)	25	(86.2)	2	(6.9)	6.9		(-2.3, 16.1)	0.491
		UPA 7.5 MG QD	29	2	(6.9)	23	(79.3)	4	(13.8)	6.9		(-2.3, 16.1)	0.491
		PLACEBO	29	0		22	(75.9)	7	(24.1)				
	EU/AUS												
		UPA 30 MG QD	10	1	(10.0)	7	(70.0)	2	(20.0)	10.0		(-8.6, 28.6)	1.000
		UPA 15 MG QD	10	0		7	(70.0)	3	(30.0)				NA
		UPA 7.5 MG QD	11	0		8	(72.7)	3	(27.3)				NA
		PLACEBO	10	0		4	(40.0)	6	(60.0)				
	JAPAN												
		UPA 30 MG QD	3	0		3	(100)	0					NA
		UPA 15 MG QD	3	0		3	(100)	0					NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:												
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA											
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA											

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
NRI													
WEEK 16													
	ALL												
		UPA 30 MG QD	42	10	(23.8)	29	(69.0)	3	(7.1)	23.8	23.3	(10.4, 36.2)	<0.001***
		UPA 15 MG QD	42	4	(9.5)	30	(71.4)	8	(19.0)	9.5	9.4	(0.1, 18.8)	0.048*
		UPA 7.5 MG QD	42	1	(2.4)	32	(76.2)	9	(21.4)	2.4	2.4	(-3.4, 8.1)	0.426
		PLACEBO	41	0		24	(58.5)	17	(41.5)				
	US/PR/CANADA												
		UPA 30 MG QD	29	8	(27.6)	21	(72.4)	0		27.6		(11.3, 43.9)	0.004**
		UPA 15 MG QD	29	4	(13.8)	21	(72.4)	4	(13.8)	13.8		(1.2, 26 3)	0.112
		UPA 7.5 MG QD	29	1	(3.4)	24	(82.8)	4	(13.8)	3.4		(-3.2, 10.1)	1.000
		PLACEBO	29	0		20	(69.0)	9	(31.0)				
	EU/AUS												
		UPA 30 MG QD	10	1	(10.0)	6	(60.0)	3	(30.0)	10.0		(-8.6, 28.6)	1.000
		UPA 15 MG QD	10	0		7	(70.0)	3	(30.0)				NA
		UPA 7.5 MG QD	11	0		6	(54.5)	5	(45.5)				NA
		PLACEBO	10	0		2	(20.0)	8	(80.0)				
	JAPAN												
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	0		33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		2	(66.7)	1	(33.3)				NA
		UPA 7.5 MG QD	2	0		2	(100)	0					NA
		PLACEBO	2	0		2	(100)	0					

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = NA
UPA 15 MG QD VS. PLACEBO: P-VALUE = NA
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 2											
	ALL										
		UPA 30 MG QD	41	1	(2.4)	40	(97.6)	2.4	2.3	(-3.8, 8.4)	0.454
		UPA 15 MG QD	41	0		41	(100)		-0.2	(-4.1, 3.8)	0.935
		UPA 7.5 MG QD	40	1	(2.5)	39	(97.5)	2.5	2.4	(-3.9, 8.7)	0.447
		PLACEBO	35	0		35	(100)				
	US/PR/CANADA										
		UPA 30 MG QD	29	1	(3.4)	28	(96.6)	3.4		(-3.2, 10.1)	1.000
		UPA 15 MG QD	29	0		29	(100)				NA
		UPA 7.5 MG QD	27	1	(3.7)	26	(96.3)	3.7		(-3.4, 10.8)	1.000
		PLACEBO	25	0		25	(100)				
	EU/AUS										
		UPA 30 MG QD	10	0		10	(100)				NA
		UPA 15 MG QD	9	0		9	(100)				NA
		UPA 7.5 MG QD	11	0		11	(100)				NA
		PLACEBO	8	0		8	(100)				
	JAPAN										
		UPA 30 MG QD	2	0		2	(100)				NA
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA									

IMPUTATION / VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	3	(7.1)	39	(92.9)	7.1	7.0	(-1.6, 15.5)	0.109
		UPA 15 MG QD	42	0		42	(100)		-0.1	(-3.9, 3.6)	0.944
		UPA 7.5 MG QD	40	1	(2.5)	39	(97.5)	2.5	2.5	(-3.7, 8.7)	0.430
		PLACEBO	38	0		38	(100)				
	US/PR/CANADA										
		UPA 30 MG QD	29	2	(6.9)	27	(93.1)	6.9		(-2.3, 16.1)	0.492
		UPA 15 MG QD	29	0		29	(100)				NA
		UPA 7.5 MG QD	27	1	(3.7)	26	(96.3)	3.7		(-3.4, 10.8)	1.000
		PLACEBO	27	0		27	(100)				
	EU/AUS										
		UPA 30 MG QD	10	1	(10.0)	9	(90.0)	10.0		(-8.6, 28.6)	1.000
		UPA 15 MG QD	10	0		10	(100)				NA
		UPA 7.5 MG QD	11	0		11	(100)				NA
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	0		3	(100)				NA
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA									

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 8											
	ALL										
		UPA 30 MG QD	42	6	(14.3)	36	(85.7)	14.3	14.1	(3.1, 25.1)	0.012*
		UPA 15 MG QD	42	1	(2.4)	41	(97.6)	2.4	2.2	(-3.5, 7.9)	0.448
		UPA 7.5 MG QD	40	2	(5.0)	38	(95.0)	5.0	4.8	(-2.7, 12.2)	0.212
		PLACEBO	38	0		38	(100)				
	US/PR/CANADA										
		UPA 30 MG QD	29	4	(13.8)	25	(86.2)	13.8		(1.2, 26.3)	0.112
		UPA 15 MG QD	29	0		29	(100)				NA
		UPA 7.5 MG QD	27	1	(3.7)	26	(96.3)	3.7		(-3.4, 10.8)	1.000
		PLACEBO	27	0		27	(100)				
	EU/AUS										
		UPA 30 MG QD	10	2	(20.0)	8	(80.0)	20.0		(-4.8, 44.8)	0.474
		UPA 15 MG QD	10	1	(10.0)	9	(90.0)	10.0		(-8.6, 28.6)	1.000
		UPA 7.5 MG QD	11	1	(9.1)	10	(90.9)	9.1		(-7.9, 26.1)	1.000
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	0		3	(100)				NA
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				

BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:
UPA 30 MG QD VS. PLACEBO: P-VALUE = NA
UPA 15 MG QD VS. PLACEBO: P-VALUE = NA
UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 12											
	ALL										
		UPA 30 MG QD	42	7	(16.7)	35	(83.3)	16.7	16.5	(4.9, 28.2)	0.005**
		UPA 15 MG QD	42	2	(4.8)	40	(95.2)	4.8	4.6	(-2.7, 12.0)	0.218
		UPA 7.5 MG QD	40	2	(5.0)	38	(95.0)	5.0	5.0	(-2.7, 12.7)	0.204
		PLACEBO	38	0		38	(100)				
	US/PR/CANADA										
		UPA 30 MG QD	29	6	(20.7)	23	(79.3)	20.7		(5.9, 35.4)	0.024*
		UPA 15 MG QD	29	2	(6.9)	27	(93.1)	6.9		(-2.3, 16.1)	0.492
		UPA 7.5 MG QD	27	2	(7.4)	25	(92.6)	7.4		(-2.5, 17.3)	0.491
		PLACEBO	27	0		27	(100)				
	EU/AUS										
		UPA 30 MG QD	10	1	(10.0)	9	(90.0)	10.0		(-8.6, 28.6)	1.000
		UPA 15 MG QD	10	0		10	(100)				NA
		UPA 7.5 MG QD	11	0		11	(100)				NA
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	0		3	(100)				NA
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA									

IMPUTATION VISIT	STRATA	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	ADJUSTED DIFF %	95 % CI [A]	P-VALUE [B]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	42	10	(23.8)	32	(76.2)	23.8	23.3	(10.3, 36.3)	<0.001***
		UPA 15 MG QD	42	4	(9.5)	38	(90.5)	9.5	9.4	(-0.0, 18.8)	0.050*
		UPA 7.5 MG QD	40	1	(2.5)	39	(97.5)	2.5	2.5	(-3.7, 8.7)	0.430
		PLACEBO	38	0		38	(100)				
	US/PR/CANADA										
		UPA 30 MG QD	29	8	(27.6)	21	(72.4)	27.6		(11.3, 43.9)	0.005**
		UPA 15 MG QD	29	4	(13.8)	25	(86.2)	13.8		(1.2, 26.3)	0.112
		UPA 7.5 MG QD	27	1	(3.7)	26	(96.3)	3.7		(-3.4, 10.8)	1.000
		PLACEBO	27	0		27	(100)				
	EU/AUS										
		UPA 30 MG QD	10	1	(10.0)	9	(90.0)	10.0		(-8.6, 28.6)	1.000
		UPA 15 MG QD	10	0		10	(100)				NA
		UPA 7.5 MG QD	11	0		11	(100)				NA
		PLACEBO	9	0		9	(100)				
	JAPAN										
		UPA 30 MG QD	3	1	(33.3)	2	(66.7)	33.3		(-20.0, 86.7)	1.000
		UPA 15 MG QD	3	0		3	(100)				NA
		UPA 7.5 MG QD	2	0		2	(100)				NA
		PLACEBO	2	0		2	(100)				
	BRESLOW-DAY TEST OF HOMOGENEITY ACROSS STRATA:										
		UPA 30 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 15 MG QD VS. PLACEBO: P-VALUE = NA									
		UPA 7.5 MG QD VS. PLACEBO: P-VALUE = NA									

NA = NOT APPLICABLE.
[A]: ACROSS THE STRATA, 95% CI FOR ADJUSTED DIFFERENCE WAS CALCULATED ACCORDING TO THE COCHRAN-MANTEL-HAENSZEL TEST FOR THE COMPARISON OF TWO TREATMENT GROUPS. WITHIN EACH STRATUM, 95% CI FOR DIFFERENCE WAS CALCULATED BASED ON NORMAL APPROXIMATION TO THE BINOMIAL DISTRIBUTION.
[B]: ACROSS THE STRATA, P-VALUE WAS CALCULATED FROM THE COCHRAN-MANTEL-HAENSZEL TEST ADJUSTED FOR STRATA. WITHIN EACH STRATUM, P-VALUE WAS CALCULATED BASED ON CHI-SQUARE TEST (OR FISHER'S EXACT TEST IF >= 25% OF THE CELLS HAVE EXPECTED CELL COUNT < 5).
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.11

表 2.7.3.6-62. ベースライン時の HADS-A が 8 以上又は HADS-D が 8 以上であった被験者のうち，二重盲検投与期の来院時点別の HADS-A 8 未満及び HADS-D 8 未満を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

Time Point / Strata / Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo: Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 12								
All								
Placebo	126	16 (12.7) [6.9, 18.5]	0					
UPA 15 mg QD	145	67 (46.2) [38.1, 54.3]	0	33.5	33.4	[23.4, 43.4]	<0.001***	0.710
UPA 30 mg QD	144	69 (48.2) [40.0, 56.4]	1	35.5	35.5	[25.5, 45.5]	<0.001***	0.682
vIGA-AD 3 (Moderate)								
Placebo	59	8 (13.6) [4.8, 22.3]	0					
UPA 15 mg QD	82	39 (47.6) [36.8, 58.4]	0	34.0		[20.1, 47.9]	<0.001***	
UPA 30 mg QD	67	32 (48.3) [36.3, 60.4]	1	34.7		[19.9, 49.6]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	67	8 (11.9) [4.2, 19.7]	0					
UPA 15 mg QD	63	28 (44.4) [32.2, 56.7]	0	32.5		[18.0, 47.0]	<0.001***	
UPA 30 mg QD	77	37 (48.1) [36.9, 59.2]	0	36.1		[22.5, 49.7]	<0.001***	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 12 (Cont.)								
US/Puerto Rico/Canada								
Placebo	63	7 (11.1) [3.4, 18.9]	0					
UPA 15 mg QD	65	26 (40.0) [28.1, 51.9]	0	28.9		[14.7, 43.1]	<0.001***	
UPA 30 mg QD	65	24 (36.9) [25.2, 48.7]	0	25.8		[11.7, 39.9]	<0.001***	
Japan								
Placebo	7	0	0					
UPA 15 mg QD	3	3 (100) [100.0, 100.0]	0	100.0			NA	
UPA 30 mg QD	6	4 (66.7) [28.9, 100.0]	0	66.7		[28.9, 100.0]	0.001**	
China								
Placebo	7	1 (14.3) [0.0, 40.2]	0					
UPA 15 mg QD	10	5 (50.0) [19.0, 81.0]	0	35.7		[-4.7, 76.1]	0.083	
UPA 30 mg QD	8	7 (87.5) [64.6, 100.0]	0	73.2		[38.6, 100.0]	<0.001***	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 12 (Cont.)								
Other								
Placebo	49	8 (16.3) [6.0, 26.7]	0					
UPA 15 mg QD	67	33 (49.3) [37.3, 61.2]	0		32.9	[17.1, 48.8]	<0.001***	
UPA 30 mg QD	65	34 (52.9) [40.6, 65.1]	1		36.5	[20.5, 52.6]	<0.001***	
Adolescent								
Placebo	18	2 (11.1) [0.0, 25.6]	0					
UPA 15 mg QD	22	10 (45.5) [24.6, 66.3]	0		34.3	[9.0, 59.7]	0.008**	
UPA 30 mg QD	21	10 (47.6) [26.3, 69.0]	0		36.5	[10.7, 62.3]	0.006**	
Adult								
Placebo	108	14 (13.0) [6.6, 19.3]	0					
UPA 15 mg QD	123	57 (46.3) [37.5, 55.2]	0		33.4	[22.5, 44.2]	<0.001***	
UPA 30 mg QD	123	59 (48.3) [39.4, 57.1]	1		35.3	[24.4, 46.2]	<0.001***	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo	126	18 (14.3) [8.2, 20.4]	0					
UPA 15 mg QD	145	66 (45.5) [37.4, 53.6]	0	31.2	31.5	[21.4, 41.6]	<0.001***	0.267
UPA 30 mg QD	144	71 (49.2) [41.0, 57.4]	2	34.9	34.9	[24.8, 45.1]	<0.001***	0.370
vIGA-AD 3 (Moderate)								
Placebo	59	8 (13.6) [4.8, 22.3]	0					
UPA 15 mg QD	82	36 (43.9) [33.2, 54.6]	0	30.3		[16.5, 44.2]	<0.001***	
UPA 30 mg QD	67	30 (45.3) [33.3, 57.3]	1	31.7		[16.9, 46.6]	<0.001***	
vIGA-AD 4 (Severe)								
Placebo	67	10 (14.9) [6.4, 23.5]	0					
UPA 15 mg QD	63	30 (47.6) [35.3, 60.0]	0	32.7		[17.7, 47.7]	<0.001***	
UPA 30 mg QD	77	41 (52.6) [41.4, 63.8]	1	37.7		[23.6, 51.8]	<0.001***	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo	63	7 (11.1) [3.4, 18.9]	0					
UPA 15 mg QD	65	29 (44.6) [32.5, 56.7]	0	33.5		[19.1, 47.9]	<0.001***	
UPA 30 mg QD	65	27 (41.5) [29.6, 53.5]	0	30.4		[16.2, 44.7]	<0.001***	
Japan								
Placebo	7	0	0					
UPA 15 mg QD	3	3 (100) [100.0, 100.0]	0	100.0			NA	
UPA 30 mg QD	6	4 (66.7) [28.9, 100.0]	0	66.7		[28.9, 100.0]	0.001**	
China								
Placebo	7	1 (14.3) [0.0, 40.2]	0					
UPA 15 mg QD	10	4 (40.0) [9.6, 70.4]	0	25.7		[-14.2, 65.6]	0.207	
UPA 30 mg QD	8	6 (75.0) [45.0, 100.0]	0	60.7		[21.1, 100.0]	0.003**	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo	49	10 (20.4) [9.1, 31.7]	0					
UPA 15 mg QD	67	30 (44.8) [32.9, 56.7]	0	24.4		[8.0, 40.8]	0.004**	
UPA 30 mg QD	65	34 (52.1) [39.8, 64.3]	2	31.6		[15.0, 48.3]	<0.001***	
Adolescent								
Placebo	18	0	0					
UPA 15 mg QD	22	11 (50.0) [29.1, 70.9]	0	50.0		[29.1, 70.9]	<0.001***	
UPA 30 mg QD	21	10 (47.6) [26.3, 69.0]	0	47.6		[26.3, 69.0]	<0.001***	
Adult								
Placebo	108	18 (16.7) [9.6, 23.7]	0					
UPA 15 mg QD	123	55 (44.7) [35.9, 53.5]	0	28.0		[16.8, 39.3]	<0.001***	
UPA 30 mg QD	123	61 (49.5) [40.6, 58.3]	2	32.8		[21.5, 44.1]	<0.001***	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　9.1.1

表 2.7.3.6-63.　二重盲検投与期の来院時点別の HADS 合計スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-045 試験

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 12										
All										
Placebo	148	12.2	10.8	2.37	[-8.74, 13.47]	5.654				
UPA 15 mg QD	249	12.5	8.7	-26.30	[-35.08, -17.52]	4.470	-28.67	[-41.37, -15.97]	6.467	<0.001***
UPA 30 mg QD	259	12.4	8.3	-25.86	[-34.49, -17.24]	4.393	-28.23	[-40.85, -15.61]	6.426	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	99	11.5	10.8	11.74	[-1.44, 24.92]	6.698				
UPA 15 mg QD	135	13.1	9.1	-14.84	[-26.12, -3.56]	5.732	-26.58	[-43.95, -9.22]	8.822	0.003**
UPA 30 mg QD	135	11.1	7.8	-18.02	[-29.27, -6.78]	5.714	-29.77	[-47.08, -12.45]	8.800	0.001**
vIGA-AD 4 (Severe)										
Placebo	49	13.5	10.7	-1.58	[-16.93, 13.77]	7.798				
UPA 15 mg QD	114	11.8	8.3	-31.82	[-41.93, -21.71]	5.136	-30.24	[-48.65, -11.84]	9.350	0.001**
UPA 30 mg QD	124	13.8	8.7	-28.20	[-37.85, -18.56]	4.901	-26.62	[-44.73, -8.51]	9.201	0.004**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo	70	11.9	11.4	15.92	[-1.40, 33.25]	8.795				
UPA 15 mg QD	109	12.5	9.3	-14.37	[-28.23, -0.52]	7.032	-30.30	[-52.49, -8.11]	11.262	0.008**
UPA 30 mg QD	114	12.2	8.6	-13.68	[-27.14, -0.21]	6.835	-29.60	[-51.55, -7.65]	11.141	0.008**
Japan										
Placebo	3	14.3	13.7	3.58	[-69.00, 76.17]	35.484				
UPA 15 mg QD	14	8.1	3.6	-50.93	[-84.49, -17.36]	16.423	-54.51	[-135.58, 26.56]	39.641	0.180
UPA 30 mg QD	15	12.5	8.9	-12.80	[-45.35, 19.75]	15.914	-16.38	[-95.20, 62.44]	38.531	0.674
China										
Placebo	7	13.3	12.9	8.58	[-38.20, 55.36]	23.019				
UPA 15 mg QD	14	13.5	11.2	-7.51	[-40.63, 25.62]	16.299	-16.09	[-73.36, 41.18]	28.183	0.572
UPA 30 mg QD	17	12.0	8.3	-13.27	[-43.38, 16.83]	14.813	-21.86	[-77.55, 33.83]	27.403	0.431

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 12 (Cont.)										
Other										
Placebo	68	12.3	9.8	-1.82	[-13.66, 10.03]	6.019				
UPA 15 mg QD	112	12.9	8.5	-28.64	[-37.86, -19.42]	4.685	-26.82	[-41.84, -11.81]	7.629	0.001**
UPA 30 mg QD	113	12.5	7.8	-33.96	[-43.14, -24.78]	4.664	-32.14	[-47.12, -17.15]	7.614	<0.001***
Adolescent										
Placebo	19	11.1	9.2	-5.46	[-35.97, 25.05]	15.363				
UPA 15 mg QD	38	12.1	7.7	-28.59	[-50.14, -7.05]	10.849	-23.14	[-60.49, 14.22]	18.810	0.222
UPA 30 mg QD	39	12.3	7.8	-25.08	[-46.33, -3.82]	10.702	-19.62	[-56.81, 17.58]	18.729	0.298
Adult										
Placebo	129	12.3	11.0	9.18	[-1.57, 19.94]	5.473				
UPA 15 mg QD	211	12.5	8.9	-21.59	[-29.98, -13.20]	4.269	-30.77	[-44.41, -17.13]	6.941	<0.001***
UPA 30 mg QD	220	12.4	8.3	-22.11	[-30.32, -13.91]	4.176	-31.29	[-44.82, -17.77]	6.884	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 16										
All										
Placebo	121	11.6	9.7	-11.02	[-22.40, 0.36]	5.795				
UPA 15 mg QD	237	12.5	8.8	-25.49	[-34.15, -16.82]	4.413	-14.46	[-27.33, -1.59]	6.554	0.028*
UPA 30 mg QD	253	12.4	7.7	-33.03	[-41.49, -24.57]	4.307	-22.01	[-34.77, -9.25]	6.500	0.001**
vIGA-AD 3 (Moderate)										
Placebo	81	11.1	9.9	-8.91	[-22.18, 4.35]	6.745				
UPA 15 mg QD	133	12.6	9.1	-13.94	[-24.57, -3.32]	5.402	-5.03	[-22.04, 11.98]	8.650	0.561
UPA 30 mg QD	134	11.1	7.4	-26.95	[-37.52, -16.38]	5.374	-18.03	[-34.98, -1.08]	8.618	0.037*
vIGA-AD 4 (Severe)										
Placebo	40	12.7	9.2	1.55	[-15.70, 18.81]	8.764				
UPA 15 mg QD	104	12.2	8.5	-30.34	[-41.43, -19.25]	5.632	-31.89	[-52.42, -11.36]	10.425	0.002**
UPA 30 mg QD	119	13.8	7.9	-33.16	[-43.65, -22.67]	5.325	-34.71	[-54.89, -14.53]	10.248	0.001**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	60	11.5	10.4	4.08	[-12.90, 21.06]	8.628				
UPA 15 mg QD	106	12.2	9.0	-15.13	[-28.26, -2.00]	6.668	-19.21	[-40.68, 2.26]	10.905	0.079
UPA 30 mg QD	115	12.4	8.0	-25.97	[-38.61, -13.33]	6.421	-30.05	[-51.22, -8.87]	10.758	0.006**
Japan										
Placebo	1	3.0	2.0	-32.23	[-137.56, 73.10]	51.546				
UPA 15 mg QD	13	8.3	4.2	-34.42	[-72.02, 3.18]	18.007	-2.19	[-114.42, 110.04]	54.770	0.968
UPA 30 mg QD	14	12.9	8.4	-15.12	[-51.63, 21.39]	17.457	17.12	[-93.86, 128.09]	54.283	0.755
China										
Placebo	7	13.3	14.1	21.03	[-31.19, 73.24]	25.674				
UPA 15 mg QD	14	13.5	10.1	-24.97	[-61.93, 11.99]	18.174	-46.00	[-109.93, 17.93]	31.435	0.153
UPA 30 mg QD	16	12.1	6.4	-12.97	[-46.79, 20.85]	16.646	-34.00	[-96.26, 28.27]	30.624	0.275

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 16 (Cont.)										
Other										
Placebo	53	11.6	8.4	-19.38	[-31.94, -6.82]	6.380				
UPA 15 mg QD	104	13.1	9.1	-25.81	[-34.93, -16.69]	4.632	-6.43	[-21.96, 9.09]	7.887	0.415
UPA 30 mg QD	108	12.4	7.4	-37.45	[-46.42, -28.48]	4.558	-18.07	[-33.50, -2.64]	7.839	0.022*
Adolescent										
Placebo	16	10.8	9.7	-24.81	[-50.67, 1.04]	13.016				
UPA 15 mg QD	37	11.9	7.7	-23.26	[-40.31, -6.22]	8.579	1.55	[-29.42, 32.52]	15.590	0.921
UPA 30 mg QD	40	12.3	7.7	-37.08	[-53.49, -20.66]	8.261	-12.26	[-42.90, 18.38]	15.425	0.429
Adult										
Placebo	105	11.7	9.6	-2.35	[-13.61, 8.92]	5.735				
UPA 15 mg QD	200	12.6	9.1	-21.52	[-29.96, -13.07]	4.298	-19.17	[-33.25, -5.09]	7.167	0.008**
UPA 30 mg QD	213	12.4	7.7	-28.39	[-36.60, -20.17]	4.182	-26.04	[-39.98, -12.10]	7.098	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 12										
All										
Placebo	148	7.1	6.1	0.78	[-10.55, 12.12]	5.773				
UPA 15 mg QD	248	7.4	5.4	-19.71	[-28.67, -10.75]	4.565	-20.49	[-33.73, -7.25]	6.744	0.002**
UPA 30 mg QD	255	7.5	5.5	-17.67	[-26.51, -8.82]	4.506	-18.45	[-31.63, -5.27]	6.710	0.006**
vIGA-AD 3 (Moderate)										
Placebo	99	6.6	6.1	9.95	[-4.01, 23.92]	7.101				
UPA 15 mg QD	134	7.8	5.7	-10.34	[-22.33, 1.65]	6.095	-20.29	[-38.73, -1.86]	9.372	0.031*
UPA 30 mg QD	133	7.1	5.4	-11.59	[-23.58, 0.40]	6.096	-21.54	[-39.95, -3.14]	9.357	0.022*
vIGA-AD 4 (Severe)										
Placebo	49	8.1	6.3	-8.53	[-24.11, 7.05]	7.915				
UPA 15 mg QD	114	7.0	5.1	-25.98	[-36.22, -15.75]	5.200	-17.46	[-36.13, 1.21]	9.486	0.067
UPA 30 mg QD	122	7.9	5.6	-21.21	[-31.04, -11.37]	4.996	-12.68	[-31.09, 5.73]	9.352	0.176

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo	69	7.1	6.7	12.53	[-4.23, 29.29]	8.513				
UPA 15 mg QD	109	7.7	6.1	-10.11	[-23.43, 3.21]	6.764	-22.64	[-44.06, -1.23]	10.876	0.038*
UPA 30 mg QD	114	7.5	6.1	-4.79	[-17.77, 8.19]	6.592	-17.32	[-38.52, 3.89]	10.769	0.109
Japan										
Placebo	3	6.7	5.7	-5.47	[-82.05, 71.11]	37.424				
UPA 15 mg QD	14	4.2	1.9	-47.39	[-83.39, -11.39]	17.614	-41.92	[-126.95, 43.11]	41.571	0.322
UPA 30 mg QD	15	6.9	5.5	-2.63	[-37.29, 32.02]	16.944	2.84	[-80.89, 86.57]	40.915	0.945
China										
Placebo	7	8.3	8.0	6.40	[-31.33, 44.12]	18.563				
UPA 15 mg QD	14	7.2	5.6	-9.90	[-36.55, 16.75]	13.114	-16.30	[-62.57, 29.98]	22.770	0.479
UPA 30 mg QD	17	7.6	4.7	-23.87	[-48.02, 0.27]	11.881	-30.27	[-75.06, 14.52]	22.041	0.179

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 12 (Cont.)										
Other										
Placebo	69	7.0	5.4	-3.98	[-18.34, 10.38]	7.297				
UPA 15 mg QD	111	7.6	5.2	-22.62	[-33.93, -11.31]	5.744	-18.64	[-36.92, -0.35]	9.290	0.046*
UPA 30 mg QD	109	7.5	5.0	-27.77	[-39.13, -16.40]	5.776	-23.79	[-42.10, -5.47]	9.306	0.011*
Adolescent										
Placebo	20	5.8	5.5	8.82	[-23.80, 41.45]	16.430				
UPA 15 mg QD	38	7.7	5.1	-21.64	[-45.15, 1.86]	11.836	-30.47	[-70.72, 9.79]	20.274	0.136
UPA 30 mg QD	38	8.1	5.6	-21.26	[-44.77, 2.25]	11.839	-30.08	[-70.40, 10.24]	20.307	0.142
Adult										
Placebo	128	7.3	6.3	3.63	[-7.46, 14.73]	5.646				
UPA 15 mg QD	210	7.3	5.5	-17.10	[-25.74, -8.45]	4.401	-20.73	[-34.80, -6.67]	7.159	0.004**
UPA 30 mg QD	217	7.4	5.5	-15.09	[-23.58, -6.60]	4.321	-18.72	[-32.69, -4.76]	7.109	0.009**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16										
All										
Placebo	120	7.0	5.7	-18.91	[-29.69, -8.13]	5.492				
UPA 15 mg QD	236	7.4	5.4	-21.95	[-30.08, -13.81]	4.143	-3.04	[-15.24, 9.16]	6.212	0.625
UPA 30 mg QD	252	7.4	4.9	-27.38	[-35.31, -19.45]	4.038	-8.47	[-20.56, 3.62]	6.158	0.170
vIGA-AD 3 (Moderate)										
Placebo	81	6.6	5.7	-15.47	[-28.36, -2.58]	6.555				
UPA 15 mg QD	132	7.5	5.7	-10.82	[-21.05, -0.59]	5.201	4.64	[-11.84, 21.13]	8.381	0.580
UPA 30 mg QD	134	7.0	5.0	-22.33	[-32.48, -12.19]	5.156	-6.87	[-23.26, 9.53]	8.336	0.411
vIGA-AD 4 (Severe)										
Placebo	39	7.8	5.6	-14.27	[-30.24, 1.69]	8.105				
UPA 15 mg QD	104	7.2	5.0	-29.98	[-40.06, -19.91]	5.112	-15.71	[-34.60, 3.18]	9.593	0.103
UPA 30 mg QD	118	7.9	4.9	-29.42	[-38.95, -19.89]	4.836	-15.14	[-33.72, 3.43]	9.432	0.110

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	59	7.1	6.3	-6.80	[-20.68, 7.08]	7.051				
UPA 15 mg QD	106	7.5	5.8	-16.03	[-26.53, -5.53]	5.332	-9.23	[-26.64, 8.17]	8.842	0.297
UPA 30 mg QD	115	7.6	5.4	-23.33	[-33.43, -13.24]	5.127	-16.53	[-33.70, 0.64]	8.721	0.059
Japan										
Placebo	1	1.0	1.0	-15.16	[-141.44, 111.11]	61.508				
UPA 15 mg QD	13	4.4	2.4	-36.13	[-72.66, 0.40]	17.622	-20.97	[-151.67, 109.74]	63.610	0.744
UPA 30 mg QD	14	7.1	4.5	-7.82	[-43.10, 27.45]	17.014	7.34	[-124.24, 138.92]	64.142	0.910
China										
Placebo	7	8.3	8.4	20.55	[-26.25, 67.36]	22.984				
UPA 15 mg QD	14	7.2	4.9	-31.38	[-64.46, 1.70]	16.242	-51.94	[-109.32, 5.45]	28.179	0.075
UPA 30 mg QD	16	7.7	4.0	-13.00	[-43.55, 17.54]	15.014	-33.56	[-89.44, 22.33]	27.452	0.230

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16 (Cont.)										
Other										
Placebo	53	6.8	4.8	-29.90	[-44.58, -15.23]	7.457				
UPA 15 mg QD	103	7.7	5.4	-20.44	[-31.18, -9.71]	5.453	9.46	[-8.74, 27.66]	9.245	0.307
UPA 30 mg QD	107	7.3	4.6	-31.63	[-42.19, -21.06]	5.366	-1.72	[-19.80, 16.36]	9.183	0.851
Adolescent										
Placebo	16	6.3	6.1	-14.96	[-41.69, 11.78]	13.457				
UPA 15 mg QD	37	7.7	5.3	-17.69	[-35.21, -0.17]	8.818	-2.74	[-34.74, 29.27]	16.110	0.865
UPA 30 mg QD	40	7.9	4.8	-37.18	[-54.05, -20.31]	8.491	-22.22	[-53.91, 9.46]	15.951	0.167
Adult										
Placebo	104	7.1	5.6	-15.01	[-25.69, -4.34]	5.435				
UPA 15 mg QD	199	7.3	5.4	-20.30	[-28.19, -12.42]	4.012	-5.29	[-18.56, 7.98]	6.756	0.434
UPA 30 mg QD	212	7.3	5.0	-23.50	[-31.15, -15.84]	3.898	-8.48	[-21.62, 4.66]	6.688	0.205

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Parameter Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-D Total Score										
Week 12										
All										
Placebo	142	5.3	4.7	-2.13	[-14.15, 9.89]	6.122				
UPA 15 mg QD	244	5.2	3.3	-30.11	[-39.61, -20.62]	4.835	-27.98	[-41.71, -14.25]	6.993	<0.001***
UPA 30 mg QD	254	5.1	2.8	-41.17	[-50.48, -31.86]	4.742	-39.03	[-52.68, -25.39]	6.950	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	94	5.1	4.8	11.75	[-2.27, 25.77]	7.129				
UPA 15 mg QD	132	5.5	3.5	-18.96	[-30.84, -7.08]	6.041	-30.71	[-49.07, -12.34]	9.338	0.001**
UPA 30 mg QD	131	4.2	2.5	-33.24	[-45.15, -21.33]	6.055	-44.99	[-63.40, -26.58]	9.361	<0.001***
vIGA-AD 4 (Severe)										
Placebo	48	5.5	4.4	-7.59	[-25.40, 10.22]	9.049				
UPA 15 mg QD	112	4.9	3.2	-29.62	[-41.38, -17.86]	5.975	-22.03	[-43.37, -0.69]	10.841	0.043*
UPA 30 mg QD	123	6.1	3.2	-38.08	[-49.27, -26.88]	5.687	-30.49	[-51.53, -9.44]	10.691	0.005**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-D Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo	66	5.1	4.8	8.65	[-9.55, 26.85]	9.246				
UPA 15 mg QD	107	4.9	3.3	-19.55	[-33.90, -5.20]	7.288	-28.20	[-51.38, -5.03]	11.774	0.017*
UPA 30 mg QD	110	4.9	2.6	-34.95	[-49.01, -20.90]	7.142	-43.60	[-66.60, -20.61]	11.683	<0.001***
Japan										
Placebo	3	7.7	8.0	10.66	[-63.88, 85.20]	36.477				
UPA 15 mg QD	15	3.6	1.6	-35.84	[-69.26, -2.42]	16.357	-46.50	[-129.08, 36.09]	40.435	0.259
UPA 30 mg QD	15	5.6	3.4	-22.02	[-55.04, 11.00]	16.149	-32.67	[-113.75, 48.40]	39.660	0.417
China										
Placebo	7	5.0	4.9	38.86	[-14.27, 91.98]	26.101				
UPA 15 mg QD	13	6.8	5.7	8.47	[-30.99, 47.92]	19.401	-30.39	[-96.82, 36.04]	32.657	0.359
UPA 30 mg QD	16	4.7	3.6	-19.84	[-55.19, 15.52]	17.377	-58.69	[-122.32, 4.94]	31.262	0.069

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-D Total Score										
Week 12 (Cont.)										
Other										
Placebo	66	5.3	4.3	-2.98	[-16.63, 10.68]	6.938				
UPA 15 mg QD	109	5.5	3.3	-29.89	[-40.53, -19.25]	5.406	-26.91	[-44.23, -9.60]	8.797	0.002**
UPA 30 mg QD	113	5.3	2.9	-40.01	[-50.48, -29.54]	5.319	-37.03	[-54.24, -19.82]	8.742	<0.001***
Adolescent										
Placebo	19	5.0	3.4	-29.77	[-55.16, -4.38]	12.783				
UPA 15 mg QD	37	4.4	2.6	-39.55	[-57.62, -21.47]	9.103	-9.78	[-40.95, 21.40]	15.697	0.535
UPA 30 mg QD	39	4.4	2.3	-37.67	[-55.20, -20.13]	8.832	-7.90	[-38.77, 22.97]	15.545	0.613
Adult										
Placebo	123	5.3	4.9	9.94	[-2.00, 21.89]	6.081				
UPA 15 mg QD	207	5.3	3.5	-21.17	[-30.40, -11.94]	4.700	-31.11	[-46.21, -16.02]	7.685	<0.001***
UPA 30 mg QD	215	5.3	2.9	-34.78	[-43.83, -25.74]	4.605	-44.72	[-59.71, -29.74]	7.628	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-D Total Score										
Week 16										
All										
Placebo	116	4.9	4.1	-7.97	[-22.23, 6.29]	7.264				
UPA 15 mg QD	230	5.2	3.5	-26.15	[-36.77, -15.52]	5.413	-18.18	[-34.62, -1.73]	8.375	0.030*
UPA 30 mg QD	245	5.2	2.8	-36.17	[-46.51, -25.83]	5.265	-28.20	[-44.50, -11.90]	8.300	0.001**
vIGA-AD 3 (Moderate)										
Placebo	78	4.7	4.2	-1.08	[-16.45, 14.29]	7.814				
UPA 15 mg QD	127	5.4	3.5	-20.80	[-33.03, -8.56]	6.221	-19.72	[-39.37, -0.07]	9.991	0.049*
UPA 30 mg QD	127	4.3	2.5	-27.17	[-39.40, -14.95]	6.214	-26.09	[-45.72, -6.46]	9.980	0.009**
vIGA-AD 4 (Severe)										
Placebo	38	5.3	3.8	3.44	[-21.61, 28.50]	12.727				
UPA 15 mg QD	103	5.0	3.5	-18.06	[-33.68, -2.44]	7.932	-21.50	[-51.02, 8.01]	14.990	0.153
UPA 30 mg QD	118	6.1	3.1	-34.21	[-48.88, -19.54]	7.447	-37.66	[-66.70, -8.61]	14.751	0.011*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-D Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	58	4.7	4.3	-2.61	[-22.27, 17.05]	9.988				
UPA 15 mg QD	101	5.0	3.3	-16.78	[-31.86, -1.71]	7.655	-14.17	[-38.95, 10.60]	12.584	0.261
UPA 30 mg QD	111	5.0	2.6	-28.72	[-43.12, -14.31]	7.315	-26.11	[-50.48, -1.73]	12.380	0.036*
Japan										
Placebo	1	2.0	1.0	-48.62	[-137.19, 39.95]	43.183				
UPA 15 mg QD	13	3.9	1.8	-34.21	[-62.70, -5.73]	13.640	14.40	[-78.51, 107.31]	45.231	0.753
UPA 30 mg QD	13	6.3	3.9	-30.61	[-58.92, -2.30]	13.592	18.01	[-74.86, 110.87]	45.290	0.694
China										
Placebo	7	5.0	5.7	24.34	[-28.25, 76.94]	25.802				
UPA 15 mg QD	13	6.8	5.6	1.11	[-37.97, 40.19]	19.184	-23.23	[-89.02, 42.55]	32.289	0.477
UPA 30 mg QD	15	4.7	2.3	-16.90	[-53.04, 19.24]	17.739	-41.25	[-104.89, 22.40]	31.222	0.196

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-D Total Score										
Week 16 (Cont.)										
Other										
Placebo	50	5.1	3.7	-0.64	[-20.90, 19.63]	10.295				
UPA 15 mg QD	103	5.5	3.7	-23.18	[-37.60, -8.75]	7.325	-22.54	[-47.42, 2.34]	12.637	0.076
UPA 30 mg QD	106	5.3	2.9	-34.84	[-49.08, -20.61]	7.229	-34.20	[-58.97, -9.44]	12.578	0.007**
Adolescent										
Placebo	16	4.5	3.6	-17.35	[-54.80, 20.09]	18.853				
UPA 15 mg QD	36	4.3	2.4	-37.95	[-63.40, -12.50]	12.803	-20.60	[-65.88, 24.69]	22.793	0.369
UPA 30 mg QD	39	4.5	2.9	-21.43	[-45.90, 3.03]	12.309	-4.08	[-48.82, 40.66]	22.519	0.857
Adult										
Placebo	100	4.9	4.2	0.78	[-13.46, 15.01]	7.246				
UPA 15 mg QD	194	5.4	3.7	-16.76	[-27.13, -6.38]	5.281	-17.53	[-35.15, 0.08]	8.967	0.051
UPA 30 mg QD	206	5.3	2.7	-31.71	[-41.78, -21.63]	5.129	-32.48	[-49.92, -15.05]	8.877	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　9.2.1

表 2.7.3.6-64. 二重盲検投与期の来院時点別の HADS 合計スコアのベースラインからの変化量（MMRM，ITT_M 集団）：M16-045 試験

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 12										
All										
Placebo	150	12.0	10.6	-1.8	[-2.7, -0.9]	0.47				
UPA 15 mg QD	250	12.4	8.7	-3.9	[-4.6, -3.1]	0.38	-2.0	[-3.1, -1.0]	0.53	<0.001***
UPA 30 mg QD	262	12.2	8.2	-4.3	[-5.0, -3.5]	0.37	-2.4	[-3.5, -1.4]	0.53	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	99	11.5	10.8	-0.8	[-1.8, 0.2]	0.51				
UPA 15 mg QD	136	13.0	9.1	-3.3	[-4.2, -2.5]	0.43	-2.5	[-3.8, -1.2]	0.67	<0.001***
UPA 30 mg QD	138	10.9	7.7	-3.5	[-4.3, -2.7]	0.43	-2.7	[-4.0, -1.4]	0.66	<0.001***
vIGA-AD 4 (Severe)										
Placebo	51	13.0	10.4	-2.5	[-4.0, -1.1]	0.74				
UPA 15 mg QD	114	11.8	8.3	-4.0	[-5.0, -3.0]	0.50	-1.5	[-3.2, 0.3]	0.89	0.099
UPA 30 mg QD	124	13.8	8.7	-4.5	[-5.5, -3.6]	0.47	-2.0	[-3.7, -0.3]	0.88	0.024*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo	70	11.9	11.4	-0.6	[-1.8, 0.6]	0.63				
UPA 15 mg QD	109	12.5	9.3	-3.0	[-3.9, -2.0]	0.50	-2.4	[-3.9, -0.8]	0.80	0.004**
UPA 30 mg QD	116	12.0	8.5	-3.5	[-4.4, -2.5]	0.48	-2.9	[-4.4, -1.3]	0.79	<0.001***
Japan										
Placebo	3	14.3	13.7	1.8	[-2.6, 6.2]	2.14				
UPA 15 mg QD	15	7.5	3.5	-5.8	[-7.8, -3.8]	0.98	-7.6	[-12.5, -2.7]	2.39	0.004**
UPA 30 mg QD	15	12.5	8.9	-2.2	[-4.2, -0.3]	0.96	-4.0	[-8.8, 0.7]	2.32	0.093
China										
Placebo	7	13.3	12.9	-0.2	[-4.1, 3.8]	1.93				
UPA 15 mg QD	14	13.5	11.2	-1.9	[-4.7, 0.9]	1.37	-1.7	[-6.5, 3.1]	2.36	0.469
UPA 30 mg QD	17	12.0	8.3	-4.2	[-6.7, -1.7]	1.24	-4.0	[-8.7, 0.6]	2.30	0.088

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS Total Score										
Week 12 (Cont.)										
Other										
Placebo	70	11.9	9.5	-2.6	[-3.8, -1.4]	0.61				
UPA 15 mg QD	112	12.9	8.5	-4.2	[-5.1, -3.2]	0.48	-1.5	[-3.0, -0.0]	0.77	0.049*
UPA 30 mg QD	114	12.4	7.7	-4.7	[-5.7, -3.8]	0.47	-2.1	[-3.6, -0.6]	0.77	0.007**
Adolescent										
Placebo	20	10.6	8.8	-2.4	[-4.5, -0.3]	1.06				
UPA 15 mg QD	38	12.1	7.7	-4.1	[-5.6, -2.6]	0.76	-1.7	[-4.3, 0.9]	1.31	0.192
UPA 30 mg QD	40	12.0	7.7	-4.1	[-5.6, -2.6]	0.74	-1.7	[-4.3, 0.9]	1.30	0.191
Adult										
Placebo	130	12.2	10.9	-1.3	[-2.2, -0.4]	0.46				
UPA 15 mg QD	212	12.5	8.9	-3.5	[-4.2, -2.8]	0.36	-2.2	[-3.3, -1.0]	0.58	<0.001***
UPA 30 mg QD	222	12.3	8.3	-4.0	[-4.7, -3.3]	0.35	-2.6	[-3.8, -1.5]	0.58	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 16										
All										
Placebo	123	11.4	9.5	-2.4	[-3.4, -1.4]	0.53				
UPA 15 mg QD	237	12.5	8.8	-3.6	[-4.4, -2.8]	0.41	-1.2	[-2.4, -0.0]	0.61	0.042*
UPA 30 mg QD	253	12.4	7.7	-4.7	[-5.5, -3.9]	0.40	-2.3	[-3.5, -1.1]	0.60	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	81	11.1	9.9	-1.6	[-2.7, -0.4]	0.58				
UPA 15 mg QD	133	12.6	9.1	-3.0	[-3.9, -2.1]	0.47	-1.5	[-2.9, 0.0]	0.75	0.052
UPA 30 mg QD	134	11.1	7.4	-3.8	[-4.7, -2.9]	0.47	-2.2	[-3.7, -0.8]	0.74	0.003**
vIGA-AD 4 (Severe)										
Placebo	42	12.0	8.9	-2.7	[-4.4, -1.0]	0.86				
UPA 15 mg QD	104	12.2	8.5	-3.9	[-5.0, -2.8]	0.57	-1.1	[-3.2, 0.9]	1.03	0.267
UPA 30 mg QD	119	13.8	7.9	-5.1	[-6.2, -4.1]	0.54	-2.4	[-4.4, -0.4]	1.02	0.019*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups: Compared to Placebo LS Mean	Between Groups: Compared to Placebo [95% CI]	Between Groups: Compared to Placebo SE	Between Groups: Compared to Placebo P-value
HADS Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	60	11.5	10.4	-1.0	[-2.3, 0.3]	0.67				
UPA 15 mg QD	106	12.2	9.0	-3.0	[-4.0, -2.0]	0.52	-2.0	[-3.7, -0.3]	0.85	0.019*
UPA 30 mg QD	115	12.4	8.0	-4.0	[-5.0, -3.0]	0.50	-3.0	[-4.6, -1.4]	0.83	<0.001***
Japan										
Placebo	1	3.0	2.0	0.1	[-8.3, 8.6]	4.15				
UPA 15 mg QD	13	8.3	4.2	-5.1	[-7.8, -2.3]	1.33	-5.2	[-14.1, 3.7]	4.37	0.242
UPA 30 mg QD	14	12.9	8.4	-3.0	[-5.7, -0.4]	1.30	-3.2	[-12.0, 5.7]	4.34	0.470
China										
Placebo	7	13.3	14.1	1.1	[-3.6, 5.8]	2.31				
UPA 15 mg QD	14	13.5	10.1	-3.0	[-6.3, 0.4]	1.64	-4.1	[-9.9, 1.7]	2.83	0.159
UPA 30 mg QD	16	12.1	6.4	-5.4	[-8.5, -2.3]	1.50	-6.5	[-12.2, -0.9]	2.76	0.024*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups: Compared to Placebo LS Mean	Between Groups: Compared to Placebo [95% CI]	Between Groups: Compared to Placebo SE	Between Groups: Compared to Placebo P-value
HADS Total Score										
Week 16 (Cont.)										
Other										
Placebo	55	11.2	8.1	-3.6	[-5.1, -2.2]	0.74				
UPA 15 mg QD	104	13.1	9.1	-3.5	[-4.6, -2.4]	0.56	0.1	[-1.7, 1.9]	0.93	0.912
UPA 30 mg QD	108	12.4	7.4	-4.9	[-6.0, -3.8]	0.55	-1.2	[-3.1, 0.6]	0.93	0.179
Adolescent										
Placebo	17	10.1	9.2	-2.1	[-4.9, 0.7]	1.39				
UPA 15 mg QD	37	11.9	7.7	-4.0	[-5.9, -2.0]	0.97	-1.9	[-5.2, 1.5]	1.70	0.274
UPA 30 mg QD	40	12.3	7.7	-4.1	[-5.9, -2.2]	0.94	-2.0	[-5.3, 1.4]	1.68	0.242
Adult										
Placebo	106	11.6	9.6	-2.1	[-3.1, -1.0]	0.52				
UPA 15 mg QD	200	12.6	9.1	-3.2	[-4.0, -2.5]	0.39	-1.2	[-2.5, 0.1]	0.65	0.069
UPA 30 mg QD	213	12.4	7.7	-4.5	[-5.2, -3.7]	0.38	-2.4	[-3.7, -1.2]	0.64	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 12										
All										
Placebo	150	7.0	6.1	-1.2	[-1.7, -0.7]	0.28				
UPA 15 mg QD	250	7.3	5.4	-2.0	[-2.4, -1.5]	0.22	-0.8	[-1.4, -0.2]	0.31	0.013*
UPA 30 mg QD	262	7.3	5.4	-2.0	[-2.4, -1.6]	0.22	-0.8	[-1.4, -0.2]	0.31	0.013*
vIGA-AD 3 (Moderate)										
Placebo	99	6.6	6.1	-0.8	[-1.3, -0.2]	0.29				
UPA 15 mg QD	136	7.6	5.7	-1.7	[-2.2, -1.2]	0.25	-1.0	[-1.7, -0.2]	0.39	0.012*
UPA 30 mg QD	138	6.8	5.2	-1.7	[-2.2, -1.2]	0.25	-1.0	[-1.7, -0.2]	0.38	0.013*
vIGA-AD 4 (Severe)										
Placebo	51	7.8	6.1	-1.5	[-2.4, -0.6]	0.44				
UPA 15 mg QD	114	7.0	5.1	-2.1	[-2.7, -1.5]	0.30	-0.6	[-1.6, 0.5]	0.54	0.277
UPA 30 mg QD	124	7.7	5.5	-2.0	[-2.6, -1.5]	0.28	-0.5	[-1.6, 0.5]	0.53	0.308

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups: Compared to Placebo LS Mean	Between Groups: Compared to Placebo [95% CI]	Between Groups: Compared to Placebo SE	Between Groups: Compared to Placebo P-value
HADS-A Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo	70	7.0	6.6	-0.5	[-1.3, 0.2]	0.37				
UPA 15 mg QD	109	7.7	6.1	-1.4	[-2.0, -0.9]	0.29	-0.9	[-1.8, 0.0]	0.47	0.054
UPA 30 mg QD	116	7.3	6.0	-1.4	[-1.9, -0.8]	0.28	-0.8	[-1.7, 0.1]	0.46	0.073
Japan										
Placebo	3	6.7	5.7	-0.3	[-2.8, 2.2]	1.22				
UPA 15 mg QD	15	3.9	1.9	-3.1	[-4.2, -1.9]	0.56	-2.8	[-5.6, -0.0]	1.36	0.049*
UPA 30 mg QD	15	6.9	5.5	-0.5	[-1.6, 0.7]	0.56	-0.2	[-2.9, 2.5]	1.34	0.881
China										
Placebo	7	8.3	8.0	0.2	[-2.2, 2.6]	1.17				
UPA 15 mg QD	14	7.2	5.6	-1.8	[-3.5, -0.2]	0.83	-2.0	[-4.9, 0.9]	1.44	0.171
UPA 30 mg QD	17	7.6	4.7	-2.9	[-4.4, -1.4]	0.75	-3.1	[-5.9, -0.2]	1.39	0.034*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	SE	Between Groups Difference: Compared to Placebo LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 12 (Cont.)										
Other										
Placebo	70	6.9	5.4	-1.7	[-2.4, -1.0]	0.35				
UPA 15 mg QD	112	7.5	5.2	-2.1	[-2.7, -1.6]	0.28	-0.5	[-1.3, 0.4]	0.45	0.312
UPA 30 mg QD	114	7.2	4.9	-2.4	[-2.9, -1.8]	0.28	-0.7	[-1.6, 0.2]	0.45	0.135
Adolescent										
Placebo	20	5.8	5.5	-1.1	[-2.5, 0.3]	0.71				
UPA 15 mg QD	38	7.7	5.1	-2.4	[-3.4, -1.4]	0.50	-1.4	[-3.1, 0.3]	0.87	0.116
UPA 30 mg QD	40	7.7	5.4	-2.1	[-3.1, -1.1]	0.49	-1.0	[-2.7, 0.7]	0.86	0.237
Adult										
Placebo	130	7.2	6.2	-1.0	[-1.6, -0.5]	0.26				
UPA 15 mg QD	212	7.3	5.5	-1.8	[-2.2, -1.4]	0.21	-0.7	[-1.4, -0.1]	0.34	0.031*
UPA 30 mg QD	222	7.2	5.4	-1.8	[-2.2, -1.4]	0.20	-0.8	[-1.4, -0.1]	0.33	0.017*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups: Compared to Placebo LS Mean	Between Groups: Compared to Placebo [95% CI]	Between Groups: Compared to Placebo SE	Between Groups: Compared to Placebo P-value
HADS-A Total Score										
Week 16										
All										
Placebo	123	6.8	5.6	-1.6	[-2.2, -1.0]	0.31				
UPA 15 mg QD	237	7.4	5.4	-2.0	[-2.5, -1.5]	0.24	-0.4	[-1.1, 0.3]	0.35	0.225
UPA 30 mg QD	253	7.4	4.9	-2.4	[-2.9, -2.0]	0.23	-0.8	[-1.5, -0.2]	0.35	0.015*
vIGA-AD 3 (Moderate)										
Placebo	81	6.6	5.7	-1.1	[-1.8, -0.4]	0.34				
UPA 15 mg QD	133	7.5	5.7	-1.6	[-2.1, -1.1]	0.27	-0.5	[-1.3, 0.4]	0.43	0.259
UPA 30 mg QD	134	7.0	5.0	-2.0	[-2.5, -1.5]	0.27	-0.9	[-1.7, -0.0]	0.43	0.039*
vIGA-AD 4 (Severe)										
Placebo	42	7.2	5.3	-1.9	[-2.9, -0.9]	0.50				
UPA 15 mg QD	104	7.2	5.0	-2.3	[-2.9, -1.6]	0.33	-0.4	[-1.6, 0.8]	0.60	0.495
UPA 30 mg QD	119	7.8	4.8	-2.7	[-3.3, -2.0]	0.31	-0.8	[-1.9, 0.4]	0.59	0.185

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	60	7.0	6.2	-0.8	[-1.5, 0.0]	0.39				
UPA 15 mg QD	106	7.5	5.8	-1.6	[-2.2, -1.0]	0.30	-0.8	[-1.8, 0.1]	0.49	0.086
UPA 30 mg QD	115	7.6	5.4	-2.0	[-2.5, -1.4]	0.29	-1.2	[-2.2, -0.2]	0.48	0.014*
Japan										
Placebo	1	1.0	1.0	-1.0	[-6.7, 4.7]	2.79				
UPA 15 mg QD	13	4.4	2.4	-2.7	[-4.4, -1.0]	0.83	-1.7	[-7.7, 4.3]	2.91	0.565
UPA 30 mg QD	14	7.1	4.5	-1.6	[-3.3, 0.0]	0.81	-0.6	[-6.5, 5.3]	2.91	0.838
China										
Placebo	7	8.3	8.4	0.6	[-2.3, 3.5]	1.43				
UPA 15 mg QD	14	7.2	4.9	-2.6	[-4.7, -0.6]	1.01	-3.2	[-6.8, 0.4]	1.76	0.076
UPA 30 mg QD	16	7.7	4.0	-3.3	[-5.2, -1.4]	0.93	-3.9	[-7.4, -0.4]	1.71	0.030*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	SE	Between Groups Difference: Compared to Placebo LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16 (Cont.)										
Other										
Placebo	55	6.5	4.6	-2.4	[-3.2, -1.6]	0.41				
UPA 15 mg QD	104	7.6	5.4	-2.0	[-2.6, -1.4]	0.31	0.4	[-0.6, 1.4]	0.51	0.434
UPA 30 mg QD	108	7.2	4.6	-2.6	[-3.2, -2.0]	0.31	-0.2	[-1.2, 0.8]	0.51	0.671
Adolescent										
Placebo	17	5.9	5.8	-0.9	[-2.5, 0.8]	0.84				
UPA 15 mg QD	37	7.7	5.3	-2.2	[-3.3, -1.0]	0.58	-1.3	[-3.3, 0.7]	1.02	0.204
UPA 30 mg QD	40	7.9	4.8	-2.8	[-3.9, -1.7]	0.56	-1.9	[-3.9, 0.1]	1.01	0.060
Adult										
Placebo	106	6.9	5.5	-1.5	[-2.1, -0.9]	0.30				
UPA 15 mg QD	200	7.3	5.4	-1.8	[-2.3, -1.4]	0.22	-0.3	[-1.1, 0.4]	0.37	0.370
UPA 30 mg QD	213	7.3	4.9	-2.2	[-2.6, -1.8]	0.22	-0.7	[-1.5, -0.0]	0.37	0.050*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS-D Total Score										
Week 12										
All										
Placebo	150	5.0	4.5	-0.6	[-1.1, -0.1]	0.25				
UPA 15 mg QD	250	5.1	3.3	-1.9	[-2.3, -1.5]	0.20	-1.3	[-1.8, -0.7]	0.29	<0.001***
UPA 30 mg QD	262	5.0	2.8	-2.3	[-2.7, -1.9]	0.20	-1.7	[-2.2, -1.1]	0.28	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	99	4.9	4.7	-0.1	[-0.6, 0.5]	0.27				
UPA 15 mg QD	136	5.3	3.4	-1.6	[-2.0, -1.1]	0.23	-1.5	[-2.2, -0.8]	0.36	<0.001***
UPA 30 mg QD	138	4.0	2.5	-1.8	[-2.3, -1.4]	0.23	-1.8	[-2.5, -1.1]	0.36	<0.001***
vIGA-AD 4 (Severe)										
Placebo	51	5.2	4.3	-1.1	[-1.8, -0.3]	0.40				
UPA 15 mg QD	114	4.8	3.2	-2.0	[-2.5, -1.5]	0.27	-0.9	[-1.9, 0.0]	0.48	0.056
UPA 30 mg QD	124	6.0	3.2	-2.5	[-3.0, -2.0]	0.26	-1.4	[-2.3, -0.5]	0.47	0.003**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups: Compared to Placebo LS Mean	Between Groups: Compared to Placebo [95% CI]	Between Groups: Compared to Placebo SE	Between Groups: Compared to Placebo P-value
HADS-D Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo	70	4.8	4.7	-0.0	[-0.7, 0.6]	0.34				
UPA 15 mg QD	109	4.8	3.2	-1.5	[-2.0, -1.0]	0.27	-1.5	[-2.3, -0.6]	0.43	0.001**
UPA 30 mg QD	116	4.7	2.6	-2.1	[-2.6, -1.6]	0.26	-2.0	[-2.9, -1.2]	0.43	<0.001***
Japan										
Placebo	3	7.7	8.0	2.0	[-0.5, 4.4]	1.19				
UPA 15 mg QD	15	3.6	1.6	-2.7	[-3.8, -1.6]	0.53	-4.7	[-7.4, -2.0]	1.32	0.001**
UPA 30 mg QD	15	5.6	3.4	-1.8	[-2.8, -0.7]	0.53	-3.7	[-6.4, -1.1]	1.29	0.007**
China										
Placebo	7	5.0	4.9	-0.3	[-2.3, 1.7]	0.99				
UPA 15 mg QD	14	6.3	5.6	-0.1	[-1.5, 1.3]	0.71	0.2	[-2.3, 2.7]	1.22	0.889
UPA 30 mg QD	17	4.4	3.6	-1.3	[-2.6, 0.0]	0.64	-1.0	[-3.4, 1.4]	1.18	0.393

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups Difference: Compared to Placebo LS Mean	Between Groups Difference: Compared to Placebo [95% CI]	Between Groups Difference: Compared to Placebo SE	Between Groups Difference: Compared to Placebo P-value
HADS-D Total Score										
Week 12 (Cont.)										
Other										
Placebo	70	5.0	4.2	-1.0	[-1.6, -0.3]	0.33				
UPA 15 mg QD	112	5.4	3.3	-2.0	[-2.5, -1.5]	0.26	-1.1	[-1.9, -0.2]	0.42	0.013*
UPA 30 mg QD	114	5.2	2.9	-2.4	[-2.9, -1.9]	0.26	-1.4	[-2.2, -0.6]	0.42	0.001**
Adolescent										
Placebo	20	4.8	3.3	-1.2	[-2.3, -0.2]	0.53				
UPA 15 mg QD	38	4.3	2.6	-1.7	[-2.4, -0.9]	0.38	-0.4	[-1.7, 0.8]	0.65	0.492
UPA 30 mg QD	40	4.3	2.2	-2.0	[-2.8, -1.3]	0.37	-0.8	[-2.1, 0.5]	0.65	0.220
Adult										
Placebo	130	5.0	4.7	-0.3	[-0.8, 0.2]	0.25				
UPA 15 mg QD	212	5.2	3.4	-1.7	[-2.1, -1.4]	0.19	-1.4	[-2.0, -0.8]	0.32	<0.001***
UPA 30 mg QD	222	5.1	2.9	-2.2	[-2.5, -1.8]	0.19	-1.8	[-2.5, -1.2]	0.31	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS-D Total Score										
Week 16										
All										
Placebo	123	4.6	3.9	-0.8	[-1.4, -0.3]	0.28				
UPA 15 mg QD	237	5.1	3.5	-1.6	[-2.1, -1.2]	0.21	-0.8	[-1.4, -0.2]	0.32	0.013*
UPA 30 mg QD	253	5.0	2.8	-2.3	[-2.7, -1.9]	0.21	-1.4	[-2.1, -0.8]	0.32	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	81	4.5	4.1	-0.4	[-1.0, 0.2]	0.31				
UPA 15 mg QD	133	5.2	3.4	-1.4	[-1.9, -0.9]	0.25	-1.0	[-1.7, -0.2]	0.39	0.014*
UPA 30 mg QD	134	4.1	2.5	-1.8	[-2.3, -1.3]	0.25	-1.4	[-2.2, -0.6]	0.39	<0.001***
vIGA-AD 4 (Severe)										
Placebo	42	4.8	3.6	-1.0	[-1.9, -0.1]	0.45				
UPA 15 mg QD	104	5.0	3.5	-1.7	[-2.3, -1.1]	0.29	-0.7	[-1.7, 0.4]	0.54	0.214
UPA 30 mg QD	119	6.0	3.1	-2.5	[-3.0, -1.9]	0.28	-1.5	[-2.5, -0.4]	0.53	0.006**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups: Compared to Placebo LS Mean	Between Groups: Compared to Placebo [95% CI]	Between Groups: Compared to Placebo SE	Between Groups: Compared to Placebo P-value
HADS-D Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	60	4.6	4.2	-0.3	[-1.0, 0.4]	0.35				
UPA 15 mg QD	106	4.7	3.2	-1.4	[-2.0, -0.9]	0.27	-1.2	[-2.0, -0.3]	0.44	0.010**
UPA 30 mg QD	115	4.8	2.6	-2.1	[-2.6, -1.6]	0.26	-1.8	[-2.7, -0.9]	0.44	<0.001***
Japan										
Placebo	1	2.0	1.0	-1.0	[-6.2, 4.2]	2.52				
UPA 15 mg QD	13	3.9	1.8	-2.5	[-4.0, -1.0]	0.71	-1.5	[-6.9, 3.9]	2.61	0.574
UPA 30 mg QD	14	5.9	3.9	-1.4	[-2.8, 0.0]	0.69	-0.4	[-5.8, 5.0]	2.61	0.880
China										
Placebo	7	5.0	5.7	0.6	[-1.7, 2.8]	1.10				
UPA 15 mg QD	14	6.3	5.3	-0.4	[-2.0, 1.2]	0.78	-1.0	[-3.7, 1.8]	1.35	0.477
UPA 30 mg QD	16	4.4	2.4	-2.2	[-3.7, -0.7]	0.72	-2.8	[-5.4, -0.1]	1.31	0.042*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups: Compared to Placebo LS Mean	Between Groups: Compared to Placebo [95% CI]	Between Groups: Compared to Placebo SE	Between Groups: Compared to Placebo P-value
HADS-D Total Score										
Week 16 (Cont.)										
Other										
Placebo	55	4.7	3.5	-1.3	[-2.1, -0.5]	0.40				
UPA 15 mg QD	104	5.5	3.7	-1.6	[-2.2, -1.0]	0.30	-0.3	[-1.3, 0.7]	0.50	0.572
UPA 30 mg QD	108	5.2	2.9	-2.3	[-2.9, -1.7]	0.30	-1.0	[-2.0, -0.0]	0.50	0.044*
Adolescent										
Placebo	17	4.2	3.4	-1.1	[-2.5, 0.4]	0.71				
UPA 15 mg QD	37	4.2	2.4	-1.8	[-2.8, -0.8]	0.49	-0.7	[-2.5, 1.0]	0.87	0.391
UPA 30 mg QD	40	4.4	2.9	-1.3	[-2.3, -0.4]	0.48	-0.3	[-2.0, 1.5]	0.86	0.769
Adult										
Placebo	106	4.7	4.0	-0.6	[-1.2, -0.1]	0.27				
UPA 15 mg QD	200	5.3	3.7	-1.4	[-1.8, -1.0]	0.20	-0.8	[-1.5, -0.1]	0.34	0.017*
UPA 30 mg QD	213	5.1	2.7	-2.3	[-2.7, -1.9]	0.20	-1.7	[-2.3, -1.0]	0.34	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　9.3.1

表 2.7.3.6-65. ベースライン時の HADS-A が 8 以上又は HADS-D が 8 以上であった被験者のうち，二重盲検投与期の来院時点別の HADS-A 8 未満及び HADS-D 8 未満を達成した被験者の割合（NRI-C，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Responder n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff Compared to Placebo Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 12								
All								
Placebo + TCS	143	37 (25.9) [18.7, 33.1]	0					
UPA 15 mg QD + TCS	157	72 (45.9) [38.1, 53.7]	0	20.0	20.1	[9.5, 30.6]	<0.001***	0.248
UPA 30 mg QD + TCS	155	80 (51.6) [43.7, 59.5]	0	25.7	25.3	[14.7, 35.9]	<0.001***	0.453
vIGA-AD 3 (Moderate)								
Placebo + TCS	62	18 (29.0) [17.7, 40.3]	0					
UPA 15 mg QD + TCS	74	34 (45.9) [34.6, 57.3]	0	16.9		[0.9, 32.9]	0.038*	
UPA 30 mg QD + TCS	74	42 (56.8) [45.5, 68.0]	0	27.7		[11.8, 43.7]	0.001**	
vIGA-AD 4 (Severe)								
Placebo + TCS	81	19 (23.5) [14.2, 32.7]	0					
UPA 15 mg QD + TCS	83	38 (45.8) [35.1, 56.5]	0	22.3		[8.2, 36.5]	0.002**	
UPA 30 mg QD + TCS	81	38 (46.9) [36.0, 57.8]	0	23.5		[9.2, 37.7]	0.001**	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 12 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	50	18 (36.0) [22.7, 49.3]	0					
UPA 15 mg QD + TCS	58	27 (46.6) [33.7, 59.4]	0	10.6		[-7.9, 29.0]	0.263	
UPA 30 mg QD + TCS	60	26 (43.3) [30.8, 55.9]	0	7.3		[-10.9, 25.6]	0.432	
Japan								
Placebo + TCS	7	2 (28.6) [0.0, 62.0]	0					
UPA 15 mg QD + TCS	6	3 (50.0) [10.0, 90.0]	0	21.4		[-30.7, 73.6]	0.421	
UPA 30 mg QD + TCS	7	3 (42.9) [6.2, 79.5]	0	14.3		[-35.4, 63.9]	0.573	
China								
Placebo + TCS	14	0	0					
UPA 15 mg QD + TCS	11	3 (27.3) [1.0, 53.6]	0	27.3		[1.0, 53.6]	0.042*	
UPA 30 mg QD + TCS	12	5 (41.7) [13.8, 69.6]	0	41.7		[13.8, 69.6]	0.003**	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 12 (Cont.)								
Other								
Placebo + TCS	72	17 (23.6) [13.8, 33.4]	0					
UPA 15 mg QD + TCS	82	39 (47.6) [36.8, 58.4]	0	23.9		[9.4, 38.5]	0.001**	
UPA 30 mg QD + TCS	76	46 (60.5) [49.5, 71.5]	0	36.9		[22.2, 51.6]	<0.001***	
Adolescent								
Placebo + TCS	15	2 (13.3) [0.0, 30.5]	0					
UPA 15 mg QD + TCS	17	10 (58.8) [35.4, 82.2]	0	45.5		[16.5, 74.5]	0.002**	
UPA 30 mg QD + TCS	17	11 (64.7) [42.0, 87.4]	0	51.4		[22.9, 79.9]	<0.001***	
Adult								
Placebo + TCS	128	35 (27.3) [19.6, 35.1]	0					
UPA 15 mg QD + TCS	140	62 (44.3) [36.1, 52.5]	0	16.9		[5.7, 28.2]	0.003**	
UPA 30 mg QD + TCS	138	69 (50.0) [41.7, 58.3]	0	22.7		[11.3, 34.0]	<0.001***	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16								
All								
Placebo + TCS	143	39 (27.4) [20.1, 34.8]	1					
UPA 15 mg QD + TCS	157	72 (45.7) [37.9, 53.6]	2	18.3	18.0	[7.3, 28.7]	0.001**	0.219
UPA 30 mg QD + TCS	155	75 (48.4) [40.5, 56.2]	1	20.9	20.4	[9.7, 31.2]	<0.001***	0.776
vIGA-AD 3 (Moderate)								
Placebo + TCS	62	19 (31.0) [19.4, 42.6]	1					
UPA 15 mg QD + TCS	74	34 (45.9) [34.6, 57.3]	0	14.9		[-1.3, 31.2]	0.071	
UPA 30 mg QD + TCS	74	40 (54.1) [42.7, 65.4]	0	23.0		[6.8, 39.3]	0.005**	
vIGA-AD 4 (Severe)								
Placebo + TCS	81	20 (24.7) [15.3, 34.1]	0					
UPA 15 mg QD + TCS	83	38 (45.5) [34.6, 56.4]	2	20.8		[6.4, 35.2]	0.005**	
UPA 30 mg QD + TCS	81	35 (43.2) [32.4, 54.0]	1	18.5		[4.2, 32.8]	0.011*	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
US/Puerto Rico/Canada								
Placebo + TCS	50	14 (28.5) [15.8, 41.1]	1					
UPA 15 mg QD + TCS	58	32 (55.2) [42.4, 68.0]	0	26.7		[8.7, 44.7]	0.004**	
UPA 30 mg QD + TCS	60	22 (36.7) [24.5, 48.9]	0	8.2		[-9.4, 25.8]	0.360	
Japan								
Placebo + TCS	7	1 (14.3) [0.0, 40.2]	0					
UPA 15 mg QD + TCS	6	3 (50.0) [10.0, 90.0]	0	35.7		[-12.0, 83.4]	0.142	
UPA 30 mg QD + TCS	7	4 (57.1) [20.5, 93.8]	0	42.9		[-2.0, 87.8]	0.061	
China								
Placebo + TCS	14	5 (35.7) [10.6, 60.8]	0					
UPA 15 mg QD + TCS	11	5 (45.5) [16.0, 74.9]	0	9.7		[-28.9, 48.4]	0.622	
UPA 30 mg QD + TCS	12	6 (50.0) [21.7, 78.3]	0	14.3		[-23.5, 52.1]	0.459	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	---- Responder ---- n (%) [95% CI]&	Missing Due to COVID-19 n	Response Rate Diff ---------- Compared to Placebo ---------- Diff(%)	Adjusted Diff(%)	[95% CI]#	P-value@	Breslow-Day P-value
Week 16 (Cont.)								
Other								
Placebo + TCS	72	19 (26.4) [16.2, 36.6]	0					
UPA 15 mg QD + TCS	82	32 (38.7) [28.0, 49.5]	2	12.4		[-2.4, 27.1]	0.102	
UPA 30 mg QD + TCS	76	43 (56.5) [45.4, 67.7]	1	30.1		[15.0, 45.2]	<0.001***	
Adolescent								
Placebo + TCS	15	3 (20.0) [0.0, 40.2]	0					
UPA 15 mg QD + TCS	17	11 (64.7) [42.0, 87.4]	0	44.7		[14.3, 75.1]	0.004**	
UPA 30 mg QD + TCS	17	7 (41.2) [17.8, 64.6]	0	21.2		[-9.8, 52.1]	0.180	
Adult								
Placebo + TCS	128	36 (28.3) [20.5, 36.1]	1					
UPA 15 mg QD + TCS	140	61 (43.4) [35.1, 51.7]	2	15.1		[3.7, 26.5]	0.009**	
UPA 30 mg QD + TCS	138	68 (49.3) [40.9, 57.6]	1	20.9		[9.5, 32.4]	<0.001***	

Note: HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression;
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19.
& 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.
# @ Across the strata, 95% CI for adjusted difference and P-value are calculated according to the Cochran-Mantel-Haenszel test adjusted for strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) for the comparison of two treatment groups. Within each stratum, 95% CI for difference and P-value are calculated using Cochran-Mantel-Haenszel test without adjustment of strata. The calculations at each visit are based on non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 or non-responder imputation only if there are no missing data due to COVID-19.
***, **, * Statistically significant at the 0.001, 0.01, 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　9.1.1

表 2.7.3.6-66.　二重盲検投与期の来院時点別の HADS 合計スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-047 試験

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 12										
All										
Placebo + TCS	217	13.0	10.9	-1.60	[-12.66, 9.45]	5.634				
UPA 15 mg QD + TCS	279	13.1	8.7	-26.42	[-36.43, -16.40]	5.102	-24.81	[-38.49, -11.14]	6.967	<0.001***
UPA 30 mg QD + TCS	278	13.2	8.1	-31.76	[-41.75, -21.77]	5.089	-30.16	[-43.84, -16.47]	6.972	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	111	11.7	10.2	6.61	[-11.91, 25.13]	9.416				
UPA 15 mg QD + TCS	130	12.4	8.8	-20.12	[-37.19, -3.04]	8.683	-26.73	[-51.91, -1.54]	12.807	0.038*
UPA 30 mg QD + TCS	133	13.3	8.3	-28.93	[-45.82, -12.04]	8.589	-35.54	[-60.61, -10.46]	12.751	0.006**
vIGA-AD 4 (Severe)										
Placebo + TCS	106	14.4	11.6	-7.50	[-16.86, 1.87]	4.765				
UPA 15 mg QD + TCS	149	13.7	8.6	-29.35	[-37.29, -21.41]	4.038	-21.86	[-34.14, -9.58]	6.246	0.001**
UPA 30 mg QD + TCS	145	13.1	8.0	-33.03	[-41.08, -24.97]	4.097	-25.53	[-37.90, -13.17]	6.290	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	90	12.4	10.0	-11.56	[-21.77, -1.34]	5.189				
UPA 15 mg QD + TCS	108	13.2	9.3	-20.02	[-29.33, -10.70]	4.733	-8.46	[-22.28, 5.37]	7.025	0.230
UPA 30 mg QD + TCS	100	13.5	8.8	-28.49	[-38.16, -18.82]	4.912	-16.93	[-31.01, -2.86]	7.151	0.019*
Japan										
Placebo + TCS	12	14.8	8.8	-26.20	[-67.14, 14.73]	20.241				
UPA 15 mg QD + TCS	15	11.1	7.1	-23.89	[-60.46, 12.68]	18.080	2.31	[-52.99, 57.61]	27.343	0.933
UPA 30 mg QD + TCS	16	12.6	7.4	-36.73	[-71.90, -1.56]	17.387	-10.53	[-64.55, 43.50]	26.713	0.696
China										
Placebo + TCS	17	19.3	16.2	-12.46	[-29.33, 4.40]	8.356				
UPA 15 mg QD + TCS	13	16.7	10.2	-34.87	[-53.99, -15.76]	9.469	-22.41	[-48.02, 3.19]	12.688	0.085
UPA 30 mg QD + TCS	16	16.4	12.3	-21.83	[-39.11, -4.56]	8.558	-9.37	[-33.69, 14.94]	12.047	0.441

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 12 (Cont.)										
Other										
Placebo + TCS	98	12.2	11.0	14.77	[-4.38, 33.91]	9.736				
UPA 15 mg QD + TCS	143	12.9	8.3	-28.14	[-44.05, -12.23]	8.091	-42.91	[-67.80, -18.02]	12.660	0.001**
UPA 30 mg QD + TCS	146	12.7	7.3	-32.37	[-48.13, -16.61]	8.017	-47.14	[-71.93, -22.34]	12.612	<0.001***
Adolescent										
Placebo + TCS	29	12.1	10.6	4.14	[-17.21, 25.50]	10.752				
UPA 15 mg QD + TCS	34	11.6	7.3	-32.84	[-52.57, -13.11]	9.935	-36.98	[-66.06, -7.91]	14.641	0.013*
UPA 30 mg QD + TCS	36	12.0	7.2	-29.85	[-49.01, -10.68]	9.650	-33.99	[-62.68, -5.30]	14.447	0.021*
Adult										
Placebo + TCS	188	13.1	10.9	-1.26	[-12.60, 10.09]	5.777				
UPA 15 mg QD + TCS	245	13.3	8.9	-24.22	[-34.18, -14.27]	5.070	-22.97	[-38.06, -7.87]	7.687	0.003**
UPA 30 mg QD + TCS	242	13.4	8.3	-30.75	[-40.77, -20.73]	5.102	-29.50	[-44.63, -14.36]	7.708	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 16										
All										
Placebo + TCS	199	13.2	10.8	-14.13	[-22.46, -5.80]	4.243				
UPA 15 mg QD + TCS	270	13.0	8.6	-28.57	[-36.17, -20.98]	3.869	-14.44	[-24.02, -4.86]	4.880	0.003**
UPA 30 mg QD + TCS	269	13.3	8.3	-33.09	[-40.67, -25.51]	3.860	-18.96	[-28.54, -9.38]	4.882	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	101	11.8	10.2	-10.45	[-20.16, -0.74]	4.938				
UPA 15 mg QD + TCS	127	12.5	8.5	-30.14	[-38.89, -21.39]	4.450	-19.70	[-32.77, -6.63]	6.647	0.003**
UPA 30 mg QD + TCS	132	13.3	8.2	-35.59	[-44.22, -26.96]	4.388	-25.14	[-38.16, -12.13]	6.619	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	98	14.6	11.4	-15.21	[-25.90, -4.53]	5.436				
UPA 15 mg QD + TCS	143	13.4	8.7	-24.74	[-33.70, -15.79]	4.553	-9.53	[-23.47, 4.41]	7.091	0.180
UPA 30 mg QD + TCS	137	13.2	8.4	-29.06	[-38.18, -19.94]	4.640	-13.84	[-27.90, 0.22]	7.152	0.054

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
HADS Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	12.4	10.2	-18.96	[-29.73, -8.20]	5.470				
UPA 15 mg QD + TCS	104	13.1	8.4	-24.92	[-34.48, -15.37]	4.854	-5.96	[-20.35, 8.44]	7.314	0.416
UPA 30 mg QD + TCS	97	13.6	9.5	-25.94	[-35.83, -16.04]	5.027	-6.97	[-21.61, 7.66]	7.434	0.349
Japan										
Placebo + TCS	11	15.8	11.1	-23.72	[-66.33, 18.88]	21.090				
UPA 15 mg QD + TCS	15	11.1	6.2	-26.61	[-64.30, 11.08]	18.635	-2.88	[-60.17, 54.41]	28.348	0.920
UPA 30 mg QD + TCS	16	12.6	7.8	-31.69	[-67.96, 4.57]	17.928	-7.97	[-63.98, 48.04]	27.710	0.775
China										
Placebo + TCS	17	19.3	14.8	-17.12	[-37.86, 3.63]	10.274				
UPA 15 mg QD + TCS	13	16.7	9.8	-38.88	[-62.47, -15.30]	11.678	-21.77	[-53.27, 9.73]	15.603	0.170
UPA 30 mg QD + TCS	16	16.4	11.1	-20.55	[-41.84, 0.75]	10.545	-3.43	[-33.29, 26.43]	14.793	0.818

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 16 (Cont.)										
Other										
Placebo + TCS	91	12.4	10.5	-5.91	[-16.88, 5.06]	5.579				
UPA 15 mg QD + TCS	138	12.8	8.9	-28.02	[-37.02, -19.02]	4.577	-22.11	[-36.30, -7.92]	7.217	0.002**
UPA 30 mg QD + TCS	140	12.8	7.2	-37.31	[-46.25, -28.38]	4.544	-31.40	[-45.55, -17.25]	7.196	<0.001***
Adolescent										
Placebo + TCS	27	12.0	10.7	-8.99	[-29.69, 11.71]	10.419				
UPA 15 mg QD + TCS	33	11.8	6.6	-41.12	[-60.06, -22.18]	9.533	-32.13	[-60.18, -4.07]	14.123	0.025*
UPA 30 mg QD + TCS	33	12.6	8.8	-22.60	[-41.24, -3.95]	9.388	-13.61	[-41.46, 14.25]	14.024	0.334
Adult										
Placebo + TCS	172	13.4	10.8	-13.81	[-21.56, -6.07]	3.946				
UPA 15 mg QD + TCS	237	13.2	8.8	-25.55	[-32.22, -18.88]	3.397	-11.73	[-21.96, -1.51]	5.207	0.025*
UPA 30 mg QD + TCS	236	13.4	8.2	-33.03	[-39.73, -26.34]	3.409	-19.22	[-29.46, -8.98]	5.214	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 12										
All										
Placebo + TCS	216	7.6	6.6	-0.33	[-9.30, 8.64]	4.568				
UPA 15 mg QD + TCS	279	7.5	5.6	-20.02	[-28.18, -11.85]	4.162	-19.69	[-30.34, -9.03]	5.427	<0.001***
UPA 30 mg QD + TCS	277	7.7	5.1	-26.67	[-34.85, -18.50]	4.164	-26.34	[-37.01, -15.68]	5.434	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	110	7.1	6.1	-2.44	[-15.38, 10.50]	6.579				
UPA 15 mg QD + TCS	129	7.4	5.7	-16.82	[-28.72, -4.93]	6.049	-14.39	[-31.96, 3.19]	8.935	0.108
UPA 30 mg QD + TCS	132	7.8	5.2	-24.26	[-36.03, -12.49]	5.986	-21.82	[-39.33, -4.32]	8.903	0.015*
vIGA-AD 4 (Severe)										
Placebo + TCS	106	8.1	7.1	0.38	[-9.24, 9.99]	4.890				
UPA 15 mg QD + TCS	150	7.6	5.5	-23.91	[-32.02, -15.80]	4.127	-24.29	[-36.87, -11.70]	6.400	<0.001***
UPA 30 mg QD + TCS	145	7.6	5.1	-30.39	[-38.65, -22.14]	4.198	-30.77	[-43.45, -18.10]	6.448	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	90	7.3	6.3	-7.58	[-17.95, 2.79]	5.271				
UPA 15 mg QD + TCS	107	7.9	6.3	-14.68	[-24.17, -5.19]	4.820	-7.10	[-21.16, 6.96]	7.143	0.321
UPA 30 mg QD + TCS	100	8.4	6.0	-26.22	[-36.05, -16.40]	4.992	-18.64	[-32.97, -4.32]	7.279	0.011*
Japan										
Placebo + TCS	12	7.8	5.1	-10.94	[-45.21, 23.33]	16.942				
UPA 15 mg QD + TCS	15	5.7	3.5	-38.79	[-69.44, -8.14]	15.152	-27.85	[-74.17, 18.47]	22.902	0.231
UPA 30 mg QD + TCS	16	6.6	4.2	-31.16	[-60.61, -1.71]	14.559	-20.22	[-65.41, 24.97]	22.342	0.371
China										
Placebo + TCS	17	11.5	10.1	-7.92	[-26.73, 10.89]	9.325				
UPA 15 mg QD + TCS	13	9.4	6.6	-26.52	[-47.79, -5.24]	10.543	-18.60	[-47.27, 10.08]	14.214	0.198
UPA 30 mg QD + TCS	16	9.6	7.1	-25.68	[-44.83, -6.53]	9.491	-17.76	[-44.83, 9.32]	13.421	0.193

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 12 (Cont.)										
Other										
Placebo + TCS	97	7.2	6.5	7.65	[-5.98, 21.28]	6.932				
UPA 15 mg QD + TCS	144	7.2	5.2	-22.48	[-33.71, -11.25]	5.713	-30.13	[-47.79, -12.47]	8.983	0.001**
UPA 30 mg QD + TCS	145	7.1	4.4	-28.07	[-39.28, -16.85]	5.703	-35.72	[-53.37, -18.07]	8.977	<0.001***
Adolescent										
Placebo + TCS	29	7.7	7.4	3.66	[-20.04, 27.36]	11.941				
UPA 15 mg QD + TCS	35	7.0	5.1	-24.89	[-46.30, -3.48]	10.789	-28.56	[-60.56, 3.44]	16.123	0.080
UPA 30 mg QD + TCS	36	7.4	4.7	-21.69	[-42.94, -0.44]	10.707	-25.35	[-57.19, 6.48]	16.038	0.117
Adult										
Placebo + TCS	187	7.6	6.5	-1.71	[-10.21, 6.79]	4.330				
UPA 15 mg QD + TCS	244	7.6	5.7	-20.16	[-27.61, -12.70]	3.798	-18.45	[-29.76, -7.14]	5.760	0.001**
UPA 30 mg QD + TCS	241	7.7	5.2	-28.21	[-35.71, -20.71]	3.819	-26.50	[-37.84, -15.16]	5.774	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16										
All										
Placebo + TCS	199	7.7	6.3	-13.48	[-22.17, -4.79]	4.427				
UPA 15 mg QD + TCS	270	7.4	5.3	-22.57	[-30.42, -14.72]	3.999	-9.09	[-19.27, 1.08]	5.184	0.080
UPA 30 mg QD + TCS	269	7.7	5.2	-24.92	[-32.79, -17.06]	4.006	-11.44	[-21.63, -1.26]	5.188	0.028*
vIGA-AD 3 (Moderate)										
Placebo + TCS	101	7.1	6.2	-13.89	[-25.05, -2.73]	5.676				
UPA 15 mg QD + TCS	127	7.3	5.4	-25.48	[-35.55, -15.41]	5.121	-11.59	[-26.62, 3.44]	7.642	0.130
UPA 30 mg QD + TCS	132	7.8	5.2	-25.89	[-35.82, -15.96]	5.048	-12.00	[-26.95, 2.96]	7.605	0.116
vIGA-AD 4 (Severe)										
Placebo + TCS	98	8.2	6.5	-14.14	[-24.77, -3.50]	5.410				
UPA 15 mg QD + TCS	143	7.5	5.2	-21.19	[-30.07, -12.31]	4.518	-7.05	[-20.92, 6.81]	7.051	0.318
UPA 30 mg QD + TCS	137	7.7	5.2	-25.50	[-34.56, -16.44]	4.609	-11.36	[-25.34, 2.62]	7.110	0.111

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	7.3	6.1	-20.40	[-31.29, -9.50]	5.535				
UPA 15 mg QD + TCS	103	7.8	5.6	-19.66	[-29.32, -10.00]	4.908	0.73	[-13.83, 15.29]	7.398	0.921
UPA 30 mg QD + TCS	97	8.5	6.2	-23.92	[-33.90, -13.95]	5.069	-3.53	[-18.34, 11.28]	7.524	0.639
Japan										
Placebo + TCS	11	8.2	6.0	-11.20	[-53.53, 31.13]	20.957				
UPA 15 mg QD + TCS	15	5.7	3.1	-25.04	[-61.92, 11.84]	18.231	-13.84	[-70.28, 42.59]	27.931	0.623
UPA 30 mg QD + TCS	16	6.6	4.3	-22.36	[-57.89, 13.17]	17.559	-11.16	[-66.43, 44.11]	27.344	0.685
China										
Placebo + TCS	17	11.5	8.5	-20.84	[-39.43, -2.25]	9.215				
UPA 15 mg QD + TCS	13	9.4	5.3	-42.23	[-63.25, -21.22]	10.416	-21.39	[-49.73, 6.94]	14.046	0.135
UPA 30 mg QD + TCS	16	9.6	6.6	-26.67	[-45.58, -7.75]	9.376	-5.82	[-32.58, 20.93]	13.263	0.663

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16 (Cont.)										
Other										
Placebo + TCS	91	7.2	6.2	-8.24	[-20.51, 4.03]	6.242				
UPA 15 mg QD + TCS	139	7.2	5.4	-23.89	[-33.93, -13.85]	5.105	-15.65	[-31.50, 0.21]	8.064	0.053
UPA 30 mg QD + TCS	140	7.1	4.5	-27.24	[-37.25, -17.22]	5.096	-18.99	[-34.84, -3.15]	8.058	0.019*
Adolescent										
Placebo + TCS	27	7.6	7.0	-8.02	[-33.24, 17.19]	12.708				
UPA 15 mg QD + TCS	34	7.0	4.5	-34.01	[-56.65, -11.37]	11.410	-25.98	[-59.93, 7.96]	17.108	0.132
UPA 30 mg QD + TCS	33	7.7	5.4	-12.74	[-35.40, 9.93]	11.423	-4.71	[-38.62, 29.19]	17.086	0.783
Adult										
Placebo + TCS	172	7.7	6.2	-14.96	[-22.95, -6.97]	4.069				
UPA 15 mg QD + TCS	236	7.5	5.4	-21.85	[-28.74, -14.96]	3.511	-6.89	[-17.44, 3.67]	5.374	0.200
UPA 30 mg QD + TCS	236	7.7	5.2	-27.40	[-34.30, -20.49]	3.516	-12.43	[-22.99, -1.88]	5.378	0.021*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
HADS-D Total Score										
Week 12										
All										
Placebo + TCS	210	5.6	4.3	-13.36	[-26.24, -0.48]	6.562				
UPA 15 mg QD + TCS	274	5.7	3.1	-29.52	[-41.22, -17.82]	5.960	-16.17	[-31.27, -1.06]	7.696	0.036*
UPA 30 mg QD + TCS	269	5.7	3.0	-34.23	[-45.95, -22.50]	5.975	-20.87	[-36.03, -5.71]	7.723	0.007**
vIGA-AD 3 (Moderate)										
Placebo + TCS	106	4.9	4.1	-2.57	[-20.16, 15.01]	8.942				
UPA 15 mg QD + TCS	128	5.2	3.1	-18.29	[-34.19, -2.39]	8.085	-15.72	[-39.41, 7.97]	12.049	0.193
UPA 30 mg QD + TCS	130	5.6	3.1	-31.26	[-47.08, -15.44]	8.043	-28.69	[-52.36, -5.02]	12.038	0.018*
vIGA-AD 4 (Severe)										
Placebo + TCS	104	6.3	4.5	-20.29	[-34.85, -5.74]	7.403				
UPA 15 mg QD + TCS	146	6.1	3.1	-35.60	[-47.97, -23.23]	6.291	-15.31	[-34.41, 3.79]	9.714	0.116
UPA 30 mg QD + TCS	139	5.8	3.0	-33.48	[-46.13, -20.82]	6.436	-13.18	[-32.48, 6.11]	9.816	0.180

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
HADS-D Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	87	5.3	3.7	-19.84	[-37.58, -2.09]	9.017				
UPA 15 mg QD + TCS	105	5.5	3.1	-21.62	[-37.74, -5.50]	8.191	-1.78	[-25.76, 22.19]	12.182	0.884
UPA 30 mg QD + TCS	95	5.3	3.0	-31.33	[-48.12, -14.55]	8.529	-11.50	[-35.92, 12.93]	12.411	0.355
Japan										
Placebo + TCS	12	7.1	3.7	-42.95	[-82.73, -3.16]	19.662				
UPA 15 mg QD + TCS	14	5.9	3.6	-35.99	[-72.74, 0.76]	18.160	6.96	[-47.32, 61.24]	26.828	0.797
UPA 30 mg QD + TCS	16	5.9	3.3	-17.81	[-52.17, 16.56]	16.982	25.14	[-27.53, 77.81]	26.033	0.340
China										
Placebo + TCS	17	7.8	6.2	-14.20	[-35.21, 6.82]	10.414				
UPA 15 mg QD + TCS	13	7.3	3.6	-43.11	[-67.10, -19.12]	11.887	-28.91	[-60.82, 2.99]	15.809	0.074
UPA 30 mg QD + TCS	16	6.8	5.2	-9.28	[-30.98, 12.43]	10.757	4.92	[-25.38, 35.21]	15.012	0.745

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-D Total Score										
Week 12 (Cont.)										
Other										
Placebo + TCS	94	5.3	4.6	1.29	[-16.76, 19.33]	9.177				
UPA 15 mg QD + TCS	142	5.7	3.0	-29.30	[-44.07, -14.54]	7.508	-30.59	[-53.90, -7.28]	11.856	0.010**
UPA 30 mg QD + TCS	142	5.9	2.8	-37.85	[-52.69, -23.02]	7.543	-39.14	[-62.51, -15.77]	11.885	0.001**
Adolescent										
Placebo + TCS	27	4.7	3.2	-7.32	[-48.38, 33.74]	20.683				
UPA 15 mg QD + TCS	35	4.3	2.0	-36.58	[-72.89, -0.27]	18.286	-29.26	[-84.07, 25.55]	27.607	0.292
UPA 30 mg QD + TCS	35	4.8	2.5	-28.01	[-64.12, 8.10]	18.189	-20.69	[-75.37, 33.99]	27.544	0.454
Adult										
Placebo + TCS	183	5.8	4.4	-12.03	[-23.62, -0.43]	5.906				
UPA 15 mg QD + TCS	239	5.9	3.3	-26.41	[-36.57, -16.25]	5.174	-14.39	[-29.81, 1.03]	7.852	0.067
UPA 30 mg QD + TCS	234	5.9	3.1	-32.96	[-43.22, -22.69]	5.229	-20.93	[-36.42, -5.44]	7.888	0.008**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group --- Percent Change from Baseline --- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
HADS-D Total Score										
Week 16										
All										
Placebo + TCS	194	5.7	4.5	-13.45	[-26.34, -0.56]	6.567				
UPA 15 mg QD + TCS	267	5.6	3.3	-27.50	[-39.10, -15.89]	5.914	-14.05	[-29.10, 1.00]	7.665	0.067
UPA 30 mg QD + TCS	260	5.8	3.2	-36.84	[-48.49, -25.19]	5.934	-23.39	[-38.51, -8.28]	7.700	0.002**
vIGA-AD 3 (Moderate)										
Placebo + TCS	97	4.9	4.1	-8.72	[-25.11, 7.66]	8.333				
UPA 15 mg QD + TCS	127	5.2	3.0	-28.82	[-43.34, -14.30]	7.386	-20.10	[-41.98, 1.79]	11.129	0.072
UPA 30 mg QD + TCS	129	5.7	3.0	-36.94	[-51.39, -22.48]	7.350	-28.21	[-50.09, -6.34]	11.124	0.012*
vIGA-AD 4 (Severe)										
Placebo + TCS	97	6.4	4.9	-13.91	[-29.87, 2.04]	8.111				
UPA 15 mg QD + TCS	140	6.0	3.5	-22.59	[-36.03, -9.15]	6.832	-8.68	[-29.54, 12.18]	10.605	0.414
UPA 30 mg QD + TCS	131	5.8	3.3	-33.05	[-46.87, -19.23]	7.026	-19.13	[-40.25, 1.99]	10.738	0.076

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
HADS-D Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	78	5.3	4.2	-9.81	[-29.22, 9.59]	9.860				
UPA 15 mg QD + TCS	102	5.5	2.9	-28.76	[-46.01, -11.51]	8.764	-18.94	[-44.91, 7.02]	13.192	0.152
UPA 30 mg QD + TCS	96	5.2	3.4	-22.65	[-40.42, -4.87]	9.032	-12.83	[-39.15, 13.48]	13.371	0.338
Japan										
Placebo + TCS	11	7.6	5.1	-38.35	[-104.83, 28.14]	32.886				
UPA 15 mg QD + TCS	14	5.9	3.2	-41.87	[-102.87, 19.13]	30.143	-3.53	[-93.80, 86.74]	44.634	0.937
UPA 30 mg QD + TCS	16	5.9	3.5	-3.75	[-60.80, 53.30]	28.193	34.60	[-53.05, 122.24]	43.337	0.430
China										
Placebo + TCS	17	7.8	6.3	-7.91	[-31.48, 15.66]	11.677				
UPA 15 mg QD + TCS	13	7.3	4.5	-28.54	[-55.45, -1.62]	13.334	-20.63	[-56.41, 15.16]	17.729	0.251
UPA 30 mg QD + TCS	15	7.3	4.6	-24.64	[-49.40, 0.12]	12.276	-16.73	[-50.97, 17.51]	16.970	0.330

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: LS Mean (Percent Change from Baseline)	[95% CI]	SE	Between Groups Difference: LS Mean (Compared to Placebo)	[95% CI]	SE	P-value
HADS-D Total Score										
Week 16 (Cont.)										
Other										
Placebo + TCS	88	5.4	4.4	-11.49	[-26.75, 3.76]	7.758				
UPA 15 mg QD + TCS	138	5.6	3.5	-20.91	[-33.25, -8.56]	6.275	-9.41	[-29.03, 10.21]	9.975	0.346
UPA 30 mg QD + TCS	133	6.0	2.8	-49.53	[-62.07, -36.99]	6.375	-38.03	[-57.80, -18.27]	10.049	<0.001***
Adolescent										
Placebo + TCS	26	4.5	3.8	-13.01	[-46.22, 20.21]	16.651				
UPA 15 mg QD + TCS	33	4.6	2.0	-49.01	[-78.57, -19.45]	14.816	-36.00	[-80.45, 8.45]	22.282	0.111
UPA 30 mg QD + TCS	33	4.9	3.3	-10.93	[-40.36, 18.51]	14.759	2.08	[-42.31, 46.47]	22.257	0.926
Adult										
Placebo + TCS	168	5.9	4.6	-11.17	[-23.14, 0.79]	6.093				
UPA 15 mg QD + TCS	234	5.8	3.5	-22.32	[-32.62, -12.02]	5.245	-11.15	[-26.93, 4.64]	8.040	0.166
UPA 30 mg QD + TCS	227	5.9	3.1	-39.08	[-49.51, -28.65]	5.314	-27.91	[-43.78, -12.03]	8.085	0.001**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　9.2.1

表 2.7.3.6-67. 二重盲検投与期の来院時点別の HADS 合計スコアのベースラインからの変化量（MMRM，ITT_M 集団）：M16-047 試験

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
HADS Total Score										
Week 12										
All										
Placebo + TCS	217	13.0	10.9	-2.2	[-3.0, -1.3]	0.43				
UPA 15 mg QD + TCS	282	13.0	8.7	-4.3	[-5.1, -3.6]	0.39	-2.2	[-3.1, -1.2]	0.50	<0.001***
UPA 30 mg QD + TCS	278	13.2	8.1	-5.0	[-5.8, -4.3]	0.39	-2.9	[-3.9, -1.9]	0.50	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	111	11.7	10.2	-1.8	[-2.9, -0.8]	0.52				
UPA 15 mg QD + TCS	131	12.4	8.7	-3.6	[-4.5, -2.7]	0.48	-1.8	[-3.1, -0.4]	0.71	0.013*
UPA 30 mg QD + TCS	133	13.3	8.3	-4.7	[-5.6, -3.7]	0.48	-2.8	[-4.2, -1.4]	0.71	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	106	14.4	11.6	-2.2	[-3.3, -1.2]	0.54				
UPA 15 mg QD + TCS	151	13.5	8.7	-4.9	[-5.8, -4.0]	0.45	-2.6	[-4.0, -1.2]	0.70	<0.001***
UPA 30 mg QD + TCS	145	13.1	8.0	-5.3	[-6.3, -4.4]	0.46	-3.1	[-4.5, -1.7]	0.71	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups Difference: Compared to Placebo LS Mean	Between Groups Difference: Compared to Placebo [95% CI]	Between Groups Difference: Compared to Placebo SE	Between Groups Difference: Compared to Placebo P-value
HADS Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	90	12.4	10.0	-2.7	[-3.7, -1.7]	0.53				
UPA 15 mg QD + TCS	108	13.2	9.3	-3.8	[-4.8, -2.9]	0.48	-1.1	[-2.5, 0.3]	0.72	0.122
UPA 30 mg QD + TCS	100	13.5	8.8	-4.4	[-5.4, -3.4]	0.50	-1.7	[-3.1, -0.3]	0.73	0.021*
Japan										
Placebo + TCS	12	14.8	8.8	-4.9	[-8.0, -1.7]	1.56				
UPA 15 mg QD + TCS	15	11.1	7.1	-5.1	[-7.9, -2.3]	1.39	-0.2	[-4.5, 4.0]	2.10	0.917
UPA 30 mg QD + TCS	16	12.6	7.4	-5.3	[-8.0, -2.6]	1.34	-0.4	[-4.6, 3.7]	2.05	0.841
China										
Placebo + TCS	17	19.3	16.2	-1.7	[-5.1, 1.7]	1.70				
UPA 15 mg QD + TCS	14	15.5	11.3	-5.3	[-9.1, -1.5]	1.87	-3.6	[-8.7, 1.5]	2.55	0.164
UPA 30 mg QD + TCS	16	16.4	12.3	-4.6	[-8.1, -1.1]	1.74	-2.9	[-7.8, 2.0]	2.44	0.243

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups Difference: Compared to Placebo LS Mean	Between Groups Difference: Compared to Placebo [95% CI]	Between Groups Difference: Compared to Placebo SE	Between Groups Difference: Compared to Placebo P-value
HADS Total Score										
Week 12 (Cont.)										
Other										
Placebo + TCS	98	12.2	11.0	-1.2	[-2.4, -0.1]	0.56				
UPA 15 mg QD + TCS	145	12.7	8.2	-4.4	[-5.3, -3.5]	0.47	-3.2	[-4.6, -1.7]	0.73	<0.001***
UPA 30 mg QD + TCS	146	12.7	7.3	-5.4	[-6.3, -4.5]	0.47	-4.2	[-5.6, -2.7]	0.73	<0.001***
Adolescent										
Placebo + TCS	29	12.1	10.6	-1.4	[-3.0, 0.3]	0.83				
UPA 15 mg QD + TCS	36	11.0	7.0	-4.3	[-5.8, -2.9]	0.75	-3.0	[-5.2, -0.8]	1.12	0.009**
UPA 30 mg QD + TCS	36	12.0	7.2	-4.7	[-6.2, -3.2]	0.74	-3.4	[-5.6, -1.2]	1.11	0.003**
Adult										
Placebo + TCS	188	13.1	10.9	-2.2	[-3.0, -1.4]	0.41				
UPA 15 mg QD + TCS	246	13.2	9.0	-4.3	[-5.0, -3.5]	0.36	-2.1	[-3.1, -1.0]	0.55	<0.001***
UPA 30 mg QD + TCS	242	13.4	8.3	-5.0	[-5.7, -4.3]	0.36	-2.8	[-3.9, -1.8]	0.55	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	[95% CI]	SE	LS Mean	[95% CI]	SE	P-value
				Within Group ---- Change from Baseline ----			Between Groups Difference ---------- Compared to Placebo ----------			
HADS Total Score										
Week 16										
All										
Placebo + TCS	200	13.1	10.8	-2.4	[-3.3, -1.5]	0.44				
UPA 15 mg QD + TCS	273	12.8	8.6	-4.4	[-5.2, -3.6]	0.40	-2.0	[-3.0, -1.0]	0.52	<0.001***
UPA 30 mg QD + TCS	269	13.3	8.3	-4.9	[-5.7, -4.1]	0.40	-2.5	[-3.6, -1.5]	0.52	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	102	11.7	10.2	-1.9	[-2.9, -0.8]	0.53				
UPA 15 mg QD + TCS	128	12.4	8.4	-4.1	[-5.0, -3.1]	0.48	-2.2	[-3.6, -0.8]	0.71	0.002**
UPA 30 mg QD + TCS	132	13.3	8.2	-4.8	[-5.7, -3.9]	0.47	-2.9	[-4.3, -1.5]	0.71	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	98	14.6	11.4	-2.7	[-3.8, -1.5]	0.57				
UPA 15 mg QD + TCS	145	13.2	8.7	-4.6	[-5.5, -3.6]	0.48	-1.9	[-3.4, -0.5]	0.75	0.011*
UPA 30 mg QD + TCS	137	13.2	8.4	-5.0	[-5.9, -4.0]	0.49	-2.3	[-3.8, -0.8]	0.76	0.002**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	12.4	10.2	-2.5	[-3.6, -1.3]	0.60				
UPA 15 mg QD + TCS	104	13.1	8.4	-4.6	[-5.6, -3.6]	0.53	-2.1	[-3.7, -0.6]	0.80	0.008**
UPA 30 mg QD + TCS	97	13.6	9.5	-3.7	[-4.8, -2.7]	0.55	-1.3	[-2.9, 0.3]	0.81	0.118
Japan										
Placebo + TCS	11	15.8	11.1	-3.1	[-6.5, 0.3]	1.67				
UPA 15 mg QD + TCS	15	11.1	6.2	-5.9	[-8.9, -3.0]	1.47	-2.8	[-7.4, 1.7]	2.24	0.212
UPA 30 mg QD + TCS	16	12.6	7.8	-4.9	[-7.8, -2.0]	1.42	-1.8	[-6.2, 2.6]	2.19	0.417
China										
Placebo + TCS	17	19.3	14.8	-3.1	[-6.4, 0.2]	1.64				
UPA 15 mg QD + TCS	14	15.5	10.4	-6.2	[-9.8, -2.5]	1.79	-3.1	[-8.0, 1.9]	2.45	0.220
UPA 30 mg QD + TCS	16	16.4	11.1	-5.8	[-9.2, -2.5]	1.67	-2.7	[-7.5, 2.0]	2.35	0.252

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups Difference: Compared to Placebo LS Mean	Between Groups Difference: Compared to Placebo [95% CI]	Between Groups Difference: Compared to Placebo SE	Between Groups Difference: Compared to Placebo P-value
HADS Total Score										
Week 16 (Cont.)										
Other										
Placebo + TCS	92	12.3	10.5	-1.9	[-3.1, -0.8]	0.57				
UPA 15 mg QD + TCS	140	12.6	8.8	-3.8	[-4.7, -2.9]	0.47	-1.9	[-3.3, -0.4]	0.74	0.013*
UPA 30 mg QD + TCS	140	12.8	7.2	-5.5	[-6.4, -4.6]	0.47	-3.6	[-5.0, -2.1]	0.74	<0.001***
Adolescent										
Placebo + TCS	27	12.0	10.7	-1.1	[-3.3, 1.0]	1.08				
UPA 15 mg QD + TCS	35	11.1	6.5	-4.9	[-6.8, -3.0]	0.96	-3.8	[-6.7, -0.9]	1.45	0.011*
UPA 30 mg QD + TCS	33	12.6	8.8	-3.1	[-5.1, -1.2]	0.98	-2.0	[-4.9, 0.9]	1.46	0.174
Adult										
Placebo + TCS	173	13.3	10.8	-2.5	[-3.3, -1.7]	0.42				
UPA 15 mg QD + TCS	238	13.1	8.9	-4.3	[-5.0, -3.5]	0.36	-1.8	[-2.8, -0.7]	0.55	0.002**
UPA 30 mg QD + TCS	236	13.4	8.2	-5.1	[-5.8, -4.4]	0.37	-2.6	[-3.7, -1.5]	0.56	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	[95% CI]	SE	LS Mean	[95% CI]	SE	P-value
				Within Group ---- Change from Baseline ----			Between Groups Difference ---------- Compared to Placebo ----------			
HADS-A Total Score										
Week 12										
All										
Placebo + TCS	217	7.6	6.6	-0.9	[-1.4, -0.4]	0.25				
UPA 15 mg QD + TCS	282	7.4	5.6	-1.8	[-2.3, -1.4]	0.23	-0.9	[-1.5, -0.4]	0.30	0.002**
UPA 30 mg QD + TCS	278	7.7	5.1	-2.4	[-2.9, -2.0]	0.23	-1.6	[-2.2, -1.0]	0.30	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	111	7.0	6.1	-1.0	[-1.6, -0.4]	0.31				
UPA 15 mg QD + TCS	131	7.2	5.7	-1.6	[-2.1, -1.0]	0.28	-0.6	[-1.4, 0.3]	0.42	0.186
UPA 30 mg QD + TCS	133	7.8	5.2	-2.4	[-3.0, -1.9]	0.28	-1.4	[-2.2, -0.6]	0.42	0.001**
vIGA-AD 4 (Severe)										
Placebo + TCS	106	8.1	7.1	-0.7	[-1.3, -0.1]	0.32				
UPA 15 mg QD + TCS	151	7.6	5.5	-2.1	[-2.6, -1.6]	0.27	-1.4	[-2.2, -0.6]	0.42	0.001**
UPA 30 mg QD + TCS	145	7.6	5.1	-2.6	[-3.1, -2.0]	0.27	-1.9	[-2.7, -1.0]	0.42	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS-A Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	90	7.3	6.3	-1.2	[-1.8, -0.5]	0.33				
UPA 15 mg QD + TCS	108	7.9	6.3	-1.6	[-2.2, -1.0]	0.30	-0.4	[-1.3, 0.4]	0.45	0.333
UPA 30 mg QD + TCS	100	8.4	6.0	-2.2	[-2.9, -1.6]	0.32	-1.1	[-2.0, -0.2]	0.46	0.020*
Japan										
Placebo + TCS	12	7.8	5.1	-2.0	[-3.6, -0.3]	0.81				
UPA 15 mg QD + TCS	15	5.7	3.5	-2.8	[-4.3, -1.4]	0.72	-0.9	[-3.1, 1.3]	1.09	0.436
UPA 30 mg QD + TCS	16	6.6	4.2	-2.5	[-3.9, -1.1]	0.69	-0.5	[-2.6, 1.7]	1.06	0.650
China										
Placebo + TCS	17	11.5	10.1	-0.6	[-2.7, 1.5]	1.03				
UPA 15 mg QD + TCS	14	8.7	7.2	-2.3	[-4.5, -0.0]	1.12	-1.7	[-4.8, 1.4]	1.54	0.282
UPA 30 mg QD + TCS	16	9.6	7.1	-2.7	[-4.8, -0.6]	1.04	-2.1	[-5.1, 0.8]	1.47	0.156

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS-A Total Score										
Week 12 (Cont.)										
Other										
Placebo + TCS	98	7.1	6.4	-0.6	[-1.2, 0.1]	0.33				
UPA 15 mg QD + TCS	145	7.2	5.2	-1.9	[-2.5, -1.4]	0.27	-1.4	[-2.2, -0.5]	0.42	0.002**
UPA 30 mg QD + TCS	146	7.0	4.4	-2.6	[-3.2, -2.1]	0.27	-2.0	[-2.9, -1.2]	0.42	<0.001***
Adolescent										
Placebo + TCS	29	7.7	7.4	-0.1	[-1.2, 1.0]	0.56				
UPA 15 mg QD + TCS	36	6.8	5.1	-1.9	[-2.9, -0.9]	0.51	-1.8	[-3.3, -0.3]	0.76	0.021*
UPA 30 mg QD + TCS	36	7.4	4.7	-2.6	[-3.6, -1.6]	0.51	-2.5	[-4.0, -1.0]	0.76	0.001**
Adult										
Placebo + TCS	188	7.5	6.5	-1.0	[-1.5, -0.6]	0.24				
UPA 15 mg QD + TCS	246	7.5	5.7	-1.8	[-2.3, -1.4]	0.21	-0.8	[-1.4, -0.2]	0.32	0.011*
UPA 30 mg QD + TCS	242	7.7	5.2	-2.5	[-2.9, -2.0]	0.21	-1.4	[-2.1, -0.8]	0.32	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	[95% CI]	SE	LS Mean	[95% CI]	SE	P-value
				Within Group ---- Change from Baseline ----			Between Groups Difference ---------- Compared to Placebo ----------			
HADS-A Total Score										
Week 16										
All										
Placebo + TCS	200	7.6	6.3	-1.3	[-1.8, -0.8]	0.26				
UPA 15 mg QD + TCS	273	7.4	5.3	-2.0	[-2.5, -1.6]	0.23	-0.8	[-1.4, -0.2]	0.30	0.010**
UPA 30 mg QD + TCS	269	7.7	5.2	-2.4	[-2.9, -2.0]	0.23	-1.2	[-1.7, -0.6]	0.30	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	102	7.0	6.1	-1.0	[-1.6, -0.4]	0.31				
UPA 15 mg QD + TCS	128	7.3	5.4	-1.9	[-2.5, -1.4]	0.28	-0.9	[-1.7, -0.1]	0.41	0.034*
UPA 30 mg QD + TCS	132	7.8	5.2	-2.4	[-3.0, -1.9]	0.28	-1.4	[-2.2, -0.6]	0.41	0.001**
vIGA-AD 4 (Severe)										
Placebo + TCS	98	8.2	6.5	-1.5	[-2.2, -0.9]	0.33				
UPA 15 mg QD + TCS	145	7.4	5.3	-2.2	[-2.8, -1.7]	0.28	-0.7	[-1.6, 0.1]	0.43	0.101
UPA 30 mg QD + TCS	137	7.7	5.2	-2.5	[-3.1, -2.0]	0.28	-1.0	[-1.8, -0.1]	0.43	0.023*

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups Difference: Compared to Placebo LS Mean	Between Groups Difference: Compared to Placebo [95% CI]	Between Groups Difference: Compared to Placebo SE	Between Groups Difference: Compared to Placebo P-value
HADS-A Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	7.3	6.1	-1.4	[-2.1, -0.7]	0.36				
UPA 15 mg QD + TCS	104	7.8	5.5	-2.2	[-2.8, -1.5]	0.32	-0.8	[-1.7, 0.2]	0.48	0.113
UPA 30 mg QD + TCS	97	8.5	6.2	-2.1	[-2.7, -1.4]	0.33	-0.7	[-1.6, 0.3]	0.49	0.178
Japan										
Placebo + TCS	11	8.2	6.0	-1.3	[-3.2, 0.6]	0.95				
UPA 15 mg QD + TCS	15	5.7	3.1	-3.2	[-4.8, -1.5]	0.83	-1.8	[-4.4, 0.7]	1.26	0.151
UPA 30 mg QD + TCS	16	6.6	4.3	-2.3	[-3.9, -0.7]	0.80	-1.0	[-3.5, 1.5]	1.24	0.414
China										
Placebo + TCS	17	11.5	8.5	-2.1	[-4.1, -0.2]	0.96				
UPA 15 mg QD + TCS	14	8.7	5.7	-3.8	[-5.9, -1.6]	1.05	-1.7	[-4.6, 1.3]	1.45	0.262
UPA 30 mg QD + TCS	16	9.6	6.6	-3.2	[-5.2, -1.2]	0.97	-1.1	[-3.9, 1.7]	1.38	0.433

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group Change from Baseline [95% CI]	SE	Between Groups Difference Compared to Placebo LS Mean	[95% CI]	SE	P-value
HADS-A Total Score										
Week 16 (Cont.)										
Other										
Placebo + TCS	92	7.1	6.2	-1.0	[-1.7, -0.4]	0.32				
UPA 15 mg QD + TCS	140	7.1	5.4	-1.8	[-2.3, -1.3]	0.27	-0.7	[-1.6, 0.1]	0.42	0.078
UPA 30 mg QD + TCS	140	7.1	4.5	-2.7	[-3.2, -2.1]	0.27	-1.6	[-2.4, -0.8]	0.42	<0.001***
Adolescent										
Placebo + TCS	27	7.6	7.0	-0.5	[-1.8, 0.8]	0.65				
UPA 15 mg QD + TCS	35	6.8	4.5	-2.5	[-3.6, -1.3]	0.58	-2.0	[-3.7, -0.3]	0.87	0.025*
UPA 30 mg QD + TCS	33	7.7	5.4	-2.0	[-3.2, -0.8]	0.58	-1.5	[-3.2, 0.2]	0.87	0.089
Adult										
Placebo + TCS	173	7.6	6.2	-1.4	[-1.9, -1.0]	0.24				
UPA 15 mg QD + TCS	238	7.4	5.4	-2.0	[-2.4, -1.6]	0.21	-0.6	[-1.2, 0.0]	0.32	0.062
UPA 30 mg QD + TCS	236	7.7	5.2	-2.5	[-2.9, -2.1]	0.21	-1.1	[-1.7, -0.5]	0.32	0.001**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups Difference: Compared to Placebo LS Mean	Between Groups Difference: Compared to Placebo [95% CI]	Between Groups Difference: Compared to Placebo SE	Between Groups Difference: Compared to Placebo P-value
HADS-D Total Score										
Week 12										
All										
Placebo + TCS	217	5.5	4.3	-1.3	[-1.8, -0.9]	0.22				
UPA 15 mg QD + TCS	282	5.5	3.1	-2.6	[-2.9, -2.2]	0.20	-1.2	[-1.7, -0.7]	0.26	<0.001***
UPA 30 mg QD + TCS	278	5.5	3.0	-2.7	[-3.1, -2.3]	0.20	-1.3	[-1.8, -0.8]	0.26	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	111	4.7	4.1	-0.8	[-1.3, -0.3]	0.26				
UPA 15 mg QD + TCS	131	5.1	3.1	-2.0	[-2.5, -1.5]	0.24	-1.2	[-1.9, -0.5]	0.36	0.001**
UPA 30 mg QD + TCS	133	5.5	3.1	-2.2	[-2.7, -1.8]	0.24	-1.4	[-2.1, -0.7]	0.36	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	106	6.2	4.4	-1.5	[-2.1, -1.0]	0.28				
UPA 15 mg QD + TCS	151	5.9	3.1	-2.8	[-3.2, -2.3]	0.24	-1.2	[-2.0, -0.5]	0.37	0.001**
UPA 30 mg QD + TCS	145	5.6	3.0	-2.8	[-3.3, -2.3]	0.24	-1.3	[-2.0, -0.5]	0.37	0.001**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS-D Total Score										
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	90	5.2	3.7	-1.5	[-2.0, -0.9]	0.27				
UPA 15 mg QD + TCS	108	5.3	3.1	-2.2	[-2.7, -1.7]	0.25	-0.7	[-1.4, -0.0]	0.36	0.048*
UPA 30 mg QD + TCS	100	5.0	2.9	-2.2	[-2.7, -1.7]	0.26	-0.8	[-1.5, -0.0]	0.37	0.041*
Japan										
Placebo + TCS	12	7.1	3.7	-2.8	[-4.7, -0.9]	0.95				
UPA 15 mg QD + TCS	15	5.5	3.6	-2.3	[-4.0, -0.6]	0.85	0.5	[-2.1, 3.1]	1.28	0.693
UPA 30 mg QD + TCS	16	5.9	3.3	-2.8	[-4.5, -1.2]	0.82	-0.0	[-2.5, 2.5]	1.25	0.994
China										
Placebo + TCS	17	7.8	6.2	-1.2	[-2.7, 0.4]	0.78				
UPA 15 mg QD + TCS	14	6.8	4.1	-3.0	[-4.7, -1.2]	0.86	-1.8	[-4.2, 0.5]	1.17	0.129
UPA 30 mg QD + TCS	16	6.8	5.2	-1.9	[-3.5, -0.2]	0.80	-0.7	[-3.0, 1.6]	1.13	0.540

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS-D Total Score										
Week 12 (Cont.)										
Other										
Placebo + TCS	98	5.1	4.5	-0.7	[-1.3, -0.1]	0.30				
UPA 15 mg QD + TCS	145	5.6	3.0	-2.5	[-3.0, -2.0]	0.24	-1.8	[-2.5, -1.0]	0.38	<0.001***
UPA 30 mg QD + TCS	146	5.7	2.8	-2.8	[-3.2, -2.3]	0.24	-2.0	[-2.8, -1.3]	0.38	<0.001***
Adolescent										
Placebo + TCS	29	4.4	3.2	-1.3	[-2.1, -0.4]	0.42				
UPA 15 mg QD + TCS	36	4.2	1.9	-2.4	[-3.2, -1.7]	0.38	-1.1	[-2.3, -0.0]	0.56	0.045*
UPA 30 mg QD + TCS	36	4.6	2.5	-2.1	[-2.8, -1.3]	0.38	-0.8	[-1.9, 0.3]	0.56	0.166
Adult										
Placebo + TCS	188	5.6	4.4	-1.2	[-1.6, -0.8]	0.21				
UPA 15 mg QD + TCS	246	5.7	3.3	-2.4	[-2.8, -2.0]	0.19	-1.2	[-1.8, -0.7]	0.28	<0.001***
UPA 30 mg QD + TCS	242	5.7	3.1	-2.6	[-2.9, -2.2]	0.19	-1.4	[-2.0, -0.8]	0.28	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	[95% CI]	SE	LS Mean	[95% CI]	SE	P-value
				Within Group ---- Change from Baseline ----			Between Groups Difference ---------- Compared to Placebo ----------			
HADS-D Total Score										
Week 16										
All										
Placebo + TCS	200	5.5	4.4	-1.2	[-1.6, -0.7]	0.24				
UPA 15 mg QD + TCS	273	5.5	3.3	-2.4	[-2.8, -2.0]	0.21	-1.2	[-1.8, -0.7]	0.28	<0.001***
UPA 30 mg QD + TCS	269	5.6	3.1	-2.6	[-3.0, -2.1]	0.22	-1.4	[-2.0, -0.8]	0.28	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	102	4.7	4.0	-0.9	[-1.4, -0.3]	0.28				
UPA 15 mg QD + TCS	128	5.2	3.0	-2.1	[-2.6, -1.6]	0.25	-1.3	[-2.0, -0.5]	0.38	0.001**
UPA 30 mg QD + TCS	132	5.6	3.0	-2.3	[-2.8, -1.9]	0.25	-1.5	[-2.2, -0.7]	0.38	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	98	6.4	4.9	-1.1	[-1.8, -0.5]	0.32				
UPA 15 mg QD + TCS	145	5.8	3.5	-2.3	[-2.9, -1.8]	0.27	-1.2	[-2.0, -0.4]	0.42	0.004**
UPA 30 mg QD + TCS	137	5.6	3.3	-2.5	[-3.0, -1.9]	0.27	-1.3	[-2.2, -0.5]	0.42	0.002**

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Within Group: Baseline Mean	Within Group: Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
HADS-D Total Score										
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	80	5.1	4.1	-1.0	[-1.7, -0.4]	0.33				
UPA 15 mg QD + TCS	104	5.3	2.8	-2.4	[-3.0, -1.9]	0.29	-1.4	[-2.3, -0.5]	0.44	0.001**
UPA 30 mg QD + TCS	97	5.1	3.4	-1.8	[-2.4, -1.2]	0.30	-0.7	[-1.6, 0.1]	0.44	0.094
Japan										
Placebo + TCS	11	7.6	5.1	-1.7	[-3.7, 0.3]	1.01				
UPA 15 mg QD + TCS	15	5.5	3.1	-2.8	[-4.6, -1.1]	0.88	-1.1	[-3.9, 1.6]	1.34	0.401
UPA 30 mg QD + TCS	16	5.9	3.5	-2.6	[-4.3, -0.9]	0.85	-0.9	[-3.5, 1.8]	1.32	0.511
China										
Placebo + TCS	17	7.8	6.3	-1.0	[-2.7, 0.6]	0.81				
UPA 15 mg QD + TCS	14	6.8	4.7	-2.3	[-4.1, -0.5]	0.89	-1.3	[-3.7, 1.1]	1.20	0.293
UPA 30 mg QD + TCS	16	6.8	4.4	-2.6	[-4.3, -0.9]	0.83	-1.6	[-3.9, 0.8]	1.16	0.184

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Parameter / Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group: Change from Baseline [95% CI]	Within Group: Change from Baseline SE	Between Groups Difference: Compared to Placebo LS Mean	Between Groups Difference: Compared to Placebo [95% CI]	Between Groups Difference: Compared to Placebo SE	Between Groups Difference: Compared to Placebo P-value
HADS-D Total Score										
Week 16 (Cont.)										
Other										
Placebo + TCS	92	5.2	4.3	-0.9	[-1.5, -0.3]	0.31				
UPA 15 mg QD + TCS	140	5.5	3.5	-2.0	[-2.5, -1.5]	0.26	-1.1	[-1.9, -0.3]	0.41	0.007**
UPA 30 mg QD + TCS	140	5.7	2.8	-2.8	[-3.3, -2.3]	0.26	-1.9	[-2.7, -1.1]	0.41	<0.001***
Adolescent										
Placebo + TCS	27	4.3	3.7	-0.7	[-1.9, 0.5]	0.59				
UPA 15 mg QD + TCS	35	4.3	2.0	-2.4	[-3.5, -1.4]	0.52	-1.7	[-3.3, -0.2]	0.79	0.031*
UPA 30 mg QD + TCS	33	4.9	3.3	-1.2	[-2.2, -0.1]	0.53	-0.5	[-2.1, 1.1]	0.80	0.548
Adult										
Placebo + TCS	173	5.7	4.6	-1.1	[-1.5, -0.6]	0.23				
UPA 15 mg QD + TCS	238	5.7	3.4	-2.2	[-2.6, -1.8]	0.20	-1.1	[-1.7, -0.6]	0.30	<0.001***
UPA 30 mg QD + TCS	236	5.7	3.1	-2.6	[-3.0, -2.2]	0.20	-1.5	[-2.1, -0.9]	0.30	<0.001***

Note: HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　9.3.1

表 2.7.3.6-68.　二重盲検投与期の来院時点別のアトピー性皮膚炎罹患 BSA のベースラインからの変化量（MMRM，ITT_M 集団）：：M16-045 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 1										
All										
Placebo	267	45.89	43.49	-2.13	[-4.02, -0.23]	0.966				
UPA 15 mg QD	268	48.66	35.63	-11.59	[-13.48, -9.70]	0.963	-9.47	[-11.88, -7.05]	1.230	<0.001***
UPA 30 mg QD	275	47.61	32.92	-13.76	[-15.63, -11.89]	0.953	-11.63	[-14.03, -9.23]	1.222	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	147	36.42	33.98	-2.47	[-4.34, -0.61]	0.948				
UPA 15 mg QD	147	37.55	26.39	-10.75	[-12.61, -8.89]	0.947	-8.28	[-10.91, -5.64]	1.340	<0.001***
UPA 30 mg QD	147	37.58	24.40	-12.71	[-14.57, -10.85]	0.946	-10.23	[-12.87, -7.60]	1.340	<0.001***
vIGA-AD 4 (Severe)										
Placebo	120	57.48	55.15	-2.96	[-5.94, 0.01]	1.514				
UPA 15 mg QD	121	62.17	46.85	-14.00	[-16.97, -11.04]	1.507	-11.04	[-15.25, -6.83]	2.138	<0.001***
UPA 30 mg QD	128	59.13	42.71	-16.44	[-19.32, -13.55]	1.468	-13.47	[-17.62, -9.32]	2.108	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 1 (Cont.)										
US/Puerto Rico/Canada										
Placebo	122	40.79	38.73	-2.33	[-4.49, -0.18]	1.098				
UPA 15 mg QD	123	44.50	33.86	-9.89	[-12.03, -7.75]	1.089	-7.55	[-10.60, -4.51]	1.547	<0.001***
UPA 30 mg QD	123	42.78	29.54	-12.90	[-15.04, -10.77]	1.085	-10.57	[-13.60, -7.53]	1.543	<0.001***
Japan										
Placebo	13	51.92	56.08	4.15	[-2.41, 10.72]	3.243				
UPA 15 mg QD	15	51.20	36.80	-14.40	[-20.51, -8.29]	3.019	-18.56	[-27.52, -9.59]	4.431	<0.001***
UPA 30 mg QD	16	54.31	45.44	-8.87	[-14.80, -2.94]	2.934	-13.02	[-21.87, -4.18]	4.372	0.005**
China										
Placebo	14	49.25	40.64	-15.21	[-26.86, -3.56]	5.774				
UPA 15 mg QD	14	63.59	33.28	-27.49	[-39.01, -15.97]	5.709	-12.28	[-28.75, 4.19]	8.168	0.140
UPA 30 mg QD	17	62.71	43.07	-17.40	[-27.85, -6.95]	5.178	-2.19	[-17.91, 13.53]	7.795	0.780

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 1 (Cont.)										
Other										
Placebo	118	50.10	47.37	-2.52	[-5.18, 0.13]	1.351				
UPA 15 mg QD	116	50.95	37.63	-12.40	[-15.08, -9.72]	1.364	-9.87	[-13.65, -6.10]	1.919	<0.001***
UPA 30 mg QD	119	49.55	33.29	-16.11	[-18.77, -13.45]	1.351	-13.59	[-17.35, -9.83]	1.911	<0.001***
Adolescent										
Placebo	37	54.28	49.43	-2.91	[-7.39, 1.58]	2.262				
UPA 15 mg QD	40	50.69	37.88	-12.04	[-16.34, -7.73]	2.171	-9.13	[-15.33, -2.93]	3.130	0.004**
UPA 30 mg QD	40	46.34	32.59	-14.81	[-19.12, -10.50]	2.174	-11.91	[-18.14, -5.67]	3.147	<0.001***
Adult										
Placebo	230	44.54	42.54	-2.60	[-4.46, -0.73]	0.949				
UPA 15 mg QD	228	48.31	35.23	-12.18	[-14.04, -10.31]	0.951	-9.58	[-12.22, -6.94]	1.345	<0.001***
UPA 30 mg QD	235	47.83	32.98	-14.19	[-16.03, -12.35]	0.938	-11.60	[-14.22, -8.97]	1.335	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo	265	45.49	41.97	-2.99	[-5.11, -0.86]	1.082				
UPA 15 mg QD	273	48.60	26.57	-20.66	[-22.76, -18.56]	1.071	-17.67	[-20.43, -14.91]	1.405	<0.001***
UPA 30 mg QD	280	47.33	22.00	-24.57	[-26.65, -22.49]	1.060	-21.58	[-24.32, -18.84]	1.397	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	149	36.71	33.50	-3.16	[-5.31, -1.00]	1.097				
UPA 15 mg QD	149	37.76	18.52	-18.79	[-20.94, -16.64]	1.094	-15.63	[-18.68, -12.59]	1.550	<0.001***
UPA 30 mg QD	150	37.00	15.87	-21.05	[-23.20, -18.90]	1.092	-17.89	[-20.93, -14.85]	1.548	<0.001***
vIGA-AD 4 (Severe)										
Placebo	116	56.77	52.85	-3.92	[-7.37, -0.48]	1.750				
UPA 15 mg QD	124	61.62	36.25	-24.26	[-27.63, -20.90]	1.711	-20.34	[-25.16, -15.52]	2.450	<0.001***
UPA 30 mg QD	130	59.24	29.07	-30.10	[-33.39, -26.81]	1.675	-26.18	[-30.94, -21.41]	2.422	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo	121	40.22	36.26	-4.28	[-6.77, -1.80]	1.264				
UPA 15 mg QD	126	44.29	24.57	-18.79	[-21.24, -16.35]	1.244	-14.51	[-18.00, -11.02]	1.775	<0.001***
UPA 30 mg QD	127	42.25	20.08	-21.95	[-24.38, -19.52]	1.237	-17.67	[-21.15, -14.19]	1.769	<0.001***
Japan										
Placebo	10	46.60	50.70	4.37	[-4.00, 12.74]	4.152				
UPA 15 mg QD	15	51.20	28.00	-23.20	[-30.40, -16.00]	3.560	-27.57	[-38.61, -16.54]	5.468	<0.001***
UPA 30 mg QD	16	54.31	33.19	-21.12	[-28.11, -14.14]	3.455	-25.49	[-36.40, -14.59]	5.406	<0.001***
China										
Placebo	14	49.25	43.57	-12.28	[-23.93, -0.63]	5.778				
UPA 15 mg QD	14	63.59	23.31	-37.46	[-48.99, -25.93]	5.713	-25.18	[-41.66, -8.70]	8.173	0.004**
UPA 30 mg QD	17	62.71	25.96	-34.50	[-44.96, -24.05]	5.182	-22.22	[-37.95, -6.49]	7.801	0.007**

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo	120	50.28	46.81	-2.71	[-5.85, 0.44]	1.601				
UPA 15 mg QD	118	51.09	28.92	-21.56	[-24.72, -18.40]	1.608	-18.85	[-23.32, -14.39]	2.268	<0.001***
UPA 30 mg QD	120	49.58	21.97	-27.60	[-30.76, -24.45]	1.604	-24.90	[-29.35, -20.44]	2.266	<0.001***
Adolescent										
Placebo	38	53.62	51.77	-0.29	[-5.68, 5.09]	2.719				
UPA 15 mg QD	42	50.59	29.84	-20.21	[-25.37, -15.04]	2.607	-19.91	[-27.36, -12.46]	3.763	<0.001***
UPA 30 mg QD	42	45.92	20.48	-26.60	[-31.77, -21.44]	2.611	-26.31	[-33.79, -18.83]	3.778	<0.001***
Adult										
Placebo	227	44.13	40.33	-4.04	[-6.15, -1.92]	1.076				
UPA 15 mg QD	231	48.24	25.98	-21.40	[-23.50, -19.31]	1.068	-17.37	[-20.34, -14.39]	1.517	<0.001***
UPA 30 mg QD	238	47.57	22.26	-24.83	[-26.90, -22.76]	1.055	-20.80	[-23.76, -17.84]	1.508	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 4										
All										
Placebo	258	45.25	40.49	-4.53	[-6.79, -2.27]	1.153				
UPA 15 mg QD	274	48.74	18.97	-28.21	[-30.43, -25.99]	1.129	-23.68	[-26.63, -20.73]	1.504	<0.001***
UPA 30 mg QD	278	47.24	13.13	-33.47	[-35.67, -31.27]	1.121	-28.94	[-31.88, -26.00]	1.498	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	147	36.62	31.29	-5.72	[-8.08, -3.36]	1.200				
UPA 15 mg QD	150	37.88	13.61	-23.65	[-25.99, -21.31]	1.190	-17.93	[-21.25, -14.61]	1.690	<0.001***
UPA 30 mg QD	148	37.09	9.73	-27.23	[-29.57, -24.88]	1.193	-21.51	[-24.83, -18.18]	1.692	<0.001***
vIGA-AD 4 (Severe)										
Placebo	111	56.68	52.67	-4.12	[-7.74, -0.49]	1.844				
UPA 15 mg QD	124	61.87	25.45	-35.09	[-38.56, -31.63]	1.761	-30.98	[-35.99, -25.96]	2.552	<0.001***
UPA 30 mg QD	130	58.79	17.00	-42.10	[-45.50, -38.70]	1.727	-37.98	[-42.95, -33.02]	2.526	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 4 (Cont.)										
US/Puerto Rico/Canada										
Placebo	119	40.44	36.78	-4.05	[-7.02, -1.07]	1.513				
UPA 15 mg QD	122	44.93	19.02	-24.77	[-27.69, -21.84]	1.489	-20.72	[-24.90, -16.55]	2.123	<0.001***
UPA 30 mg QD	125	42.41	10.61	-31.49	[-34.40, -28.59]	1.475	-27.45	[-31.60, -23.29]	2.113	<0.001***
Japan										
Placebo	10	46.60	51.40	4.98	[-3.73, 13.69]	4.308				
UPA 15 mg QD	15	51.20	19.33	-31.87	[-39.11, -24.63]	3.574	-36.84	[-48.17, -25.52]	5.596	<0.001***
UPA 30 mg QD	16	54.31	22.19	-32.12	[-39.15, -25.09]	3.469	-37.10	[-48.30, -25.89]	5.541	<0.001***
China										
Placebo	14	49.25	42.85	-13.00	[-21.91, -4.09]	4.419				
UPA 15 mg QD	14	63.59	13.76	-47.01	[-55.75, -38.26]	4.334	-34.00	[-46.61, -21.40]	6.252	<0.001***
UPA 30 mg QD	17	62.71	17.30	-43.17	[-51.10, -35.24]	3.929	-30.17	[-42.19, -18.14]	5.965	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 4 (Cont.)										
Other										
Placebo	115	49.63	43.08	-6.28	[-9.63, -2.92]	1.705				
UPA 15 mg QD	123	50.52	19.46	-30.37	[-33.65, -27.08]	1.671	-24.09	[-28.78, -19.40]	2.387	<0.001***
UPA 30 mg QD	120	49.13	13.96	-35.58	[-38.90, -32.27]	1.686	-29.30	[-34.02, -24.59]	2.398	<0.001***
Adolescent										
Placebo	38	54.54	50.23	-2.59	[-8.50, 3.33]	2.988				
UPA 15 mg QD	41	51.04	21.45	-28.35	[-34.03, -22.67]	2.868	-25.76	[-33.96, -17.57]	4.139	<0.001***
UPA 30 mg QD	42	45.92	13.25	-33.84	[-39.50, -28.17]	2.863	-31.25	[-39.46, -23.04]	4.147	<0.001***
Adult										
Placebo	220	43.65	38.81	-5.47	[-7.74, -3.21]	1.154				
UPA 15 mg QD	233	48.33	18.53	-28.84	[-31.05, -26.62]	1.128	-23.36	[-26.54, -20.19]	1.615	<0.001***
UPA 30 mg QD	236	47.47	13.11	-34.02	[-36.22, -31.82]	1.120	-28.55	[-31.71, -25.39]	1.609	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo	168	41.15	29.14	-8.60	[-11.09, -6.11]	1.269				
UPA 15 mg QD	264	47.99	13.07	-32.92	[-35.14, -30.70]	1.131	-24.32	[-27.45, -21.19]	1.595	<0.001***
UPA 30 mg QD	273	47.30	9.53	-36.99	[-39.19, -34.79]	1.120	-28.39	[-31.51, -25.28]	1.586	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	107	34.62	22.59	-9.13	[-11.66, -6.60]	1.286				
UPA 15 mg QD	146	37.48	10.11	-26.47	[-28.81, -24.14]	1.187	-17.35	[-20.79, -13.90]	1.750	<0.001***
UPA 30 mg QD	145	37.24	7.34	-29.60	[-31.93, -27.26]	1.190	-20.47	[-23.91, -17.02]	1.752	<0.001***
vIGA-AD 4 (Severe)										
Placebo	61	52.62	40.64	-9.15	[-13.37, -4.93]	2.145				
UPA 15 mg QD	118	60.99	16.74	-42.23	[-45.66, -38.81]	1.740	-33.08	[-38.52, -27.65]	2.765	<0.001***
UPA 30 mg QD	128	58.70	12.01	-46.95	[-50.27, -43.62]	1.688	-37.80	[-43.17, -32.43]	2.729	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo	80	36.93	26.21	-8.00	[-11.26, -4.75]	1.653				
UPA 15 mg QD	119	44.07	12.99	-29.15	[-32.11, -26.19]	1.504	-21.14	[-25.54, -16.74]	2.237	<0.001***
UPA 30 mg QD	125	42.19	7.06	-35.06	[-37.98, -32.14]	1.483	-27.06	[-31.42, -22.69]	2.221	<0.001***
Japan										
Placebo	2	28.50	22.00	3.40	[-14.69, 21.49]	8.953				
UPA 15 mg QD	15	51.20	18.53	-32.67	[-41.50, -23.84]	4.327	-36.07	[-56.13, -16.00]	9.942	0.001**
UPA 30 mg QD	14	55.71	17.93	-38.37	[-47.19, -29.55]	4.334	-41.77	[-61.86, -21.68]	9.957	<0.001***
China										
Placebo	8	50.50	46.75	-7.16	[-16.43, 2.11]	4.617				
UPA 15 mg QD	14	63.59	7.94	-52.83	[-61.04, -44.61]	4.064	-45.67	[-58.17, -33.17]	6.210	<0.001***
UPA 30 mg QD	17	62.71	10.00	-50.47	[-57.92, -43.02]	3.684	-43.31	[-55.29, -31.32]	5.956	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo	78	44.85	30.52	-11.44	[-15.12, -7.76]	1.872				
UPA 15 mg QD	116	49.70	13.08	-35.75	[-39.00, -32.49]	1.653	-24.31	[-29.22, -19.39]	2.498	<0.001***
UPA 30 mg QD	117	49.52	11.10	-38.20	[-41.46, -34.94]	1.655	-26.76	[-31.68, -21.84]	2.499	<0.001***
Adolescent										
Placebo	21	46.42	30.66	-12.51	[-19.59, -5.44]	3.577				
UPA 15 mg QD	41	51.21	15.30	-34.78	[-40.65, -28.92]	2.956	-22.27	[-31.45, -13.09]	4.638	<0.001***
UPA 30 mg QD	41	45.11	11.78	-35.11	[-40.99, -29.23]	2.963	-22.60	[-31.80, -13.39]	4.649	<0.001***
Adult										
Placebo	147	40.40	28.93	-8.73	[-11.21, -6.25]	1.263				
UPA 15 mg QD	223	47.39	12.66	-33.25	[-35.45, -31.04]	1.123	-24.52	[-27.84, -21.20]	1.692	<0.001***
UPA 30 mg QD	232	47.69	9.14	-37.94	[-40.11, -35.76]	1.108	-29.21	[-32.51, -25.91]	1.681	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 12										
All										
Placebo	142	40.43	24.94	-11.03	[-13.65, -8.40]	1.337				
UPA 15 mg QD	252	48.17	11.72	-33.80	[-36.03, -31.57]	1.137	-22.77	[-26.02, -19.53]	1.653	<0.001***
UPA 30 mg QD	266	47.12	7.94	-38.37	[-40.57, -36.17]	1.120	-27.34	[-30.56, -24.12]	1.642	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	96	34.32	20.66	-10.30	[-12.71, -7.88]	1.228				
UPA 15 mg QD	139	37.49	8.45	-27.83	[-30.02, -25.65]	1.112	-17.54	[-20.80, -14.28]	1.657	<0.001***
UPA 30 mg QD	140	36.71	5.39	-31.03	[-33.21, -28.84]	1.112	-20.73	[-23.99, -17.47]	1.657	<0.001***
vIGA-AD 4 (Severe)										
Placebo	46	53.18	33.86	-13.58	[-18.55, -8.62]	2.524				
UPA 15 mg QD	113	61.31	15.75	-42.68	[-46.32, -39.04]	1.847	-29.09	[-35.25, -22.94]	3.131	<0.001***
UPA 30 mg QD	126	58.68	10.77	-48.26	[-51.76, -44.77]	1.776	-34.68	[-40.75, -28.61]	3.085	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo	65	35.61	20.58	-10.70	[-14.13, -7.26]	1.747				
UPA 15 mg QD	112	43.80	10.29	-30.50	[-33.50, -27.49]	1.528	-19.80	[-24.37, -15.23]	2.322	<0.001***
UPA 30 mg QD	121	41.92	6.40	-35.70	[-38.65, -32.75]	1.498	-25.00	[-29.53, -20.48]	2.301	<0.001***
Japan										
Placebo	1	17.00	18.00	14.89	[-8.01, 37.79]	11.371				
UPA 15 mg QD	15	51.20	20.70	-30.50	[-39.37, -21.63]	4.341	-45.39	[-69.88, -20.89]	12.169	0.001**
UPA 30 mg QD	14	55.71	16.71	-39.25	[-48.20, -30.30]	4.388	-54.14	[-78.71, -29.57]	12.209	<0.001***
China										
Placebo	7	44.36	39.00	-8.50	[-24.18, 7.17]	7.771				
UPA 15 mg QD	14	63.59	11.61	-49.16	[-60.87, -37.44]	5.764	-40.65	[-60.28, -21.02]	9.717	<0.001***
UPA 30 mg QD	17	62.71	11.26	-49.20	[-59.83, -38.58]	5.228	-40.70	[-59.69, -21.71]	9.400	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 12 (Cont.)										
Other										
Placebo	69	44.92	27.72	-13.48	[-17.22, -9.75]	1.898				
UPA 15 mg QD	111	50.22	11.97	-36.95	[-40.12, -33.78]	1.609	-23.47	[-28.37, -18.57]	2.489	<0.001***
UPA 30 mg QD	114	49.25	7.99	-40.83	[-43.98, -37.67]	1.604	-27.34	[-32.23, -22.45]	2.485	<0.001***
Adolescent										
Placebo	19	46.74	28.00	-14.28	[-21.45, -7.11]	3.619				
UPA 15 mg QD	39	51.83	15.09	-35.59	[-41.10, -30.09]	2.771	-21.32	[-30.35, -12.28]	4.557	<0.001***
UPA 30 mg QD	41	45.11	9.20	-37.54	[-43.01, -32.07]	2.755	-23.26	[-32.28, -14.24]	4.549	<0.001***
Adult										
Placebo	123	39.46	24.47	-11.18	[-13.84, -8.52]	1.355				
UPA 15 mg QD	213	47.50	11.11	-34.05	[-36.31, -31.79]	1.149	-22.87	[-26.36, -19.38]	1.778	<0.001***
UPA 30 mg QD	225	47.48	7.71	-39.10	[-41.31, -36.88]	1.128	-27.91	[-31.38, -24.45]	1.764	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo	128	40.22	22.10	-14.55	[-17.23, -11.87]	1.365				
UPA 15 mg QD	244	47.83	10.14	-34.77	[-36.97, -32.57]	1.120	-20.22	[-23.49, -16.95]	1.665	<0.001***
UPA 30 mg QD	259	47.00	7.11	-38.95	[-41.11, -36.79]	1.100	-24.40	[-27.64, -21.15]	1.652	<0.001***
vIGA-AD 3 (Moderate)										
Placebo	86	33.78	18.79	-12.12	[-14.65, -9.59]	1.287				
UPA 15 mg QD	137	37.34	7.38	-28.53	[-30.72, -26.34]	1.113	-16.41	[-19.76, -13.06]	1.702	<0.001***
UPA 30 mg QD	138	36.49	4.42	-31.69	[-33.88, -29.50]	1.113	-19.57	[-22.92, -16.22]	1.702	<0.001***
vIGA-AD 4 (Severe)										
Placebo	42	53.42	28.90	-20.59	[-25.63, -15.55]	2.563				
UPA 15 mg QD	107	61.27	13.68	-43.94	[-47.48, -40.41]	1.794	-23.35	[-29.52, -17.19]	3.132	<0.001***
UPA 30 mg QD	121	58.98	10.18	-48.79	[-52.16, -45.41]	1.714	-28.20	[-34.26, -22.13]	3.083	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point Strata Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo	60	35.56	19.79	-11.55	[-15.31, -7.78]	1.913				
UPA 15 mg QD	109	43.90	10.14	-30.35	[-33.49, -27.20]	1.596	-18.80	[-23.71, -13.89]	2.494	<0.001***
UPA 30 mg QD	119	42.20	5.67	-36.38	[-39.45, -33.32]	1.556	-24.83	[-29.69, -19.98]	2.466	<0.001***
Japan										
Placebo	1	17.00	5.00	0.70	[-24.41, 25.81]	12.412				
UPA 15 mg QD	13	47.15	13.19	-31.47	[-40.50, -22.44]	4.419	-32.17	[-58.79, -5.55]	13.174	0.019*
UPA 30 mg QD	14	55.71	16.64	-39.50	[-48.53, -30.47]	4.425	-40.20	[-66.86, -13.54]	13.195	0.004**
China										
Placebo	7	44.36	26.43	-21.81	[-34.32, -9.31]	6.193				
UPA 15 mg QD	14	63.59	10.81	-49.96	[-59.20, -40.73]	4.540	-28.15	[-43.80, -12.50]	7.740	0.001**
UPA 30 mg QD	16	62.56	8.88	-49.78	[-58.20, -41.36]	4.141	-27.97	[-43.12, -12.81]	7.499	0.001**

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
Other										
Placebo	60	44.79	24.20	-18.19	[-21.93, -14.45]	1.900				
UPA 15 mg QD	108	49.83	9.69	-38.83	[-41.87, -35.80]	1.541	-20.65	[-25.47, -15.83]	2.448	<0.001***
UPA 30 mg QD	110	48.82	7.21	-41.44	[-44.46, -38.41]	1.535	-23.25	[-28.06, -18.44]	2.443	<0.001***
Adolescent										
Placebo	18	46.94	27.99	-14.39	[-21.17, -7.62]	3.416				
UPA 15 mg QD	38	50.83	13.80	-36.10	[-41.31, -30.88]	2.625	-21.70	[-30.25, -13.16]	4.308	<0.001***
UPA 30 mg QD	40	44.61	8.31	-37.65	[-42.82, -32.47]	2.602	-23.26	[-31.78, -14.73]	4.295	<0.001***
Adult										
Placebo	110	39.12	21.14	-15.33	[-18.08, -12.58]	1.400				
UPA 15 mg QD	206	47.28	9.47	-35.20	[-37.43, -32.97]	1.134	-19.87	[-23.41, -16.33]	1.803	<0.001***
UPA 30 mg QD	219	47.43	6.89	-39.78	[-41.96, -37.60]	1.109	-24.45	[-27.96, -20.94]	1.788	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-045 試験 CSR W16 Table 14.2　12.1.1

表 2.7.3.6-69.　二重盲検投与期の来院時点別のアトピー性皮膚炎罹患 BSA のベースラインからの変化量（MMRM，ITT_M 集団）：M16-047 試験

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group ---- Change from Baseline ---- LS Mean	[95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 2										
All										
Placebo + TCS	294	48.930	39.827	-7.676	[-9.760, -5.591]	1.0623				
UPA 15 mg QD + TCS	294	46.919	26.380	-20.049	[-22.134, -17.963]	1.0629	-12.373	[-14.964, -9.782]	1.3201	<0.001***
UPA 30 mg QD + TCS	289	48.759	22.555	-24.903	[-27.004, -22.802]	1.0707	-17.227	[-19.829, -14.626]	1.3253	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	137	37.252	30.023	-7.558	[-9.749, -5.366]	1.1146				
UPA 15 mg QD + TCS	138	35.838	18.857	-18.075	[-20.244, -15.906]	1.1034	-10.517	[-13.600, -7.435]	1.5677	<0.001***
UPA 30 mg QD + TCS	135	40.383	15.354	-23.579	[-25.771, -21.388]	1.1148	-16.021	[-19.122, -12.920]	1.5772	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	157	59.120	48.381	-9.650	[-12.472, -6.828]	1.4361				
UPA 15 mg QD + TCS	156	56.721	33.035	-23.673	[-26.514, -20.832]	1.4454	-14.023	[-18.027, -10.019]	2.0375	<0.001***
UPA 30 mg QD + TCS	154	56.101	28.868	-27.440	[-30.304, -24.577]	1.4570	-17.791	[-21.812, -13.769]	2.0463	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	106	45.744	34.866	-10.187	[-13.320, -7.054]	1.5920				
UPA 15 mg QD + TCS	106	44.969	24.222	-20.495	[-23.618, -17.371]	1.5873	-10.307	[-14.731, -5.884]	2.2478	<0.001***
UPA 30 mg QD + TCS	102	43.517	20.714	-23.060	[-26.244, -19.876]	1.6180	-12.872	[-17.340, -8.405]	2.2704	<0.001***
Japan										
Placebo + TCS	18	66.611	48.194	-17.113	[-26.367, -7.858]	4.5995				
UPA 15 mg QD + TCS	16	59.469	42.656	-18.075	[-27.883, -8.268]	4.8741	-0.963	[-14.512, 12.587]	6.7350	0.887
UPA 30 mg QD + TCS	17	66.294	37.706	-27.398	[-36.910, -17.886]	4.7273	-10.285	[-23.495, 2.924]	6.5635	0.124
China										
Placebo + TCS	17	66.088	58.741	-6.097	[-15.418, 3.224]	4.6232				
UPA 15 mg QD + TCS	17	53.412	26.147	-28.829	[-38.189, -19.470]	4.6433	-22.733	[-36.063, -9.402]	6.6149	0.001**
UPA 30 mg QD + TCS	16	59.400	32.275	-27.360	[-36.898, -17.822]	4.7299	-21.263	[-34.617, -7.909]	6.6234	0.002**

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group Change from Baseline [95% CI]	SE	Between Groups Difference Compared to Placebo LS Mean	[95% CI]	SE	P-value
Week 2 (Cont.)										
Other										
Placebo + TCS	153	47.150	40.177	-6.762	[-9.099, -4.426]	1.1889				
UPA 15 mg QD + TCS	155	46.245	26.201	-20.294	[-22.614, -17.973]	1.1808	-13.532	[-16.825, -10.239]	1.6756	<0.001***
UPA 30 mg QD + TCS	154	49.190	21.093	-27.177	[-29.509, -24.844]	1.1867	-20.414	[-23.716, -17.113]	1.6798	<0.001***
Adolescent										
Placebo + TCS	38	48.353	40.295	-5.595	[-10.873, -0.316]	2.6617				
UPA 15 mg QD + TCS	38	43.747	24.650	-19.432	[-24.698, -14.166]	2.6555	-13.837	[-21.302, -6.373]	3.7643	<0.001***
UPA 30 mg QD + TCS	37	44.281	21.778	-22.635	[-28.014, -17.256]	2.7121	-17.040	[-24.579, -9.502]	3.8011	<0.001***
Adult										
Placebo + TCS	256	49.015	39.757	-8.893	[-10.858, -6.928]	1.0008				
UPA 15 mg QD + TCS	256	47.389	26.637	-21.039	[-23.002, -19.076]	0.9997	-12.146	[-14.924, -9.369]	1.4148	<0.001***
UPA 30 mg QD + TCS	252	49.416	22.669	-26.178	[-28.156, -24.201]	1.0072	-17.286	[-20.072, -14.499]	1.4196	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
Week 4										
All										
Placebo + TCS	286	48.942	36.306	-11.222	[-13.355, -9.089]	1.0869				
UPA 15 mg QD + TCS	293	46.742	18.078	-28.017	[-30.143, -25.891]	1.0832	-16.795	[-19.457, -14.133]	1.3564	<0.001***
UPA 30 mg QD + TCS	287	48.547	13.885	-33.551	[-35.694, -31.408]	1.0921	-22.329	[-25.004, -19.654]	1.3629	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	131	37.500	26.411	-11.252	[-13.592, -8.913]	1.1900				
UPA 15 mg QD + TCS	137	35.480	12.555	-23.677	[-25.969, -21.384]	1.1663	-12.424	[-15.699, -9.150]	1.6656	<0.001***
UPA 30 mg QD + TCS	137	40.326	9.369	-29.721	[-32.027, -27.415]	1.1731	-18.469	[-21.755, -15.182]	1.6717	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	155	58.612	44.668	-13.050	[-15.918, -10.182]	1.4597				
UPA 15 mg QD + TCS	156	56.631	22.929	-33.684	[-36.566, -30.803]	1.4664	-20.634	[-24.700, -16.569]	2.0690	<0.001***
UPA 30 mg QD + TCS	150	56.055	18.009	-38.329	[-41.254, -35.404]	1.4887	-25.279	[-29.377, -21.181]	2.0854	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 4 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	100	46.099	31.591	-13.481	[-16.701, -10.260]	1.6370				
UPA 15 mg QD + TCS	107	44.609	17.872	-26.661	[-29.833, -23.488]	1.6123	-13.180	[-17.700, -8.660]	2.2973	<0.001***
UPA 30 mg QD + TCS	104	43.218	13.577	-30.095	[-33.324, -26.866]	1.6412	-16.614	[-21.176, -12.053]	2.3186	<0.001***
Japan										
Placebo + TCS	18	66.611	48.583	-16.724	[-26.063, -7.384]	4.6393				
UPA 15 mg QD + TCS	16	59.469	29.469	-31.263	[-41.160, -21.365]	4.9163	-14.539	[-28.212, -0.867]	6.7927	0.038*
UPA 30 mg QD + TCS	16	66.375	21.875	-42.010	[-51.734, -32.286]	4.8339	-25.286	[-38.707, -11.866]	6.6681	<0.001***
China										
Placebo + TCS	17	66.088	51.735	-13.103	[-23.606, -2.599]	5.2133				
UPA 15 mg QD + TCS	17	53.412	16.459	-38.518	[-49.056, -27.980]	5.2311	-25.415	[-40.400, -10.430]	7.4408	0.001**
UPA 30 mg QD + TCS	16	59.400	19.375	-40.260	[-51.026, -29.494]	5.3422	-27.157	[-42.214, -12.100]	7.4727	0.001**

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 4 (Cont.)										
Other										
Placebo + TCS	151	46.787	36.227	-10.561	[-12.991, -8.131]	1.2366				
UPA 15 mg QD + TCS	153	46.161	17.212	-28.787	[-31.195, -26.379]	1.2254	-18.226	[-21.647, -14.805]	1.7409	<0.001***
UPA 30 mg QD + TCS	151	49.177	12.669	-35.814	[-38.241, -33.388]	1.2346	-25.254	[-28.688, -21.819]	1.7476	<0.001***
Adolescent										
Placebo + TCS	38	48.405	37.903	-8.689	[-14.565, -2.813]	2.9647				
UPA 15 mg QD + TCS	37	44.146	18.943	-24.423	[-30.318, -18.528]	2.9745	-15.734	[-24.066, -7.403]	4.2040	<0.001***
UPA 30 mg QD + TCS	37	44.281	13.476	-30.938	[-36.939, -24.936]	3.0278	-22.249	[-30.650, -13.848]	4.2386	<0.001***
Adult										
Placebo + TCS	248	49.024	36.061	-12.530	[-14.529, -10.532]	1.0180				
UPA 15 mg QD + TCS	256	47.117	17.954	-29.417	[-31.396, -27.438]	1.0081	-16.887	[-19.700, -14.074]	1.4329	<0.001***
UPA 30 mg QD + TCS	250	49.178	13.946	-34.881	[-36.880, -32.882]	1.0181	-22.351	[-25.177, -19.525]	1.4395	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 8										
All										
Placebo + TCS	239	46.397	29.809	-14.523	[-16.756, -12.291]	1.1378				
UPA 15 mg QD + TCS	288	46.502	14.432	-31.187	[-33.342, -29.032]	1.0981	-16.663	[-19.427, -13.899]	1.4081	<0.001***
UPA 30 mg QD + TCS	285	48.531	10.021	-37.281	[-39.447, -35.114]	1.1039	-22.757	[-25.532, -19.982]	1.4137	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	120	37.524	22.878	-14.285	[-16.731, -11.838]	1.2444				
UPA 15 mg QD + TCS	136	35.521	9.971	-26.122	[-28.462, -23.781]	1.1903	-11.837	[-15.222, -8.453]	1.7215	<0.001***
UPA 30 mg QD + TCS	135	40.094	6.067	-32.754	[-35.108, -30.399]	1.1975	-18.469	[-21.866, -15.072]	1.7276	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	119	55.345	36.798	-16.446	[-19.524, -13.369]	1.5661				
UPA 15 mg QD + TCS	152	56.328	18.424	-37.549	[-40.463, -34.635]	1.4824	-21.103	[-25.341, -16.864]	2.1565	<0.001***
UPA 30 mg QD + TCS	150	56.124	13.579	-42.683	[-45.629, -39.736]	1.4989	-26.236	[-30.498, -21.975]	2.1681	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	96	43.697	26.565	-16.441	[-19.680, -13.202]	1.6463				
UPA 15 mg QD + TCS	108	44.687	13.652	-30.810	[-33.942, -27.678]	1.5914	-14.369	[-18.874, -9.864]	2.2895	<0.001***
UPA 30 mg QD + TCS	103	43.162	10.088	-33.487	[-36.686, -30.288]	1.6255	-17.046	[-21.599, -12.493]	2.3139	<0.001***
Japan										
Placebo + TCS	11	59.227	26.591	-28.106	[-37.823, -18.390]	4.8184				
UPA 15 mg QD + TCS	15	57.767	22.200	-35.750	[-45.076, -26.423]	4.6033	-7.644	[-21.157, 5.870]	6.6864	0.260
UPA 30 mg QD + TCS	16	66.375	15.563	-48.637	[-57.698, -39.575]	4.4703	-20.531	[-33.773, -7.288]	6.5545	0.003**
China										
Placebo + TCS	17	66.088	51.500	-13.338	[-22.403, -4.273]	4.4955				
UPA 15 mg QD + TCS	14	56.786	10.901	-45.268	[-54.819, -35.718]	4.7471	-31.930	[-45.201, -18.660]	6.5899	<0.001***
UPA 30 mg QD + TCS	16	59.400	15.688	-43.948	[-53.220, -34.675]	4.5973	-30.609	[-43.596, -17.623]	6.4396	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 8 (Cont.)										
Other										
Placebo + TCS	115	44.514	29.618	-13.765	[-16.521, -11.009]	1.4025				
UPA 15 mg QD + TCS	151	45.728	14.546	-30.879	[-33.435, -28.322]	1.3002	-17.114	[-20.872, -13.355]	1.9121	<0.001***
UPA 30 mg QD + TCS	150	49.155	8.779	-39.505	[-42.078, -36.932]	1.3087	-25.740	[-29.512, -21.968]	1.9189	<0.001***
Adolescent										
Placebo + TCS	32	44.200	31.872	-10.362	[-16.188, -4.535]	2.9383				
UPA 15 mg QD + TCS	35	44.194	15.931	-25.767	[-31.514, -20.019]	2.8970	-15.405	[-23.596, -7.214]	4.1296	<0.001***
UPA 30 mg QD + TCS	37	44.281	10.759	-33.654	[-39.443, -27.864]	2.9165	-23.292	[-31.508, -15.077]	4.1408	<0.001***
Adult										
Placebo + TCS	207	46.737	29.490	-16.071	[-18.218, -13.924]	1.0937				
UPA 15 mg QD + TCS	253	46.822	14.225	-32.811	[-34.841, -30.781]	1.0340	-16.739	[-19.694, -13.784]	1.5052	<0.001***
UPA 30 mg QD + TCS	248	49.165	9.911	-38.761	[-40.812, -36.709]	1.0448	-22.689	[-25.659, -19.720]	1.5125	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 12										
All										
Placebo + TCS	219	46.568	27.617	-16.298	[-18.601, -13.995]	1.1734				
UPA 15 mg QD + TCS	283	46.839	13.068	-32.424	[-34.599, -30.248]	1.1084	-16.126	[-18.962, -13.289]	1.4449	<0.001***
UPA 30 mg QD + TCS	280	48.606	8.203	-39.021	[-41.204, -36.838]	1.1124	-22.723	[-25.569, -19.877]	1.4498	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	113	37.495	21.730	-15.067	[-17.434, -12.701]	1.2032				
UPA 15 mg QD + TCS	132	36.087	8.567	-27.423	[-29.652, -25.193]	1.1335	-12.356	[-15.606, -9.105]	1.6526	<0.001***
UPA 30 mg QD + TCS	134	40.237	4.295	-34.483	[-36.714, -32.252]	1.1342	-19.416	[-22.669, -16.163]	1.6541	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	106	56.242	33.892	-19.193	[-22.503, -15.883]	1.6845				
UPA 15 mg QD + TCS	151	56.238	17.003	-38.814	[-41.832, -35.795]	1.5356	-19.621	[-24.101, -15.141]	2.2795	<0.001***
UPA 30 mg QD + TCS	146	56.287	11.790	-44.449	[-47.506, -41.391]	1.5553	-25.256	[-29.762, -20.749]	2.2929	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 12 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	88	43.209	24.653	-17.391	[-20.506, -14.276]	1.5828				
UPA 15 mg QD + TCS	108	44.687	11.739	-32.723	[-35.655, -29.791]	1.4893	-15.332	[-19.609, -11.054]	2.1733	<0.001***
UPA 30 mg QD + TCS	100	43.825	8.033	-35.616	[-38.626, -32.605]	1.5294	-18.224	[-22.556, -13.892]	2.2011	<0.001***
Japan										
Placebo + TCS	12	61.292	28.375	-30.480	[-41.702, -19.257]	5.5621				
UPA 15 mg QD + TCS	15	57.767	21.933	-36.376	[-46.755, -25.997]	5.1324	-5.897	[-21.201, 9.408]	7.5773	0.441
UPA 30 mg QD + TCS	16	66.375	17.056	-47.480	[-57.541, -37.420]	4.9716	-17.001	[-32.053, -1.948]	7.4537	0.028*
China										
Placebo + TCS	17	66.088	46.976	-17.862	[-27.297, -8.426]	4.6761				
UPA 15 mg QD + TCS	14	56.786	9.750	-46.494	[-56.533, -36.456]	4.9859	-28.633	[-42.503, -14.763]	6.8832	<0.001***
UPA 30 mg QD + TCS	16	59.400	11.719	-47.916	[-57.574, -38.259]	4.7849	-30.055	[-43.574, -16.535]	6.6996	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 12 (Cont.)										
Other										
Placebo + TCS	102	44.481	26.858	-15.652	[-18.654, -12.649]	1.5276				
UPA 15 mg QD + TCS	146	46.354	13.459	-31.563	[-34.268, -28.859]	1.3753	-15.912	[-19.952, -11.872]	2.0551	<0.001***
UPA 30 mg QD + TCS	148	48.748	6.981	-41.125	[-43.838, -38.412]	1.3795	-25.473	[-29.521, -21.425]	2.0589	<0.001***
Adolescent										
Placebo + TCS	30	43.013	28.993	-12.146	[-18.286, -6.005]	3.0953				
UPA 15 mg QD + TCS	35	44.194	14.737	-27.427	[-33.351, -21.504]	2.9833	-15.282	[-23.818, -6.746]	4.3008	0.001**
UPA 30 mg QD + TCS	37	44.281	9.184	-35.230	[-41.121, -29.338]	2.9649	-23.084	[-31.594, -14.573]	4.2867	<0.001***
Adult										
Placebo + TCS	189	47.133	27.398	-17.846	[-20.070, -15.622]	1.1327				
UPA 15 mg QD + TCS	248	47.212	12.833	-34.000	[-36.046, -31.954]	1.0420	-16.154	[-19.175, -13.132]	1.5390	<0.001***
UPA 30 mg QD + TCS	243	49.264	8.054	-40.529	[-42.596, -38.462]	1.0527	-22.683	[-25.719, -19.647]	1.5464	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	[95% CI]	SE	Between Groups Difference: Compared to Placebo: LS Mean	[95% CI]	SE	P-value
Week 16										
All										
Placebo + TCS	206	46.535	27.544	-16.393	[-18.742, -14.043]	1.1972				
UPA 15 mg QD + TCS	274	46.706	13.463	-31.835	[-34.024, -29.646]	1.1153	-15.442	[-18.329, -12.556]	1.4704	<0.001***
UPA 30 mg QD + TCS	276	48.562	8.246	-38.970	[-41.161, -36.779]	1.1164	-22.577	[-25.468, -19.686]	1.4728	<0.001***
vIGA-AD 3 (Moderate)										
Placebo + TCS	105	37.460	21.668	-15.186	[-17.657, -12.714]	1.2569				
UPA 15 mg QD + TCS	130	35.994	8.602	-27.130	[-29.434, -24.827]	1.1709	-11.945	[-15.322, -8.567]	1.7173	<0.001***
UPA 30 mg QD + TCS	134	40.117	4.731	-34.136	[-36.433, -31.838]	1.1677	-18.950	[-22.325, -15.574]	1.7162	<0.001***
vIGA-AD 4 (Severe)										
Placebo + TCS	101	55.970	33.653	-19.137	[-22.544, -15.731]	1.7332				
UPA 15 mg QD + TCS	144	56.376	17.851	-37.870	[-40.895, -34.846]	1.5383	-18.733	[-23.288, -14.178]	2.3175	<0.001***
UPA 30 mg QD + TCS	142	56.531	11.563	-44.686	[-47.739, -41.632]	1.5530	-25.548	[-30.123, -20.974]	2.3273	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	LS Mean	Within Group ---- Change from Baseline ---- [95% CI]	SE	Between Groups Difference ---------- Compared to Placebo ---------- LS Mean	[95% CI]	SE	P-value
Week 16 (Cont.)										
US/Puerto Rico/Canada										
Placebo + TCS	83	43.559	23.223	-18.959	[-22.307, -15.611]	1.7011				
UPA 15 mg QD + TCS	104	44.204	11.556	-32.504	[-35.605, -29.403]	1.5752	-13.544	[-18.108, -8.981]	2.3184	<0.001***
UPA 30 mg QD + TCS	99	43.394	7.762	-35.819	[-38.995, -32.642]	1.6134	-16.859	[-21.474, -12.245]	2.3446	<0.001***
Japan										
Placebo + TCS	11	63.409	28.818	-30.985	[-40.329, -21.641]	4.6277				
UPA 15 mg QD + TCS	15	57.767	22.387	-36.012	[-44.662, -27.362]	4.2668	-5.027	[-17.791, 7.737]	6.3105	0.431
UPA 30 mg QD + TCS	16	66.375	13.856	-50.639	[-59.015, -42.264]	4.1286	-19.654	[-32.173, -7.136]	6.1897	0.003**
China										
Placebo + TCS	17	66.088	42.882	-21.956	[-31.221, -12.691]	4.5964				
UPA 15 mg QD + TCS	14	56.786	10.464	-46.240	[-56.257, -36.224]	4.9760	-24.284	[-38.019, -10.549]	6.8200	0.001**
UPA 30 mg QD + TCS	16	59.400	13.625	-46.010	[-55.491, -36.529]	4.7021	-24.054	[-37.329, -10.780]	6.5849	0.001**

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

Time Point / Strata / Treatment	N	Baseline Mean	Visit Mean	Within Group: Change from Baseline: LS Mean	Within Group: Change from Baseline: [95% CI]	Within Group: Change from Baseline: SE	Between Groups Difference: Compared to Placebo: LS Mean	Between Groups Difference: Compared to Placebo: [95% CI]	Between Groups Difference: Compared to Placebo: SE	Between Groups Difference: Compared to Placebo: P-value
Week 16 (Cont.)										
Other										
Placebo + TCS	95	43.683	28.427	-13.536	[-16.589, -10.484]	1.5529				
UPA 15 mg QD + TCS	141	46.374	14.218	-30.657	[-33.352, -27.962]	1.3705	-17.121	[-21.192, -13.049]	2.0708	<0.001***
UPA 30 mg QD + TCS	145	48.929	7.363	-40.727	[-43.421, -38.033]	1.3698	-27.191	[-31.263, -23.118]	2.0715	<0.001***
Adolescent										
Placebo + TCS	30	43.013	27.000	-14.587	[-21.079, -8.096]	3.2704				
UPA 15 mg QD + TCS	35	44.194	14.826	-28.015	[-34.158, -21.871]	3.0928	-13.427	[-22.366, -4.488]	4.5016	0.004**
UPA 30 mg QD + TCS	35	43.869	8.674	-35.233	[-41.342, -29.124]	3.0746	-20.646	[-29.560, -11.732]	4.4890	<0.001***
Adult										
Placebo + TCS	176	47.136	27.637	-17.534	[-19.800, -15.268]	1.1542				
UPA 15 mg QD + TCS	239	47.074	13.264	-33.287	[-35.341, -31.234]	1.0459	-15.754	[-18.812, -12.695]	1.5575	<0.001***
UPA 30 mg QD + TCS	241	49.244	8.183	-40.459	[-42.524, -38.394]	1.0515	-22.925	[-25.991, -19.859]	1.5614	<0.001***

Note: BSA = Body Surface Area; vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis.
Measurements after receiving rescue treatment are considered as missing.
MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Within each stratum, Baseline, treatment, visit, treatment by visit interaction are in the model. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing change from Baseline values are included in analysis.
***, **, * Statistically significant at 0.001, 0.01, and 0.05 level, respectively.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.2　12.1.1

表 2.7.3.6-70.　第 1 ピリオドの来院時別の罹患 BSA のベースラインからの変化（LOCF，OC，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 2											
	ALL										
		UPA 30 MG QD	42	42.1	25.1	-17.1	2.95	-18.4	(-25.7, -11.1)	3.71	<0.001***
		UPA 15 MG QD	42	50.6	29.3	-20.6	2.94	-21.9	(-29.2, -14.6)	3.71	<0.001***
		UPA 7.5 MG QD	42	46.9	39.0	-7.6	2.99	-8.8	(-16.1, -1.5)	3.70	0.018*
		PLACEBO	37	46.2	47.2	1.2	3.12				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	23.0	-17.0	2.84	-18.7	(-26.8, -10.6)	4.10	<0.001***
		UPA 15 MG QD	29	52.8	31.4	-20.9	2.84	-22.7	(-30.8, -14.5)	4.11	<0.001***
		UPA 7.5 MG QD	29	47.6	38.8	-8.7	2.81	-10.5	(-18.6, -2.4)	4.09	0.012*
		PLACEBO	26	45.5	47.3	1.8	2.97				
	EU/AUS										
		UPA 30 MG QD	10	52.6	33.6	-17.9	6.73	-16.7	(-36.5, 3.1)	9.74	0.095
		UPA 15 MG QD	10	41.1	18.2	-24.2	6.76	-23.0	(-42.8, -3.2)	9.75	0.024*
		UPA 7.5 MG QD	11	49.1	43.8	-4.9	6.37	-3.7	(-23.0, 15.6)	9.50	0.697
		PLACEBO	9	47.0	45.9	-1.2	7.04				
	JAPAN										
		UPA 30 MG QD	3	33.3	17.7	-15.3	8.53	-14.6	(-49.7, 20.6)	13.67	0.335
		UPA 15 MG QD	3	61.0	45.7	-15.9	9.35	-15.1	(-48.6, 18.3)	13.00	0.297
		UPA 7.5 MG QD	2	25.0	15.5	-8.9	11.09	-8.1	(-48.5, 32.2)	15.71	0.626
		PLACEBO	2	51.5	51.0	-0.8	10.10				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.967

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 4											
	ALL										
		UPA 30 MG QD	42	42.1	12.5	-29.8	3.02	-30.3	(-37.7, -22.9)	3.74	<0.001***
		UPA 15 MG QD	42	50.6	24.3	-24.5	3.01	-24.9	(-32.3, -17.5)	3.75	<0.001***
		UPA 7.5 MG QD	42	46.9	29.4	-16.6	3.06	-17.0	(-24.4, -9.6)	3.74	<0.001***
		PLACEBO	39	44.6	44.6	0.4	3.15				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	10.9	-29.7	3.03	-28.9	(-37.4, -20.4)	4.29	<0.001***
		UPA 15 MG QD	29	52.8	25.0	-26.5	3.04	-25.6	(-34.2, -17.1)	4.33	<0.001***
		UPA 7.5 MG QD	29	47.6	28.3	-18.9	3.00	-18.1	(-26.6, -9.6)	4.29	<0.001***
		PLACEBO	28	43.4	43.0	-0.8	3.06				
	EU/AUS										
		UPA 30 MG QD	10	52.6	18.7	-32.2	6.47	-32.1	(-51.2, -13.1)	9.38	0.002**
		UPA 15 MG QD	10	41.1	20.1	-23.2	6.50	-23.1	(-42.1, -4.1)	9.38	0.019*
		UPA 7.5 MG QD	11	49.1	34.7	-13.8	6.13	-13.8	(-32.3, 4.8)	9.14	0.141
		PLACEBO	9	47.0	47.1	-0.1	6.77				
	JAPAN										
		UPA 30 MG QD	3	33.3	7.0	-31.3	6.54	-39.1	(-66.1, -12.2)	10.48	0.014*
		UPA 15 MG QD	3	61.0	31.0	-21.6	7.17	-29.4	(-55.0, -3.8)	9.97	0.032*
		UPA 7.5 MG QD	2	25.0	14.5	-19.5	8.51	-27.3	(-58.3, 3.6)	12.05	0.073
		PLACEBO	2	51.5	55.5	7.8	7.75				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.982

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 8											
	ALL										
		UPA 30 MG QD	42	42.1	9.3	-32.6	3.34	-31.7	(-39.9, -23.5)	4.14	<0.001***
		UPA 15 MG QD	42	50.6	22.3	-25.6	3.34	-24.7	(-32.9, -16.5)	4.16	<0.001***
		UPA 7.5 MG QD	42	46.9	30.2	-15.0	3.39	-14.1	(-22.3, -5.9)	4.14	<0.001***
		PLACEBO	39	44.6	42.7	-0.9	3.49				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	7.9	-32.8	3.30	-29.0	(-38.2, -19.7)	4.67	<0.001***
		UPA 15 MG QD	29	52.8	23.8	-27.5	3.31	-23.7	(-33.0, -14.3)	4.72	<0.001***
		UPA 7.5 MG QD	29	47.6	29.6	-17.7	3.27	-13.8	(-23.1, -4.5)	4.68	0.004**
		PLACEBO	28	43.4	40.0	-3.9	3.33				
	EU/AUS										
		UPA 30 MG QD	10	52.6	14.3	-36.0	7.09	-33.4	(-54.2, -12.6)	10.26	0.003**
		UPA 15 MG QD	10	41.1	16.8	-27.2	7.12	-24.7	(-45.5, -3.8)	10.27	0.022*
		UPA 7.5 MG QD	11	49.1	34.7	-13.6	6.71	-11.1	(-31.4, 9.2)	10.00	0.276
		PLACEBO	9	47.0	44.7	-2.6	7.41				
	JAPAN										
		UPA 30 MG QD	3	33.3	5.7	-35.5	7.50	-60.5	(-91.4, -29.7)	12.02	0.004**
		UPA 15 MG QD	3	61.0	26.3	-21.4	8.22	-46.4	(-75.8, -17.0)	11.43	0.010**
		UPA 7.5 MG QD	2	25.0	14.5	-24.7	9.75	-49.7	(-85.3, -14.2)	13.82	0.016*
		PLACEBO	2	51.5	70.5	25.0	8.88				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.767

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF WEEK 12											
	ALL										
		UPA 30 MG QD	42	42.1	8.4	-33.7	3.34	-31.1	(-39.2, -22.9)	4.14	<0.001***
		UPA 15 MG QD	42	50.6	20.3	-27.5	3.34	-24.9	(-33.1, -16.6)	4.16	<0.001***
		UPA 7.5 MG QD	42	46.9	31.7	-13.4	3.39	-10.8	(-19.0, -2.6)	4.14	0.010**
		PLACEBO	39	44.6	41.1	-2.6	3.49				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	7.5	-33.7	3.48	-29.3	(-39.0, -19.5)	4.93	<0.001***
		UPA 15 MG QD	29	52.8	20.1	-30.8	3.49	-26.3	(-36.2, -16.5)	4.98	<0.001***
		UPA 7.5 MG QD	29	47.6	32.4	-14.7	3.45	-10.3	(-20.0, -0.5)	4.93	0.040*
		PLACEBO	28	43.4	39.6	-4.5	3.51				
	EU/AUS										
		UPA 30 MG QD	10	52.6	12.4	-38.0	6.27	-29.6	(-48.1, -11.2)	9.08	0.002**
		UPA 15 MG QD	10	41.1	18.8	-25.1	6.30	-16.8	(-35.2, 1.7)	9.08	0.073
		UPA 7.5 MG QD	11	49.1	33.2	-15.2	5.94	-6.9	(-24.8, 11.1)	8.85	0.442
		PLACEBO	9	47.0	38.9	-8.3	6.56				
	JAPAN										
		UPA 30 MG QD	3	33.3	4.3	-36.7	7.68	-62.1	(-93.8, -30.5)	12.31	0.004**
		UPA 15 MG QD	3	61.0	26.7	-21.3	8.42	-46.7	(-76.8, -16.6)	11.71	0.010**
		UPA 7.5 MG QD	2	25.0	14.5	-24.5	9.99	-49.9	(-86.3, -13.5)	14.16	0.017*
		PLACEBO	2	51.5	71.0	25.4	9.10				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.593

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
WEEK 16											
	ALL										
		UPA 30 MG QD	42	42.1	10.7	-30.7	3.43	-26.5	(-34.9, -18.1)	4.25	<0.001***
		UPA 15 MG QD	42	50.6	19.7	-27.1	3.43	-23.0	(-31.4, -14.6)	4.27	<0.001***
		UPA 7.5 MG QD	42	46.9	32.6	-11.7	3.48	-7.6	(-16.0, 0.8)	4.25	0.075
		PLACEBO	39	44.6	38.7	-4.1	3.58				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	7.8	-33.6	3.64	-26.8	(-37.0, -16.6)	5.15	<0.001***
		UPA 15 MG QD	29	52.8	18.6	-32.0	3.65	-25.3	(-35.6, -15.0)	5.20	<0.001***
		UPA 7.5 MG QD	29	47.6	31.8	-15.2	3.61	-8.5	(-18.7, 1.7)	5.15	0.103
		PLACEBO	28	43.4	37.4	-6.7	3.67				
	EU/AUS										
		UPA 30 MG QD	10	52.6	17.4	-33.0	6.47	-27.6	(-46.6, -8.5)	9.38	0.006**
		UPA 15 MG QD	10	41.1	19.7	-24.2	6.50	-18.7	(-37.8, 0.3)	9.38	0.054
		UPA 7.5 MG QD	11	49.1	36.6	-11.8	6.13	-6.3	(-24.9, 12.2)	9.14	0.493
		PLACEBO	9	47.0	41.8	-5.4	6.77				
	JAPAN										
		UPA 30 MG QD	3	33.3	16.7	-22.9	8.53	-19.7	(-54.9, 15.4)	13.67	0.209
		UPA 15 MG QD	3	61.0	30.0	-20.4	9.35	-17.2	(-50.6, 16.2)	13.00	0.243
		UPA 7.5 MG QD	2	25.0	22.5	-13.8	11.10	-10.6	(-51.0, 29.8)	15.72	0.529
		PLACEBO	2	51.5	43.5	-3.2	10.10				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.977

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 2											
	ALL										
		UPA 30 MG QD	42	42.1	25.1	-17.1	2.95	-18.4	(-25.7, -11.1)	3.71	<0.001***
		UPA 15 MG QD	42	50.6	29.3	-20.6	2.94	-21.9	(-29.2, -14.6)	3.71	<0.001***
		UPA 7.5 MG QD	42	46.9	39.0	-7.6	2.99	-8.8	(-16.1, -1.5)	3.70	0.018*
		PLACEBO	37	46.2	47.2	1.2	3.12				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	23.0	-17.0	2.84	-18.7	(-26.8, -10.6)	4.10	<0.001***
		UPA 15 MG QD	29	52.8	31.4	-20.9	2.84	-22.7	(-30.8, -14.5)	4.11	<0.001***
		UPA 7.5 MG QD	29	47.6	38.8	-8.7	2.81	-10.5	(-18.6, -2.4)	4.09	0.012*
		PLACEBO	26	45.5	47.3	1.8	2.97				
	EU/AUS										
		UPA 30 MG QD	10	52.6	33.6	-17.9	6.73	-16.7	(-36.5, 3.1)	9.74	0.095
		UPA 15 MG QD	10	41.1	18.2	-24.2	6.76	-23.0	(-42.8, -3.2)	9.75	0.024*
		UPA 7.5 MG QD	11	49.1	43.8	-4.9	6.37	-3.7	(-23.0, 15.6)	9.50	0.697
		PLACEBO	9	47.0	45.9	-1.2	7.04				
	JAPAN										
		UPA 30 MG QD	3	33.3	17.7	-15.3	8.53	-14.6	(-49.7, 20.6)	13.67	0.335
		UPA 15 MG QD	3	61.0	45.7	-15.9	9.35	-15.1	(-48.6, 18.3)	13.00	0.297
		UPA 7.5 MG QD	2	25.0	15.5	-8.9	11.09	-8.1	(-48.5, 32.2)	15.71	0.626
		PLACEBO	2	51.5	51.0	-0.8	10.10				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.967

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
WEEK 4											
	ALL										
		UPA 30 MG QD	41	40.9	10.4	-30.9	2.96	-31.6	(-39.0, -24.2)	3.75	<0.001***
		UPA 15 MG QD	41	50.7	24.3	-24.3	2.94	-25.0	(-32.4, -17.6)	3.76	<0.001***
		UPA 7.5 MG QD	42	46.9	29.4	-16.4	2.96	-17.1	(-24.5, -9.7)	3.73	<0.001***
		PLACEBO	35	44.2	44.4	0.7	3.18				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	10.9	-29.8	3.03	-27.9	(-36.6, -19.3)	4.37	<0.001***
		UPA 15 MG QD	28	53.1	25.0	-26.6	3.09	-24.8	(-33.6, -15.9)	4.45	<0.001***
		UPA 7.5 MG QD	29	47.6	28.3	-18.9	3.00	-17.0	(-25.7, -8.4)	4.37	<0.001***
		PLACEBO	26	42.8	41.5	-1.8	3.17				
	EU/AUS										
		UPA 30 MG QD	9	47.9	10.1	-37.0	5.81	-42.1	(-59.9, -24.2)	8.78	<0.001***
		UPA 15 MG QD	10	41.1	20.1	-23.5	5.56	-28.6	(-46.1, -11.0)	8.64	0.002**
		UPA 7.5 MG QD	11	49.1	34.7	-13.0	5.27	-18.1	(-35.2, -0.9)	8.43	0.040*
		PLACEBO	7	47.6	52.0	5.0	6.59				
	JAPAN										
		UPA 30 MG QD	3	33.3	7.0	-31.3	6.54	-39.1	(-66.1, -12.2)	10.48	0.014*
		UPA 15 MG QD	3	61.0	31.0	-21.6	7.17	-29.4	(-55.0, -3.8)	9.97	0.032*
		UPA 7.5 MG QD	2	25.0	14.5	-19.5	8.51	-27.3	(-58.3, 3.6)	12.05	0.073
		PLACEBO	2	51.5	55.5	7.8	7.75				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.786

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 8											
	ALL										
		UPA 30 MG QD	42	42.1	9.3	-32.4	3.30	-30.2	(-38.7, -21.6)	4.34	<0.001***
		UPA 15 MG QD	40	50.5	21.3	-26.4	3.35	-24.2	(-32.9, -15.5)	4.40	<0.001***
		UPA 7.5 MG QD	40	48.3	29.9	-16.1	3.40	-13.9	(-22.6, -5.2)	4.39	0.002**
		PLACEBO	31	43.8	40.6	-2.2	3.74				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	7.9	-32.9	3.25	-26.0	(-35.6, -16.4)	4.84	<0.001***
		UPA 15 MG QD	28	53.1	23.8	-28.0	3.31	-21.1	(-30.9, -11.4)	4.91	<0.001***
		UPA 7.5 MG QD	28	48.6	29.0	-19.2	3.27	-12.3	(-21.9, -2.6)	4.88	0.013*
		PLACEBO	23	44.0	37.6	-6.9	3.61				
	EU/AUS										
		UPA 30 MG QD	10	52.6	14.3	-35.2	6.92	-33.3	(-56.5, -10.0)	11.39	0.007**
		UPA 15 MG QD	9	39.0	12.0	-31.2	7.35	-29.3	(-52.6, -6.0)	11.40	0.015*
		UPA 7.5 MG QD	10	51.9	35.3	-13.9	6.90	-11.9	(-35.2, 11.3)	11.36	0.301
		PLACEBO	6	40.5	42.0	-1.9	8.90				
	JAPAN										
		UPA 30 MG QD	3	33.3	5.7	-35.5	7.50	-60.5	(-91.4, -29.7)	12.02	0.004**
		UPA 15 MG QD	3	61.0	26.3	-21.4	8.22	-46.4	(-75.8, -17.0)	11.43	0.010**
		UPA 7.5 MG QD	2	25.0	14.5	-24.7	9.75	-49.7	(-85.3, -14.2)	13.82	0.016*
		PLACEBO	2	51.5	70.5	25.0	8.88				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.648

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 12											
	ALL										
		UPA 30 MG QD	40	39.9	6.8	-34.2	3.27	-28.1	(-36.5, -19.7)	4.26	<0.001***
		UPA 15 MG QD	39	51.1	18.7	-29.8	3.27	-23.6	(-32.2, -15.1)	4.31	<0.001***
		UPA 7.5 MG QD	36	49.8	31.0	-16.4	3.41	-10.3	(-19.0, -1.7)	4.38	0.020*
		PLACEBO	30	43.6	37.5	-6.1	3.66				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	7.5	-33.8	3.47	-26.2	(-36.4, -16.0)	5.16	<0.001***
		UPA 15 MG QD	28	53.1	19.9	-31.5	3.52	-23.8	(-34.2, -13.4)	5.23	<0.001***
		UPA 7.5 MG QD	26	49.9	32.9	-16.1	3.62	-8.5	(-19.0, 2.0)	5.29	0.112
		PLACEBO	23	44.0	37.1	-7.6	3.85				
	EU/AUS										
		UPA 30 MG QD	8	43.9	5.0	-39.7	4.98	-23.1	(-39.7, -6.5)	8.06	0.008**
		UPA 15 MG QD	8	40.4	11.6	-31.7	5.02	-15.1	(-31.6, 1.5)	8.02	0.072
		UPA 7.5 MG QD	8	55.8	28.9	-20.6	5.20	-4.0	(-21.3, 13.3)	8.40	0.640
		PLACEBO	5	38.6	26.0	-16.6	6.36				
	JAPAN										
		UPA 30 MG QD	3	33.3	4.3	-36.7	7.68	-62.1	(-93.8, -30.5)	12.31	0.004**
		UPA 15 MG QD	3	61.0	26.7	-21.3	8.42	-46.7	(-76.8, -16.6)	11.71	0.010**
		UPA 7.5 MG QD	2	25.0	14.5	-24.5	9.99	-49.9	(-86.3, -13.5)	14.16	0.017*
		PLACEBO	2	51.5	71.0	25.4	9.10				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.564

IMPUTATION VISIT	STRATA	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -CHANGE FROM BASELINE LSMEAN	- SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 16											
	ALL										
		UPA 30 MG QD	40	39.9	9.2	-30.8	3.32	-21.8	(-30.9, -12.8)	4.58	<0.001***
		UPA 15 MG QD	38	51.0	17.5	-29.9	3.35	-20.9	(-30.0, -11.7)	4.61	<0.001***
		UPA 7.5 MG QD	34	48.8	31.1	-14.6	3.55	-5.6	(-14.9, 3.7)	4.70	0.237
		PLACEBO	25	46.5	35.4	-9.0	4.04				
	US/PR/CANADA										
		UPA 30 MG QD	29	39.4	7.8	-33.7	3.45	-21.3	(-31.8, -10.9)	5.27	<0.001***
		UPA 15 MG QD	28	53.1	18.4	-33.0	3.49	-20.7	(-31.2, -10.1)	5.31	<0.001***
		UPA 7.5 MG QD	26	49.9	32.3	-16.8	3.60	-4.4	(-15.1, 6.2)	5.38	0.412
		PLACEBO	21	45.7	33.7	-12.4	3.99				
	EU/AUS										
		UPA 30 MG QD	8	43.9	11.3	-33.4	5.96	-32.7	(-60.7, -4.6)	13.37	0.025*
		UPA 15 MG QD	7	38.6	8.6	-34.7	6.49	-34.0	(-62.7, -5.2)	13.70	0.023*
		UPA 7.5 MG QD	6	51.8	28.8	-17.8	7.02	-17.1	(-46.0, 11.7)	13.75	0.229
		PLACEBO	2	50.0	45.5	-0.7	11.95				
	JAPAN										
		UPA 30 MG QD	3	33.3	16.7	-22.9	8.53	-19.7	(-54.9, 15.4)	13.67	0.209
		UPA 15 MG QD	3	61.0	30.0	-20.4	9.35	-17.2	(-50.6, 16.2)	13.00	0.243
		UPA 7.5 MG QD	2	25.0	22.5	-13.8	11.10	-10.6	(-51.0, 29.8)	15.72	0.529
		PLACEBO	2	51.5	43.5	-3.2	10.10				

TEST OF INTERACTION BETWEEN STRATA AND TREATMENT: P-VALUE @ = 0.984

[A] ACROSS THE STRATA, P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, AND TREATMENT IN THE MODEL.
WITHIN EACH STRATUM, P-VALUES WERE CALCULATED FROM ANCOVA WITH BASELINE VALUE AND THE TREATMENT IN THE MODEL.
@ P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATUM, BASELINE VALUE, TREATMENT, INTERACTION OF STRATUM AND TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.
Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.12

表 2.7.3.6-71.　人口統計学的特性の要約（ITT_M 集団，日本人部分集団）：M16-045 試験

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
Sex - n (%)					
Male	8 (57.1)	10 (66.7)	13 (81.3)	23 (74.2)	31 (68.9)
Female	6 (42.9)	5 (33.3)	3 (18.8)	8 (25.8)	14 (31.1)
Ethnicity - n (%)					
Hispanic or Latino	0	0	0	0	0
Not Hispanic or Latino	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
Race - n (%)					
White	0	0	0	0	0
Black or African American	0	0	0	0	0
Asian	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
American Indian/Alaska Native	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Other	0	0	0	0	0
Multiple	0	0	0	0	0
Age Group 1 (years) - n (%)					
< 18	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
>= 18	13 (92.9)	14 (93.3)	14 (87.5)	28 (90.3)	41 (91.1)

Note: Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
Age Group 2 (years) - n (%)					
< 18	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
18 - < 40	6 (42.9)	5 (33.3)	10 (62.5)	15 (48.4)	21 (46.7)
40 - < 65	7 (50.0)	8 (53.3)	4 (25.0)	12 (38.7)	19 (42.2)
>= 65	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Age (years)					
n	14	15	16	31	45
Mean (SD)	36.8 (10.77)	39.9 (14.17)	33.5 (11.78)	36.6 (13.18)	36.7 (12.36)
Median	38.0	42.0	32.5	34.0	34.0
Min, Max	18, 55	17, 68	18, 64	17, 68	17, 68
Weight (kg)					
n	14	15	16	31	45
Mean (SD)	63.86 (10.904)	62.89 (7.589)	63.73 (14.623)	63.32 (11.575)	63.49 (11.249)
Median	63.80	65.00	58.35	60.40	63.20
Min, Max	45.6, 82.8	49.4, 74.2	46.5, 93.6	46.5, 93.6	45.6, 93.6
Height (cm)					
n	14	15	16	31	45
Mean (SD)	162.89 (9.706)	164.52 (8.054)	168.49 (8.036)	166.57 (8.163)	165.42 (8.732)
Median	164.00	162.00	168.20	166.60	164.00
Min, Max	147.0, 179.8	151.6, 181.5	156.5, 181.0	151.6, 181.5	147.0, 181.5
BMI (kg/m^2)					
n	14	15	16	31	45
Mean (SD)	23.99 (2.938)	23.21 (2.066)	22.27 (3.785)	22.73 (3.063)	23.12 (3.050)
Median	25.30	23.30	21.20	22.50	22.90
Min, Max	19.6, 28.0	19.7, 26.1	16.7, 28.6	16.7, 28.6	16.7, 28.6

Note: Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
BMI (kg/m^2) - n (%)					
< 25	6 (42.9)	10 (66.7)	11 (68.8)	21 (67.7)	27 (60.0)
25 - < 30	8 (57.1)	5 (33.3)	5 (31.3)	10 (32.3)	18 (40.0)
>= 30	0	0	0	0	0
Geographic Region - n (%)					
US/Puerto Rico/Canada	0	0	0	0	0
Japan	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
China	0	0	0	0	0
Other	0	0	0	0	0
Tobacco$ - n (%)					
Current	3 (21.4)	3 (20.0)	5 (31.3)	8 (25.8)	11 (24.4)
Former	3 (21.4)	3 (20.0)	0	3 (9.7)	6 (13.3)
Never	8 (57.1)	9 (60.0)	11 (68.8)	20 (64.5)	28 (62.2)
Unknown	0	0	0	0	0
Alcohol$ - n (%)					
Current	10 (71.4)	10 (66.7)	8 (50.0)	18 (58.1)	28 (62.2)
Former	3 (21.4)	1 (6.7)	0	1 (3.2)	4 (8.9)
Never	1 (7.1)	4 (26.7)	8 (50.0)	12 (38.7)	13 (28.9)
Unknown	0	0	0	0	0

Note: Percentages calculated on non-missing values.
$ Percentages calculated on non-missing/non-unknown values. A subject may be a current user of one type of tobacco, a former user of another type of tobacco and never used another type of tobacco. A subject will be counted in the category closest to user.

Program Source Code: [redacted]

相互参照：M16-045 試験 W16 Japan Study Data Table 14.1　4.1_J

表 2.7.3.6-72.　ベースラインのその他の基準値の特性の要約（ITT_M 集団，日本人部分集団）：M16-045 試験

	Placebo (N=14)	Active UPA 15 mg QD (N=15)	Active UPA 30 mg QD (N=16)	Active Total (N=31)	Total (N=45)
Baseline vIGA-AD - n (%)					
3 (Moderate)	8 (57.1)	8 (53.3)	9 (56.3)	17 (54.8)	25 (55.6)
4 (Severe)	6 (42.9)	7 (46.7)	7 (43.8)	14 (45.2)	20 (44.4)
Baseline EASI - n (%)					
< Median (25.8)	6 (42.9)	8 (53.3)	7 (43.8)	15 (48.4)	21 (46.7)
>= Median (25.8)	8 (57.1)	7 (46.7)	9 (56.3)	16 (51.6)	24 (53.3)
hsCRP - n (%)					
< Median (1.4)	8 (57.1)	11 (73.3)	10 (62.5)	21 (67.7)	29 (64.4)
>= Median (1.4)	6 (42.9)	4 (26.7)	6 (37.5)	10 (32.3)	16 (35.6)
Previous Systemic Therapy - n (%)					
With	9 (64.3)	7 (46.7)	9 (56.3)	16 (51.6)	25 (55.6)
Without	5 (35.7)	8 (53.3)	7 (43.8)	15 (48.4)	20 (44.4)
EASI					
n	14	15	16	31	45
Mean (SD)	30.89 (14.628)	29.63 (11.132)	30.25 (9.206)	29.95 (10.015)	30.24 (11.481)
Median	27.45	25.40	29.05	28.50	27.70
Min, Max	16.2, 70.2	16.1, 53.3	18.8, 50.0	16.1, 53.3	16.1, 70.2

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
EASI Head/Neck					
n	14	15	16	31	45
Mean (SD)	3.47 (1.815)	3.36 (1.108)	3.76 (1.866)	3.57 (1.535)	3.54 (1.606)
Median	3.25	3.50	3.20	3.20	3.20
Min, Max	1.0, 7.2	1.4, 5.0	0.8, 7.2	0.8, 7.2	0.8, 7.2
EASI Lower Limbs					
n	14	15	16	31	45
Mean (SD)	9.74 (7.146)	10.93 (5.849)	10.50 (4.956)	10.71 (5.319)	10.41 (5.881)
Median	8.80	9.60	11.60	10.80	9.60
Min, Max	0.4, 28.8	3.2, 22.0	2.4, 20.0	2.4, 22.0	0.4, 28.8
EASI Trunk					
n	14	15	16	31	45
Mean (SD)	11.61 (5.392)	9.68 (3.943)	10.13 (3.221)	9.91 (3.535)	10.44 (4.212)
Median	12.00	9.60	10.05	9.60	9.60
Min, Max	4.5, 21.6	4.8, 18.0	4.8, 15.0	4.8, 18.0	4.5, 21.6
EASI Upper Limbs					
n	14	15	16	31	45
Mean (SD)	6.06 (3.130)	5.65 (2.228)	5.86 (2.932)	5.76 (2.574)	5.85 (2.726)
Median	5.70	5.40	5.40	5.40	5.40
Min, Max	2.0, 14.4	2.4, 10.0	2.4, 14.4	2.4, 14.4	2.0, 14.4

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
BSA in Percentage					
n	14	15	16	31	45
Mean (SD)	49.7 (24.02)	51.2 (21.06)	54.3 (15.42)	52.8 (18.12)	51.8 (19.91)
Median	52.5	46.0	55.0	50.0	50.0
Min, Max	16, 98	15, 90	25, 83	15, 90	15, 98
Overall SCORAD Score					
n	14	15	16	31	45
Mean (SD)	69.01 (17.617)	63.91 (11.884)	67.46 (14.949)	65.74 (13.450)	66.76 (14.744)
Median	66.45	63.70	67.10	65.30	65.30
Min, Max	41.7, 102.6	39.0, 85.4	42.1, 91.4	39.0, 91.4	39.0, 102.6
Objective SCORAD					
n	14	15	16	31	45
Mean (SD)	53.44 (15.333)	51.44 (12.201)	53.90 (11.917)	52.71 (11.918)	52.94 (12.900)
Median	50.45	50.60	53.50	50.70	50.70
Min, Max	30.7, 82.6	28.0, 73.4	34.1, 72.6	28.0, 73.4	28.0, 82.6
SCORAD Itch					
n	14	15	16	31	45
Mean (SD)	8.7 (0.99)	7.6 (1.64)	7.7 (1.66)	7.6 (1.62)	8.0 (1.53)
Median	8.5	7.0	7.5	7.0	8.0
Min, Max	7, 10	4, 10	6, 10	4, 10	4, 10

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
SCORAD Sleep					
n	14	15	16	31	45
Mean (SD)	6.9 (2.60)	4.9 (2.47)	5.9 (2.90)	5.4 (2.70)	5.8 (2.73)
Median	7.0	5.0	7.0	6.0	7.0
Min, Max	2, 10	1, 9	2, 10	1, 10	1, 10
DLQI					
n	14	15	16	31	45
Mean (SD)	16.5 (4.96)	10.5 (4.88)	15.1 (7.90)	12.8 (6.91)	14.0 (6.54)
Median	16.0	11.0	17.0	13.0	15.0
Min, Max	7, 25	1, 19	2, 25	1, 25	1, 25
HADS Total Score					
n	14	15	16	31	45
Mean (SD)	12.9 (7.77)	7.5 (7.54)	11.8 (8.81)	9.7 (8.37)	10.7 (8.24)
Median	13.0	6.0	9.0	8.0	8.0
Min, Max	3, 23	0, 25	2, 35	0, 35	0, 35
HADS-A Total Score					
n	14	15	16	31	45
Mean (SD)	6.6 (3.92)	3.9 (4.06)	6.6 (4.73)	5.3 (4.55)	5.7 (4.36)
Median	7.0	3.0	5.0	4.0	5.0
Min, Max	1, 13	0, 15	1, 18	0, 18	0, 18

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
HADS-D Total Score					
n	14	15	16	31	45
Mean (SD)	6.4 (4.25)	3.6 (3.89)	5.3 (4.58)	4.5 (4.27)	5.0 (4.31)
Median	6.0	2.0	4.5	3.0	4.0
Min, Max	0, 13	0, 13	0, 17	0, 17	0, 17
WPAI: AD: Absenteeism (%)					
n	5	5	4	9	14
Mean (SD)	15.977 (25.2995)	4.000 (8.9443)	20.833 (41.6667)	11.481 (27.7444)	13.087 (25.9930)
Median	9.091	0.000	0.000	0.000	0.000
Min, Max	0.00, 60.38	0.00, 20.00	0.00, 83.33	0.00, 83.33	0.00, 83.33
WPAI: AD: Presenteeism (%)					
n	5	5	4	9	14
Mean (SD)	76.0 (23.02)	46.0 (35.78)	50.0 (35.59)	47.8 (33.46)	57.9 (32.39)
Median	80.0	60.0	40.0	50.0	60.0
Min, Max	40, 100	0, 90	20, 100	0, 100	0, 100
WPAI: AD: Work Productivity Loss (%)					
n	5	5	4	9	14
Mean (SD)	77.753 (23.9001)	47.600 (36.7260)	50.000 (35.5903)	48.667 (33.9264)	59.055 (33.0643)
Median	80.000	60.000	40.000	50.000	64.000
Min, Max	40.00, 100.00	0.00, 90.00	20.00, 100.00	0.00, 100.00	0.00, 100.00

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
WPAI: AD: Activity Impairment (%)					
n	14	15	16	31	45
Mean (SD)	67.9 (24.55)	59.3 (23.74)	65.6 (25.55)	62.6 (24.49)	64.2 (24.35)
Median	75.0	60.0	70.0	70.0	70.0
Min, Max	0, 90	20, 90	20, 100	20, 100	0, 100
EQ-5D-5L Index					
n	14	15	16	31	45
Mean (SD)	0.608 (0.3595)	0.833 (0.1209)	0.673 (0.2605)	0.750 (0.2175)	0.706 (0.2736)
Median	0.783	0.866	0.750	0.809	0.803
Min, Max	-0.09, 0.94	0.54, 1.00	0.21, 1.00	0.21, 1.00	-0.09, 1.00
EQ-5D-5L VAS Score					
n	14	15	16	31	45
Mean (SD)	48.7 (22.24)	61.7 (20.63)	44.4 (27.89)	52.8 (25.77)	51.5 (24.55)
Median	53.0	65.0	50.0	56.0	56.0
Min, Max	10, 83	30, 96	3, 95	3, 96	3, 96
Worst Pruritus NRS (Daily)					
n	14	15	16	31	45
Mean (SD)	8.3 (1.14)	7.2 (1.70)	7.4 (1.97)	7.3 (1.81)	7.6 (1.68)
Median	8.0	8.0	7.0	7.0	8.0
Min, Max	6, 10	4, 10	5, 10	4, 10	4, 10

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
Worst Pruritus NRS (Weekly Average)					
n	14	15	16	31	45
Mean (SD)	7.856 (0.9274)	6.792 (1.5868)	7.100 (1.7682)	6.951 (1.6621)	7.232 (1.5223)
Median	7.757	7.000	7.286	7.000	7.571
Min, Max	6.00, 9.71	4.00, 9.43	4.71, 10.00	4.00, 10.00	4.00, 10.00
PGIS					
n	14	15	16	31	45
Mean (SD)	4.4 (0.85)	4.0 (0.85)	4.4 (0.89)	4.2 (0.88)	4.3 (0.87)
Median	4.5	4.0	4.0	4.0	4.0
Min, Max	3, 6	3, 6	3, 6	3, 6	3, 6

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
PGIS - n (%)					
Absent	0	0	0	0	0
Minimal	0	0	0	0	0
Mild	0	0	0	0	0
Moderate	2 (14.3)	4 (26.7)	2 (12.5)	6 (19.4)	8 (17.8)
Moderately Severe	5 (35.7)	8 (53.3)	7 (43.8)	15 (48.4)	20 (44.4)
Severe	6 (42.9)	2 (13.3)	5 (31.3)	7 (22.6)	13 (28.9)
Very Severe	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
PGIT - n (%)					
Extremely Dissatisfied	1 (7.1)	0	0	0	1 (2.2)
Very Dissatisfied	5 (35.7)	1 (6.7)	5 (31.3)	6 (19.4)	11 (24.4)
Somewhat Dissatisfied	2 (14.3)	4 (26.7)	2 (12.5)	6 (19.4)	8 (17.8)
Neither Dissatisfied nor Satisfied	4 (28.6)	6 (40.0)	6 (37.5)	12 (38.7)	16 (35.6)
Somewhat Satisfied	2 (14.3)	1 (6.7)	2 (12.5)	3 (9.7)	5 (11.1)
Very Satisfied	0	3 (20.0)	1 (6.3)	4 (12.9)	4 (8.9)
Extremely Satisfied	0	0	0	0	0

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
ADerm-SS Skin Pain					
n	14	15	16	31	45
Mean (SD)	6.963 (1.8596)	5.370 (2.0346)	5.621 (2.4183)	5.499 (2.2073)	5.955 (2.1940)
Median	7.267	5.143	5.393	5.286	5.714
Min, Max	2.00, 9.71	0.00, 8.00	0.00, 10.00	0.00, 10.00	0.00, 10.00
ADerm-SS TSS-7					
n	14	15	16	31	45
Mean (SD)	46.4 (10.26)	39.2 (13.35)	39.4 (15.22)	39.3 (14.11)	41.5 (13.33)
Median	47.5	39.0	41.0	41.0	41.0
Min, Max	32, 64	12, 62	11, 70	11, 70	11, 70
ADerm-SS TSS-11					
n	14	15	16	31	45
Mean (SD)	71.5 (17.32)	58.9 (22.07)	59.3 (25.68)	59.1 (23.60)	63.0 (22.41)
Median	67.0	58.0	61.5	61.0	62.0
Min, Max	45, 103	12, 98	12, 108	12, 108	12, 108
ADerm-IS Sleep Domain Score					
n	14	15	16	31	45
Mean (SD)	19.453 (6.1463)	15.568 (7.2852)	16.304 (8.1579)	15.948 (7.6278)	17.038 (7.3161)
Median	21.000	13.429	16.857	15.667	19.000
Min, Max	5.71, 24.86	0.00, 27.00	0.00, 29.43	0.00, 29.43	0.00, 29.43

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
ADerm-IS Daily Activities Domain Score					
n	14	15	16	31	45
Mean (SD)	27.3 (7.95)	20.7 (9.71)	22.6 (11.59)	21.7 (10.59)	23.4 (10.10)
Median	29.5	23.0	24.0	24.0	25.0
Min, Max	9, 35	0, 32	1, 40	0, 40	0, 40
ADerm-IS Emotional State Domain Score					
n	14	15	16	31	45
Mean (SD)	22.6 (7.68)	14.7 (9.39)	18.8 (9.63)	16.8 (9.59)	18.6 (9.36)
Median	26.5	14.0	19.5	19.0	21.0
Min, Max	7, 29	0, 29	0, 30	0, 30	0, 30
POEM					
n	14	15	16	31	45
Mean (SD)	19.8 (5.29)	18.6 (4.64)	18.8 (5.67)	18.7 (5.11)	19.0 (5.14)
Median	19.5	20.0	20.0	20.0	20.0
Min, Max	11, 28	10, 25	8, 28	8, 28	8, 28
Disease Duration since Diagnosis (years)					
n	14	15	16	31	45
Mean (SD)	21.870 (13.4243)	25.188 (17.6266)	20.356 (10.8069)	22.694 (14.4711)	22.438 (14.0063)
Median	24.995	20.047	17.962	18.097	20.047
Min, Max	0.04, 44.81	3.75, 50.20	3.33, 44.29	3.33, 50.20	0.04, 50.20

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
Disease Duration since Symptoms Started (years)					
n	14	15	16	31	45
Mean (SD)	30.248 (11.4091)	30.410 (16.2001)	23.053 (9.7770)	26.613 (13.5734)	27.744 (12.9217)
Median	30.038	27.885	23.604	25.864	27.121
Min, Max	5.37, 44.81	6.36, 50.20	7.15, 44.29	6.36, 50.20	5.37, 50.20
Duration between Symptoms and Diagnosis (years)					
n	14	15	16	31	45
Mean (SD)	8.378 (15.2635)	5.222 (11.3201)	2.697 (6.8012)	3.919 (9.1964)	5.306 (11.4393)
Median	0.000	0.000	0.000	0.000	0.000
Min, Max	0.00, 43.75	0.00, 38.56	0.00, 23.00	0.00, 38.56	0.00, 43.75

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

相互参照：M16-045 試験 W16 Japan Study Data Table 14.1__5.1_J

表 2.7.3.6-73.　疾患歴（ITT_M 集団，日本人部分集団）：M16-045 試験

MedDRA 22.1 System Organ Class Preferred Term	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
Blood and lymphatic system disorders	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Anaemia	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Eye disorders	4 (28.6)	5 (33.3)	2 (12.5)	7 (22.6)	11 (24.4)
Cataract	1 (7.1)	2 (13.3)	1 (6.3)	3 (9.7)	4 (8.9)
Conjunctivitis allergic	3 (21.4)	3 (20.0)	1 (6.3)	4 (12.9)	7 (15.6)
Dry eye	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Macular fibrosis	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Retinal detachment	0	1 (6.7)	1 (6.3)	2 (6.5)	2 (4.4)
Uveitis	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Vernal keratoconjunctivitis	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Gastrointestinal disorders	2 (14.3)	0	0	0	2 (4.4)
Constipation	1 (7.1)	0	0	0	1 (2.2)
Gastrooesophageal reflux disease	1 (7.1)	0	0	0	1 (2.2)
General disorders and administration site conditions	1 (7.1)	0	1 (6.3)	1 (3.2)	2 (4.4)
Developmental delay	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Nodule	1 (7.1)	0	0	0	1 (2.2)
Hepatobiliary disorders	1 (7.1)	1 (6.7)	1 (6.3)	2 (6.5)	3 (6.7)
Hepatic steatosis	1 (7.1)	1 (6.7)	1 (6.3)	2 (6.5)	3 (6.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
Immune system disorders	6 (42.9)	7 (46.7)	9 (56.3)	16 (51.6)	22 (48.9)
Food allergy	6 (42.9)	5 (33.3)	8 (50.0)	13 (41.9)	19 (42.2)
Seasonal allergy	0	2 (13.3)	1 (6.3)	3 (9.7)	3 (6.7)
Infections and infestations	4 (28.6)	2 (13.3)	5 (31.3)	7 (22.6)	11 (24.4)
Cellulitis	1 (7.1)	0	1 (6.3)	1 (3.2)	2 (4.4)
Dermatitis infected	1 (7.1)	0	0	0	1 (2.2)
Folliculitis	1 (7.1)	0	1 (6.3)	1 (3.2)	2 (4.4)
Herpes simplex	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Herpes zoster	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
Impetigo	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Influenza	1 (7.1)	0	0	0	1 (2.2)
Oral herpes	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Pharyngitis	1 (7.1)	0	0	0	1 (2.2)
Tinea infection	1 (7.1)	0	0	0	1 (2.2)
Tonsillitis	1 (7.1)	0	0	0	1 (2.2)
Upper respiratory tract infection	1 (7.1)	0	0	0	1 (2.2)
Varicella	0	0	2 (12.5)	2 (6.5)	2 (4.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
Metabolism and nutrition disorders	2 (14.3)	0	0	0	2 (4.4)
Dyslipidaemia	1 (7.1)	0	0	0	1 (2.2)
Hyperuricaemia	1 (7.1)	0	0	0	1 (2.2)
Musculoskeletal and connective tissue disorders	1 (7.1)	0	0	0	1 (2.2)
Myofascial pain syndrome	1 (7.1)	0	0	0	1 (2.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (7.1)	2 (13.3)	1 (6.3)	3 (9.7)	4 (8.9)
Melanocytic naevus	1 (7.1)	0	0	0	1 (2.2)
Neoplasm	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Skin papilloma	0	1 (6.7)	1 (6.3)	2 (6.5)	2 (4.4)
Nervous system disorders	1 (7.1)	1 (6.7)	1 (6.3)	2 (6.5)	3 (6.7)
Headache	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Migraine	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
Psychiatric disorders	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
Adjustment disorder	0	0	1 (6.3)	1 (3.2)	1 (2.2)
Depression	1 (7.1)	0	0	0	1 (2.2)
Insomnia	0	1 (6.7)	1 (6.3)	2 (6.5)	2 (4.4)
Reproductive system and breast disorders	1 (7.1)	0	0	0	1 (2.2)
Dysmenorrhoea	1 (7.1)	0	0	0	1 (2.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
Respiratory, thoracic and mediastinal disorders	11 (78.6)	11 (73.3)	12 (75.0)	23 (74.2)	34 (75.6)
Asthma	5 (35.7)	7 (46.7)	5 (31.3)	12 (38.7)	17 (37.8)
Pneumothorax	1 (7.1)	0	0	0	1 (2.2)
Rhinitis allergic	10 (71.4)	8 (53.3)	9 (56.3)	17 (54.8)	27 (60.0)
Skin and subcutaneous tissue disorders	4 (28.6)	4 (26.7)	1 (6.3)	5 (16.1)	9 (20.0)
Acne	2 (14.3)	1 (6.7)	1 (6.3)	2 (6.5)	4 (8.9)
Dyshidrotic eczema	1 (7.1)	0	0	0	1 (2.2)
Hyperkeratosis	1 (7.1)	0	0	0	1 (2.2)
Ingrowing nail	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Milia	1 (7.1)	0	0	0	1 (2.2)
Photosensitivity reaction	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Pigmentation disorder	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Skin erosion	1 (7.1)	0	0	0	1 (2.2)
Social circumstances	5 (35.7)	5 (33.3)	3 (18.8)	8 (25.8)	13 (28.9)
Menopause	1 (7.1)	0	0	0	1 (2.2)
Non-consummation	4 (28.6)	5 (33.3)	3 (18.8)	8 (25.8)	12 (26.7)
Vascular disorders	0	2 (13.3)	0	2 (6.5)	2 (4.4)
Hypertension	0	2 (13.3)	0	2 (6.5)	2 (4.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-045 試験 W16 Japan Study Data Table 14.1　6_J

表 2.7.3.6-74.　　前治療歴（ITT_M 集団，日本人部分集団）：M16-045 試験

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
Any Prior Medications	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
ALCLOMETASONE	1 (7.1)	2 (13.3)	1 (6.3)	3 (9.7)	4 (8.9)
ALL OTHER NON-THERAPEUTIC PRODUCTS	2 (14.3)	2 (13.3)	1 (6.3)	3 (9.7)	5 (11.1)
AMCINONIDE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
AMITRIPTYLINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
AMLODIPINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
ANGELICA ACUTILOBA ROOT W/ATRACTYLO	1 (7.1)	0	0	0	1 (2.2)
ANTIVIRALS FOR SYSTEMIC USE	1 (7.1)	0	0	0	1 (2.2)
AZELASTINE	1 (7.1)	0	0	0	1 (2.2)
BENZACLIN TOPICAL	1 (7.1)	0	0	0	1 (2.2)
BEPOTASTINE	4 (28.6)	3 (20.0)	4 (25.0)	7 (22.6)	11 (24.4)
BETAMETHASONE	9 (64.3)	10 (66.7)	13 (81.3)	23 (74.2)	32 (71.1)
BETNESOL-N	0	1 (6.7)	0	1 (3.2)	1 (2.2)
BILASTINE	2 (14.3)	3 (20.0)	2 (12.5)	5 (16.1)	7 (15.6)
BIOTIN	0	0	1 (6.3)	1 (3.2)	1 (2.2)
BREO ELLIPTA	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
BROTIZOLAM	0	0	1 (6.3)	1 (3.2)	1 (2.2)
CAMPHOR	1 (7.1)	0	0	0	1 (2.2)
CEFAZOLIN	1 (7.1)	0	0	0	1 (2.2)
CEFDITOREN	1 (7.1)	0	0	0	1 (2.2)
CELESTAMINE	0	2 (13.3)	1 (6.3)	3 (9.7)	3 (6.7)
CETIRIZINE	0	2 (13.3)	1 (6.3)	3 (9.7)	3 (6.7)
CICLOSPORIN	6 (42.9)	5 (33.3)	8 (50.0)	13 (41.9)	19 (42.2)
CINAL	0	1 (6.7)	0	1 (3.2)	1 (2.2)
CLEMASTINE	1 (7.1)	0	0	0	1 (2.2)
CLOBETASOL	3 (21.4)	5 (33.3)	6 (37.5)	11 (35.5)	14 (31.1)
CLOBETASONE	2 (14.3)	3 (20.0)	2 (12.5)	5 (16.1)	7 (15.6)
CORDRAN-N	1 (7.1)	0	0	0	1 (2.2)
DEPRODONE	1 (7.1)	0	2 (12.5)	2 (6.5)	3 (6.7)
DESLORATADINE	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
DEXAMETHASONE	9 (64.3)	4 (26.7)	3 (18.8)	7 (22.6)	16 (35.6)
DEXCHLORPHENIRAMINE	0	2 (13.3)	0	2 (6.5)	2 (4.4)
DIFLORASONE	2 (14.3)	3 (20.0)	2 (12.5)	5 (16.1)	7 (15.6)
DIFLUCORTOLONE	1 (7.1)	4 (26.7)	2 (12.5)	6 (19.4)	7 (15.6)
DIFLUPREDNATE	2 (14.3)	3 (20.0)	4 (25.0)	7 (22.6)	9 (20.0)
DIPHENHYDRAMINE	1 (7.1)	0	0	0	1 (2.2)
DULOXETINE	0	0	1 (6.3)	1 (3.2)	1 (2.2)
EBASTINE	0	1 (6.7)	1 (6.3)	2 (6.5)	2 (4.4)
EPINASTINE	2 (14.3)	3 (20.0)	1 (6.3)	4 (12.9)	6 (13.3)
FEXOFENADINE	6 (42.9)	5 (33.3)	4 (25.0)	9 (29.0)	15 (33.3)
FLAVINE ADENINE DINUCLEOTIDE	1 (7.1)	0	0	0	1 (2.2)
FLUDROXYCORTIDE	1 (7.1)	2 (13.3)	1 (6.3)	3 (9.7)	4 (8.9)
FLUMETASONE	0	1 (6.7)	1 (6.3)	2 (6.5)	2 (4.4)
FLUNITRAZEPAM	0	1 (6.7)	0	1 (3.2)	1 (2.2)
FLUOCINONIDE	1 (7.1)	0	0	0	1 (2.2)
FLUTICASONE	2 (14.3)	1 (6.7)	0	1 (3.2)	3 (6.7)
GENTAMICIN	0	1 (6.7)	0	1 (3.2)	1 (2.2)
GLICLAZIDE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
GUAIAZULENE	1 (7.1)	1 (6.7)	1 (6.3)	2 (6.5)	3 (6.7)
HEPARINOID	8 (57.1)	10 (66.7)	12 (75.0)	22 (71.0)	30 (66.7)
HERBAL	0	0	1 (6.3)	1 (3.2)	1 (2.2)
HISTADESTAL	0	0	1 (6.3)	1 (3.2)	1 (2.2)
HOCHUEKKITO	0	0	1 (6.3)	1 (3.2)	1 (2.2)
HOMOCHLORCYCLIZINE	1 (7.1)	0	1 (6.3)	1 (3.2)	2 (4.4)
HYALURONIC ACID	0	0	1 (6.3)	1 (3.2)	1 (2.2)
HYDROCORTISONE	4 (28.6)	5 (33.3)	6 (37.5)	11 (35.5)	15 (33.3)
HYDROXYZINE	0	3 (20.0)	0	3 (9.7)	3 (6.7)
IMIDAPRIL	0	1 (6.7)	0	1 (3.2)	1 (2.2)
IMMUNOTHERAPY	0	0	1 (6.3)	1 (3.2)	1 (2.2)
INFLUENZA VACCINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
IRON	0	1 (6.7)	0	1 (3.2)	1 (2.2)
JUMIHAIDOKUTO	0	0	1 (6.3)	1 (3.2)	1 (2.2)
LEVOCETIRIZINE	5 (35.7)	5 (33.3)	3 (18.8)	8 (25.8)	13 (28.9)
LEVOFLOXACIN	1 (7.1)	0	0	0	1 (2.2)
LOMERIZINE	1 (7.1)	0	0	0	1 (2.2)
LORATADINE	3 (21.4)	1 (6.7)	1 (6.3)	2 (6.5)	5 (11.1)
LORAZEPAM	0	0	1 (6.3)	1 (3.2)	1 (2.2)
LOXOPROFEN	1 (7.1)	0	1 (6.3)	1 (3.2)	2 (4.4)
LULICONAZOLE	1 (7.1)	0	0	0	1 (2.2)
MENTHA ARVENSIS	1 (7.1)	0	0	0	1 (2.2)
MENTHOL	1 (7.1)	0	0	0	1 (2.2)
MEQUITAZINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
MOMETASONE	1 (7.1)	2 (13.3)	1 (6.3)	3 (9.7)	4 (8.9)
MONTELUKAST	1 (7.1)	0	0	0	1 (2.2)
NARATRIPTAN	0	1 (6.7)	0	1 (3.2)	1 (2.2)
NEO-MEDROL EYE-EAR	1 (7.1)	0	0	0	1 (2.2)
NIZATIDINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
OLOPATADINE	4 (28.6)	6 (40.0)	7 (43.8)	13 (41.9)	17 (37.8)
ORENGEDOKUTO	0	0	1 (6.3)	1 (3.2)	1 (2.2)
PARACETAMOL	1 (7.1)	0	0	0	1 (2.2)
POLYPODIUM LEUCATOMOS	0	1 (6.7)	0	1 (3.2)	1 (2.2)
PRANLUKAST	1 (7.1)	0	2 (12.5)	2 (6.5)	3 (6.7)
PREDNISOLONE	4 (28.6)	6 (40.0)	6 (37.5)	12 (38.7)	16 (35.6)
PROCATEROL	1 (7.1)	0	0	0	1 (2.2)
PYRIDOXAL	1 (7.1)	0	0	0	1 (2.2)
RABBIT VACCINIA EXTRACT	0	0	1 (6.3)	1 (3.2)	1 (2.2)
REBAMIPIDE	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
RETINOL	0	1 (6.7)	0	1 (3.2)	1 (2.2)
RUPATADINE	3 (21.4)	0	3 (18.8)	3 (9.7)	6 (13.3)
SALBUTAMOL	0	1 (6.7)	0	1 (3.2)	1 (2.2)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
SALICYLIC ACID	0	1 (6.7)	0	1 (3.2)	1 (2.2)
STELAMIN	0	1 (6.7)	2 (12.5)	3 (9.7)	3 (6.7)
SULPIRIDE	0	0	1 (6.3)	1 (3.2)	1 (2.2)
SUPLATAST TOSILATE	1 (7.1)	1 (6.7)	1 (6.3)	2 (6.5)	3 (6.7)
TACROLIMUS	8 (57.1)	8 (53.3)	12 (75.0)	20 (64.5)	28 (62.2)
TERRA-CORTRIL	0	0	1 (6.3)	1 (3.2)	1 (2.2)
TETRACYCLINE	1 (7.1)	0	0	0	1 (2.2)
THEOPHYLLINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
TOCOPHEROL	0	2 (13.3)	0	2 (6.5)	2 (4.4)
TRALOKINUMAB	0	0	1 (6.3)	1 (3.2)	1 (2.2)
TRIAMCINOLONE	1 (7.1)	2 (13.3)	2 (12.5)	4 (12.9)	5 (11.1)
ULOBETASOL	0	1 (6.7)	0	1 (3.2)	1 (2.2)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	0	0	2 (12.5)	2 (6.5)	2 (4.4)
UREA	1 (7.1)	0	0	0	1 (2.2)
VALISONE-G	0	2 (13.3)	2 (12.5)	4 (12.9)	4 (8.9)
VALPROIC ACID	0	1 (6.7)	0	1 (3.2)	1 (2.2)
WHITE SOFT PARAFFIN	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
ZINC	2 (14.3)	3 (20.0)	1 (6.3)	4 (12.9)	6 (13.3)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

相互参照：M16-045 試験 W16 Japan Study Data Table 14.1　7.1_J

表 2.7.3.6-75.　　併用薬（二重盲検投与期）（ITT_M 集団，日本人部分集団）：M16-045 試験

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
Any Concomitant Medications	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
ACETYLSALICYLIC ACID	1 (7.1)	0	0	0	1 (2.2)
ALBUMIN TANNATE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
ALCLOMETASONE	2 (14.3)	0	0	0	2 (4.4)
ALL OTHER NON-THERAPEUTIC PRODUCTS	0	1 (6.7)	0	1 (3.2)	1 (2.2)
AMITRIPTYLINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
AMLODIPINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
AMOXICILLIN	0	1 (6.7)	0	1 (3.2)	1 (2.2)
ANGELICA ACUTILOBA ROOT W/ATRACTYLO	1 (7.1)	0	0	0	1 (2.2)
ANTIVIRALS FOR SYSTEMIC USE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
BENZACLIN TOPICAL	1 (7.1)	0	1 (6.3)	1 (3.2)	2 (4.4)
BEPOTASTINE	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
BETAMETHASONE	5 (35.7)	1 (6.7)	1 (6.3)	2 (6.5)	7 (15.6)
BILASTINE	0	3 (20.0)	3 (18.8)	6 (19.4)	6 (13.3)
BREO ELLIPTA	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
BROTIZOLAM	0	0	1 (6.3)	1 (3.2)	1 (2.2)
BUDESONIDE W/FORMOTEROL FUMARATE	1 (7.1)	0	0	0	1 (2.2)
CARBOCISTEINE	1 (7.1)	0	3 (18.8)	3 (9.7)	4 (8.9)
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	0	0	1 (6.3)	1 (3.2)	1 (2.2)
CEFAZOLIN	0	0	1 (6.3)	1 (3.2)	1 (2.2)
CEFCAPENE	1 (7.1)	1 (6.7)	1 (6.3)	2 (6.5)	3 (6.7)
CEFDITOREN	0	0	1 (6.3)	1 (3.2)	1 (2.2)
CEFPODOXIME	1 (7.1)	0	0	0	1 (2.2)
CETIRIZINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
CHLORHEXIDINE	1 (7.1)	0	0	0	1 (2.2)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
CINAL	0	1 (6.7)	0	1 (3.2)	1 (2.2)
CLINDAMYCIN	0	0	2 (12.5)	2 (6.5)	2 (4.4)
CLOBETASONE	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
CODEINE	0	0	1 (6.3)	1 (3.2)	1 (2.2)
CONTAC	0	1 (6.7)	0	1 (3.2)	1 (2.2)
DEPRODONE	1 (7.1)	0	0	0	1 (2.2)
DEXAMETHASONE	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
DEXCHLORPHENIRAMINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
DEXTROMETHORPHAN	1 (7.1)	0	2 (12.5)	2 (6.5)	3 (6.7)
DICLOFENAC	0	1 (6.7)	0	1 (3.2)	1 (2.2)
DIFLORASONE	2 (14.3)	0	0	0	2 (4.4)
DIFLUCORTOLONE	1 (7.1)	0	0	0	1 (2.2)
DIFLUPREDNATE	0	2 (13.3)	1 (6.3)	3 (9.7)	3 (6.7)
DOMPERIDONE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
DULOXETINE	0	0	1 (6.3)	1 (3.2)	1 (2.2)
DUPILUMAB	1 (7.1)	0	0	0	1 (2.2)
ENCEPHALITIS VACCINES	0	0	1 (6.3)	1 (3.2)	1 (2.2)
EPINASTINE	1 (7.1)	3 (20.0)	0	3 (9.7)	4 (8.9)
FAMCICLOVIR	1 (7.1)	2 (13.3)	1 (6.3)	3 (9.7)	4 (8.9)
FEXOFENADINE	6 (42.9)	3 (20.0)	2 (12.5)	5 (16.1)	11 (24.4)
FLAVINE ADENINE DINUCLEOTIDE	1 (7.1)	0	0	0	1 (2.2)
FLUNITRAZEPAM	0	1 (6.7)	0	1 (3.2)	1 (2.2)
FLUOCINONIDE	1 (7.1)	0	0	0	1 (2.2)
FLUOROMETHOLONE	1 (7.1)	0	0	0	1 (2.2)
FLUTICASONE	2 (14.3)	0	0	0	2 (4.4)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
GARENOXACIN	0	1 (6.7)	0	1 (3.2)	1 (2.2)
GENTAMICIN	0	2 (13.3)	1 (6.3)	3 (9.7)	3 (6.7)
GUAIAZULENE	0	2 (13.3)	0	2 (6.5)	2 (4.4)
HEPARINOID	8 (57.1)	4 (26.7)	7 (43.8)	11 (35.5)	19 (42.2)
HYALURONIC ACID	0	0	1 (6.3)	1 (3.2)	1 (2.2)
HYDROCORTISONE	0	0	1 (6.3)	1 (3.2)	1 (2.2)
HYDROTALCITE	1 (7.1)	0	0	0	1 (2.2)
HYDROXYZINE	0	2 (13.3)	0	2 (6.5)	2 (4.4)
IBUPROFEN	1 (7.1)	0	0	0	1 (2.2)
IMIDAPRIL	0	1 (6.7)	0	1 (3.2)	1 (2.2)
IRON	0	1 (6.7)	0	1 (3.2)	1 (2.2)
LACTOMIN	0	0	1 (6.3)	1 (3.2)	1 (2.2)
LANINAMIVIR	0	1 (6.7)	0	1 (3.2)	1 (2.2)
LEVOCETIRIZINE	3 (21.4)	1 (6.7)	1 (6.3)	2 (6.5)	5 (11.1)
LEVOFLOXACIN	1 (7.1)	0	0	0	1 (2.2)
LIDOCAINE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
LOMERIZINE	1 (7.1)	0	0	0	1 (2.2)
LORATADINE	1 (7.1)	0	0	0	1 (2.2)
LORAZEPAM	0	0	1 (6.3)	1 (3.2)	1 (2.2)
LOXOPROFEN	0	1 (6.7)	1 (6.3)	2 (6.5)	2 (4.4)
LULICONAZOLE	1 (7.1)	0	0	0	1 (2.2)
MECOBALAMIN	0	1 (6.7)	0	1 (3.2)	1 (2.2)
MEFENAMIC ACID	0	1 (6.7)	0	1 (3.2)	1 (2.2)
METOCLOPRAMIDE	0	0	1 (6.3)	1 (3.2)	1 (2.2)
MONTELUKAST	2 (14.3)	0	0	0	2 (4.4)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
NADIFLOXACIN	1 (7.1)	1 (6.7)	3 (18.8)	4 (12.9)	5 (11.1)
NARATRIPTAN	0	1 (6.7)	0	1 (3.2)	1 (2.2)
NEO-MEDROL EYE-EAR	1 (7.1)	0	0	0	1 (2.2)
NUTRIENTS NOS	0	0	1 (6.3)	1 (3.2)	1 (2.2)
OLOPATADINE	2 (14.3)	4 (26.7)	7 (43.8)	11 (35.5)	13 (28.9)
OSELTAMIVIR	0	0	1 (6.3)	1 (3.2)	1 (2.2)
PA	0	0	2 (12.5)	2 (6.5)	2 (4.4)
PABRON S	0	0	1 (6.3)	1 (3.2)	1 (2.2)
PAMIN	0	0	1 (6.3)	1 (3.2)	1 (2.2)
PARACETAMOL	2 (14.3)	5 (33.3)	2 (12.5)	7 (22.6)	9 (20.0)
PHENOL	0	1 (6.7)	0	1 (3.2)	1 (2.2)
POLYPODIUM LEUCATOMOS	0	1 (6.7)	0	1 (3.2)	1 (2.2)
PRANLUKAST	1 (7.1)	0	2 (12.5)	2 (6.5)	3 (6.7)
PREDNISOLONE	3 (21.4)	2 (13.3)	0	2 (6.5)	5 (11.1)
PROCATEROL	1 (7.1)	0	0	0	1 (2.2)
PYRIDOXAL	1 (7.1)	0	0	0	1 (2.2)
REBAMIPIDE	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
RUPATADINE	1 (7.1)	0	1 (6.3)	1 (3.2)	2 (4.4)
SALBUTAMOL	0	1 (6.7)	0	1 (3.2)	1 (2.2)
SALICYLIC ACID	1 (7.1)	0	0	0	1 (2.2)
SULPIRIDE	0	0	1 (6.3)	1 (3.2)	1 (2.2)
TACROLIMUS	2 (14.3)	0	1 (6.3)	1 (3.2)	3 (6.7)
TERRA-CORTRIL	1 (7.1)	0	0	0	1 (2.2)
THEOPHYLLINE	1 (7.1)	1 (6.7)	0	1 (3.2)	2 (4.4)
THIAMAZOLE	0	0	1 (6.3)	1 (3.2)	1 (2.2)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo (N=14) n (%)	Active: UPA 15 mg QD (N=15) n (%)	Active: UPA 30 mg QD (N=16) n (%)	Active: Total (N=31) n (%)	Total (N=45) n (%)
TIARAMIDE	0	1 (6.7)	0	1 (3.2)	1 (2.2)
TRANEXAMIC ACID	0	3 (20.0)	0	3 (9.7)	3 (6.7)
UREA	1 (7.1)	0	0	0	1 (2.2)
VALACICLOVIR	0	1 (6.7)	2 (12.5)	3 (9.7)	3 (6.7)
VALISONE-G	1 (7.1)	0	0	0	1 (2.2)
VALPROIC ACID	0	1 (6.7)	0	1 (3.2)	1 (2.2)
VITAMEDIN	0	0	1 (6.3)	1 (3.2)	1 (2.2)
WHITE SOFT PARAFFIN	14 (100)	15 (100)	15 (93.8)	30 (96.8)	44 (97.8)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

相互参照：M16-045 試験 W16 Japan Study Data Table 14.1　7.2.1_J

表 2.7.3.6-76. 被験者の内訳（二重盲検投与期）（ITT_M 集団，日本人部分集団）：M16-045 試験

Strata Status	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
All					
Randomized	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
Never Received Any Study Drug	0	0	0	0	0
Received Randomized Study Drug	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
Received Rescue Medication	13 (92.9)	2 (13.3)	1 (6.3)	3 (9.7)	16 (35.6)
Completed DB Period	8 (57.1)	15 (100)	15 (93.8)	30 (96.8)	38 (84.4)
Discontinued Study in DB Period	5 (35.7)	0	1 (6.3)	1 (3.2)	6 (13.3)
All Reasons for Discontinuation$					
Adverse Event	1 (7.1)	0	0	0	1 (2.2)
Withdrawal Consent	5 (35.7)	0	1 (6.3)	1 (3.2)	6 (13.3)
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	1 (7.1)	0	0	0	1 (2.2)
Withdrawal Consent	4 (28.6)	0	1 (6.3)	1 (3.2)	5 (11.1)
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
All (Cont.)					
Completed Study Drug in DB Period	8 (57.1)	15 (100)	14 (87.5)	29 (93.5)	37 (82.2)
Ongoing Study Drug in DB Period	0	0	0	0	0
Discontinued Study Drug in DB Period	6 (42.9)	0	2 (12.5)	2 (6.5)	8 (17.8)
All Reasons for Discontinuation$					
Adverse Event	4 (28.6)	0	1 (6.3)	1 (3.2)	5 (11.1)
Withdrawal Consent	4 (28.6)	0	1 (6.3)	1 (3.2)	5 (11.1)
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	2 (14.3)	0	0	0	2 (4.4)
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	1 (7.1)	0	0	0	1 (2.2)
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	2 (14.3)	0	1 (6.3)	1 (3.2)	3 (6.7)
Withdrawal Consent	3 (21.4)	0	1 (6.3)	1 (3.2)	4 (8.9)
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	1 (7.1)	0	0	0	1 (2.2)
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
Age Group: Adolescent					
Randomized	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
Never Received Any Study Drug	0	0	0	0	0
Received Randomized Study Drug	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
Received Rescue Medication	1 (7.1)	0	0	0	1 (2.2)
Completed DB Period	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
Discontinued Study in DB Period	0	0	0	0	0
All Reasons for Discontinuation$					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
Age Group: Adolescent (Cont.)					
Completed Study Drug in DB Period	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
Ongoing Study Drug in DB Period	0	0	0	0	0
Discontinued Study Drug in DB Period	0	0	0	0	0
All Reasons for Discontinuation$					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
Age Group: Adult					
Randomized	13 (92.9)	14 (93.3)	14 (87.5)	28 (90.3)	41 (91.1)
Never Received Any Study Drug	0	0	0	0	0
Received Randomized Study Drug	13 (92.9)	14 (93.3)	14 (87.5)	28 (90.3)	41 (91.1)
Received Rescue Medication	12 (85.7)	2 (13.3)	1 (6.3)	3 (9.7)	15 (33.3)
Completed DB Period	7 (50.0)	14 (93.3)	13 (81.3)	27 (87.1)	34 (75.6)
Discontinued Study in DB Period	5 (35.7)	0	1 (6.3)	1 (3.2)	6 (13.3)
All Reasons for Discontinuation$					
Adverse Event	1 (7.1)	0	0	0	1 (2.2)
Withdrawal Consent	5 (35.7)	0	1 (6.3)	1 (3.2)	6 (13.3)
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	1 (7.1)	0	0	0	1 (2.2)
Withdrawal Consent	4 (28.6)	0	1 (6.3)	1 (3.2)	5 (11.1)
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo (N=14) n (%)	Active UPA 15 mg QD (N=15) n (%)	Active UPA 30 mg QD (N=16) n (%)	Active Total (N=31) n (%)	Total (N=45) n (%)
Age Group: Adult (Cont.)					
Completed Study Drug in DB Period	7 (50.0)	14 (93.3)	12 (75.0)	26 (83.9)	33 (73.3)
Ongoing Study Drug in DB Period	0	0	0	0	0
Discontinued Study Drug in DB Period	6 (42.9)	0	2 (12.5)	2 (6.5)	8 (17.8)
All Reasons for Discontinuation$					
Adverse Event	4 (28.6)	0	1 (6.3)	1 (3.2)	5 (11.1)
Withdrawal Consent	4 (28.6)	0	1 (6.3)	1 (3.2)	5 (11.1)
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	2 (14.3)	0	0	0	2 (4.4)
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	1 (7.1)	0	0	0	1 (2.2)
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	2 (14.3)	0	1 (6.3)	1 (3.2)	3 (6.7)
Withdrawal Consent	3 (21.4)	0	1 (6.3)	1 (3.2)	4 (8.9)
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	1 (7.1)	0	0	0	1 (2.2)
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

相互参照：M16-045 試験 W16 Japan Study Data Table 14.1　3.1.1_J

表 2.7.3.6-77.　人口統計学的特性の要約（ITT_M 集団，日本人部分集団）：M16-045 試験（投与 52 週時データカットオフ）

	Placebo (N=14)	Active UPA 15 mg QD (N=15)	Active UPA 30 mg QD (N=16)	Active Total (N=31)	Total (N=45)
Sex - n (%)					
Male	8 (57.1)	10 (66.7)	13 (81.3)	23 (74.2)	31 (68.9)
Female	6 (42.9)	5 (33.3)	3 (18.8)	8 (25.8)	14 (31.1)
Ethnicity - n (%)					
Hispanic or Latino	0	0	0	0	0
Not Hispanic or Latino	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
Race - n (%)					
White	0	0	0	0	0
Black or African American	0	0	0	0	0
Asian	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
American Indian/Alaska Native	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Other	0	0	0	0	0
Multiple	0	0	0	0	0
Age Group 1 (years) - n (%)					
< 18	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
>= 18	13 (92.9)	14 (93.3)	14 (87.5)	28 (90.3)	41 (91.1)

Note: Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
Age Group 2 (years) - n (%)					
< 18	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
18 - < 40	6 (42.9)	5 (33.3)	10 (62.5)	15 (48.4)	21 (46.7)
40 - < 65	7 (50.0)	8 (53.3)	4 (25.0)	12 (38.7)	19 (42.2)
>= 65	0	1 (6.7)	0	1 (3.2)	1 (2.2)
Age (years)					
n	14	15	16	31	45
Mean (SD)	36.8 (10.77)	39.9 (14.17)	33.5 (11.78)	36.6 (13.18)	36.7 (12.36)
Median	38.0	42.0	32.5	34.0	34.0
Min, Max	18, 55	17, 68	18, 64	17, 68	17, 68
Weight (kg)					
n	14	15	16	31	45
Mean (SD)	63.86 (10.904)	62.89 (7.589)	63.73 (14.623)	63.32 (11.575)	63.49 (11.249)
Median	63.80	65.00	58.35	60.40	63.20
Min, Max	45.6, 82.8	49.4, 74.2	46.5, 93.6	46.5, 93.6	45.6, 93.6
Height (cm)					
n	14	15	16	31	45
Mean (SD)	162.89 (9.706)	164.52 (8.054)	168.49 (8.036)	166.57 (8.163)	165.42 (8.732)
Median	164.00	162.00	168.20	166.60	164.00
Min, Max	147.0, 179.8	151.6, 181.5	156.5, 181.0	151.6, 181.5	147.0, 181.5
BMI (kg/m^2)					
n	14	15	16	31	45
Mean (SD)	23.99 (2.938)	23.21 (2.066)	22.27 (3.785)	22.73 (3.063)	23.12 (3.050)
Median	25.30	23.30	21.20	22.50	22.90
Min, Max	19.6, 28.0	19.7, 26.1	16.7, 28.6	16.7, 28.6	16.7, 28.6

Note: Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
BMI (kg/m^2) - n (%)					
< 25	6 (42.9)	10 (66.7)	11 (68.8)	21 (67.7)	27 (60.0)
25 - < 30	8 (57.1)	5 (33.3)	5 (31.3)	10 (32.3)	18 (40.0)
>= 30	0	0	0	0	0
Geographic Region - n (%)					
US/Puerto Rico/Canada	0	0	0	0	0
Japan	14 (100)	15 (100)	16 (100)	31 (100)	45 (100)
China	0	0	0	0	0
Other	0	0	0	0	0
Tobacco$ - n (%)					
Current	3 (21.4)	3 (20.0)	5 (31.3)	8 (25.8)	11 (24.4)
Former	3 (21.4)	3 (20.0)	0	3 (9.7)	6 (13.3)
Never	8 (57.1)	9 (60.0)	11 (68.8)	20 (64.5)	28 (62.2)
Unknown	0	0	0	0	0
Alcohol$ - n (%)					
Current	10 (71.4)	10 (66.7)	8 (50.0)	18 (58.1)	28 (62.2)
Former	3 (21.4)	1 (6.7)	0	1 (3.2)	4 (8.9)
Never	1 (7.1)	4 (26.7)	8 (50.0)	12 (38.7)	13 (28.9)
Unknown	0	0	0	0	0

Note: Percentages calculated on non-missing values.
$ Percentages calculated on non-missing/non-unknown values. A subject may be a current user of one type of tobacco, a former user of another type of tobacco and never used another type of tobacco. A subject will be counted in the category closest to user.

Program Source Code: [redacted]

相互参照：M16-045 試験 W52 Japan Study Data Table 14.1　3.1_J

表 2.7.3.6-78.　ベースラインのその他の基準値の特性の要約（ITT_M 集団，日本人部分集団）：M16-045 試験（投与 52 週時データカットオフ）

	Placebo (N=14)	Active UPA 15 mg QD (N=15)	Active UPA 30 mg QD (N=16)	Active Total (N=31)	Total (N=45)
Baseline vIGA-AD - n (%)					
3 (Moderate)	8 (57.1)	8 (53.3)	9 (56.3)	17 (54.8)	25 (55.6)
4 (Severe)	6 (42.9)	7 (46.7)	7 (43.8)	14 (45.2)	20 (44.4)
Baseline EASI - n (%)					
< Median (25.8)#	6 (42.9)	8 (53.3)	7 (43.8)	15 (48.4)	21 (46.7)
>= Median (25.8)#	8 (57.1)	7 (46.7)	9 (56.3)	16 (51.6)	24 (53.3)
hsCRP - n (%)					
< Median (1.4)#	8 (57.1)	11 (73.3)	10 (62.5)	21 (67.7)	29 (64.4)
>= Median (1.4)#	6 (42.9)	4 (26.7)	6 (37.5)	10 (32.3)	16 (35.6)
Previous Systemic Therapy - n (%)					
With	9 (64.3)	7 (46.7)	9 (56.3)	16 (51.6)	25 (55.6)
Without	5 (35.7)	8 (53.3)	7 (43.8)	15 (48.4)	20 (44.4)
EASI					
n	14	15	16	31	45
Mean (SD)	30.89 (14.628)	29.63 (11.132)	30.25 (9.206)	29.95 (10.015)	30.24 (11.481)
Median	27.45	25.40	29.05	28.50	27.70
Min, Max	16.2, 70.2	16.1, 53.3	18.8, 50.0	16.1, 53.3	16.1, 70.2

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.
The median value is based on all randomized subjects in the main study who have non-missing baseline value.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
EASI Head/Neck					
n	14	15	16	31	45
Mean (SD)	3.47 (1.815)	3.36 (1.108)	3.76 (1.866)	3.57 (1.535)	3.54 (1.606)
Median	3.25	3.50	3.20	3.20	3.20
Min, Max	1.0, 7.2	1.4, 5.0	0.8, 7.2	0.8, 7.2	0.8, 7.2
EASI Lower Limbs					
n	14	15	16	31	45
Mean (SD)	9.74 (7.146)	10.93 (5.849)	10.50 (4.956)	10.71 (5.319)	10.41 (5.881)
Median	8.80	9.60	11.60	10.80	9.60
Min, Max	0.4, 28.8	3.2, 22.0	2.4, 20.0	2.4, 22.0	0.4, 28.8
EASI Trunk					
n	14	15	16	31	45
Mean (SD)	11.61 (5.392)	9.68 (3.943)	10.13 (3.221)	9.91 (3.535)	10.44 (4.212)
Median	12.00	9.60	10.05	9.60	9.60
Min, Max	4.5, 21.6	4.8, 18.0	4.8, 15.0	4.8, 18.0	4.5, 21.6
EASI Upper Limbs					
n	14	15	16	31	45
Mean (SD)	6.06 (3.130)	5.65 (2.228)	5.86 (2.932)	5.76 (2.574)	5.85 (2.726)
Median	5.70	5.40	5.40	5.40	5.40
Min, Max	2.0, 14.4	2.4, 10.0	2.4, 14.4	2.4, 14.4	2.0, 14.4

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
BSA in Percentage					
n	14	15	16	31	45
Mean (SD)	49.7 (24.02)	51.2 (21.06)	54.3 (15.42)	52.8 (18.12)	51.8 (19.91)
Median	52.5	46.0	55.0	50.0	50.0
Min, Max	16, 98	15, 90	25, 83	15, 90	15, 98
Overall SCORAD Score					
n	14	15	16	31	45
Mean (SD)	69.01 (17.617)	63.91 (11.884)	67.46 (14.949)	65.74 (13.450)	66.76 (14.744)
Median	66.45	63.70	67.10	65.30	65.30
Min, Max	41.7, 102.6	39.0, 85.4	42.1, 91.4	39.0, 91.4	39.0, 102.6
Objective SCORAD					
n	14	15	16	31	45
Mean (SD)	53.44 (15.333)	51.44 (12.201)	53.90 (11.917)	52.71 (11.918)	52.94 (12.900)
Median	50.45	50.60	53.50	50.70	50.70
Min, Max	30.7, 82.6	28.0, 73.4	34.1, 72.6	28.0, 73.4	28.0, 82.6
SCORAD Itch					
n	14	15	16	31	45
Mean (SD)	8.7 (0.99)	7.6 (1.64)	7.7 (1.66)	7.6 (1.62)	8.0 (1.53)
Median	8.5	7.0	7.5	7.0	8.0
Min, Max	7, 10	4, 10	6, 10	4, 10	4, 10

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
SCORAD Sleep					
n	14	15	16	31	45
Mean (SD)	6.9 (2.60)	4.9 (2.47)	5.9 (2.90)	5.4 (2.70)	5.8 (2.73)
Median	7.0	5.0	7.0	6.0	7.0
Min, Max	2, 10	1, 9	2, 10	1, 10	1, 10
DLQI					
n	14	15	16	31	45
Mean (SD)	16.5 (4.96)	10.5 (4.88)	15.1 (7.90)	12.8 (6.91)	14.0 (6.54)
Median	16.0	11.0	17.0	13.0	15.0
Min, Max	7, 25	1, 19	2, 25	1, 25	1, 25
HADS Total Score					
n	14	15	16	31	45
Mean (SD)	12.9 (7.77)	7.5 (7.54)	11.8 (8.81)	9.7 (8.37)	10.7 (8.24)
Median	13.0	6.0	9.0	8.0	8.0
Min, Max	3, 23	0, 25	2, 35	0, 35	0, 35
HADS-A Total Score					
n	14	15	16	31	45
Mean (SD)	6.6 (3.92)	3.9 (4.06)	6.6 (4.73)	5.3 (4.55)	5.7 (4.36)
Median	7.0	3.0	5.0	4.0	5.0
Min, Max	1, 13	0, 15	1, 18	0, 18	0, 18

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
HADS-D Total Score					
n	14	15	16	31	45
Mean (SD)	6.4 (4.25)	3.6 (3.89)	5.3 (4.58)	4.5 (4.27)	5.0 (4.31)
Median	6.0	2.0	4.5	3.0	4.0
Min, Max	0, 13	0, 13	0, 17	0, 17	0, 17
WPAI: AD: Absenteeism (%)					
n	5	5	4	9	14
Mean (SD)	15.977 (25.2995)	4.000 (8.9443)	20.833 (41.6667)	11.481 (27.7444)	13.087 (25.9930)
Median	9.091	0.000	0.000	0.000	0.000
Min, Max	0.00, 60.38	0.00, 20.00	0.00, 83.33	0.00, 83.33	0.00, 83.33
WPAI: AD: Presenteeism (%)					
n	5	5	4	9	14
Mean (SD)	76.0 (23.02)	46.0 (35.78)	50.0 (35.59)	47.8 (33.46)	57.9 (32.39)
Median	80.0	60.0	40.0	50.0	60.0
Min, Max	40, 100	0, 90	20, 100	0, 100	0, 100
WPAI: AD: Work Productivity Loss (%)					
n	5	5	4	9	14
Mean (SD)	77.753 (23.9001)	47.600 (36.7260)	50.000 (35.5903)	48.667 (33.9264)	59.055 (33.0643)
Median	80.000	60.000	40.000	50.000	64.000
Min, Max	40.00, 100.00	0.00, 90.00	20.00, 100.00	0.00, 100.00	0.00, 100.00

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
WPAI: AD: Activity Impairment (%)					
n	14	15	16	31	45
Mean (SD)	67.9 (24.55)	59.3 (23.74)	65.6 (25.55)	62.6 (24.49)	64.2 (24.35)
Median	75.0	60.0	70.0	70.0	70.0
Min, Max	0, 90	20, 90	20, 100	20, 100	0, 100
EQ-5D-5L Index					
n	14	15	16	31	45
Mean (SD)	0.608 (0.3595)	0.833 (0.1209)	0.673 (0.2605)	0.750 (0.2175)	0.706 (0.2736)
Median	0.783	0.866	0.750	0.809	0.803
Min, Max	-0.09, 0.94	0.54, 1.00	0.21, 1.00	0.21, 1.00	-0.09, 1.00
EQ-5D-5L VAS Score					
n	14	15	16	31	45
Mean (SD)	48.7 (22.24)	61.7 (20.63)	44.4 (27.89)	52.8 (25.77)	51.5 (24.55)
Median	53.0	65.0	50.0	56.0	56.0
Min, Max	10, 83	30, 96	3, 95	3, 96	3, 96
Worst Pruritus NRS (Daily)					
n	14	15	16	31	45
Mean (SD)	8.3 (1.14)	7.2 (1.70)	7.4 (1.97)	7.3 (1.81)	7.6 (1.68)
Median	8.0	8.0	7.0	7.0	8.0
Min, Max	6, 10	4, 10	5, 10	4, 10	4, 10

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
Worst Pruritus NRS (Weekly Average)					
n	14	15	16	31	45
Mean (SD)	7.856 (0.9274)	6.792 (1.5868)	7.100 (1.7682)	6.951 (1.6621)	7.232 (1.5223)
Median	7.757	7.000	7.286	7.000	7.571
Min, Max	6.00, 9.71	4.00, 9.43	4.71, 10.00	4.00, 10.00	4.00, 10.00
PGIS					
n	14	15	16	31	45
Mean (SD)	4.4 (0.85)	4.0 (0.85)	4.4 (0.89)	4.2 (0.88)	4.3 (0.87)
Median	4.5	4.0	4.0	4.0	4.0
Min, Max	3, 6	3, 6	3, 6	3, 6	3, 6

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
PGIS - n (%)					
Absent	0	0	0	0	0
Minimal	0	0	0	0	0
Mild	0	0	0	0	0
Moderate	2 (14.3)	4 (26.7)	2 (12.5)	6 (19.4)	8 (17.8)
Moderately Severe	5 (35.7)	8 (53.3)	7 (43.8)	15 (48.4)	20 (44.4)
Severe	6 (42.9)	2 (13.3)	5 (31.3)	7 (22.6)	13 (28.9)
Very Severe	1 (7.1)	1 (6.7)	2 (12.5)	3 (9.7)	4 (8.9)
PGIT - n (%)					
Extremely Dissatisfied	1 (7.1)	0	0	0	1 (2.2)
Very Dissatisfied	5 (35.7)	1 (6.7)	5 (31.3)	6 (19.4)	11 (24.4)
Somewhat Dissatisfied	2 (14.3)	4 (26.7)	2 (12.5)	6 (19.4)	8 (17.8)
Neither Dissatisfied nor Satisfied	4 (28.6)	6 (40.0)	6 (37.5)	12 (38.7)	16 (35.6)
Somewhat Satisfied	2 (14.3)	1 (6.7)	2 (12.5)	3 (9.7)	5 (11.1)
Very Satisfied	0	3 (20.0)	1 (6.3)	4 (12.9)	4 (8.9)
Extremely Satisfied	0	0	0	0	0

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
ADerm-SS Skin Pain					
n	14	15	16	31	45
Mean (SD)	6.963 (1.8596)	5.370 (2.0346)	5.621 (2.4183)	5.499 (2.2073)	5.955 (2.1940)
Median	7.267	5.143	5.393	5.286	5.714
Min, Max	2.00, 9.71	0.00, 8.00	0.00, 10.00	0.00, 10.00	0.00, 10.00
ADerm-SS TSS-7					
n	14	15	16	31	45
Mean (SD)	46.4 (10.26)	39.2 (13.35)	39.4 (15.22)	39.3 (14.11)	41.5 (13.33)
Median	47.5	39.0	41.0	41.0	41.0
Min, Max	32, 64	12, 62	11, 70	11, 70	11, 70
ADerm-SS TSS-11					
n	14	15	16	31	45
Mean (SD)	71.5 (17.32)	58.9 (22.07)	59.3 (25.68)	59.1 (23.60)	63.0 (22.41)
Median	67.0	58.0	61.5	61.0	62.0
Min, Max	45, 103	12, 98	12, 108	12, 108	12, 108
ADerm-IS Sleep Domain Score					
n	14	15	16	31	45
Mean (SD)	19.453 (6.1463)	15.568 (7.2852)	16.304 (8.1579)	15.948 (7.6278)	17.038 (7.3161)
Median	21.000	13.429	16.857	15.667	19.000
Min, Max	5.71, 24.86	0.00, 27.00	0.00, 29.43	0.00, 29.43	0.00, 29.43

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
ADerm-IS Daily Activities Domain Score					
n	14	15	16	31	45
Mean (SD)	27.3 (7.95)	20.7 (9.71)	22.6 (11.59)	21.7 (10.59)	23.4 (10.10)
Median	29.5	23.0	24.0	24.0	25.0
Min, Max	9, 35	0, 32	1, 40	0, 40	0, 40
ADerm-IS Emotional State Domain Score					
n	14	15	16	31	45
Mean (SD)	22.6 (7.68)	14.7 (9.39)	18.8 (9.63)	16.8 (9.59)	18.6 (9.36)
Median	26.5	14.0	19.5	19.0	21.0
Min, Max	7, 29	0, 29	0, 30	0, 30	0, 30
POEM					
n	14	15	16	31	45
Mean (SD)	19.8 (5.29)	18.6 (4.64)	18.8 (5.67)	18.7 (5.11)	19.0 (5.14)
Median	19.5	20.0	20.0	20.0	20.0
Min, Max	11, 28	10, 25	8, 28	8, 28	8, 28
Disease Duration since Diagnosis (years)					
n	14	15	16	31	45
Mean (SD)	21.870 (13.4243)	25.188 (17.6266)	20.356 (10.8069)	22.694 (14.4711)	22.438 (14.0063)
Median	24.995	20.047	17.962	18.097	20.047
Min, Max	0.04, 44.81	3.75, 50.20	3.33, 44.29	3.33, 50.20	0.04, 50.20

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo (N=14)	Active: UPA 15 mg QD (N=15)	Active: UPA 30 mg QD (N=16)	Active: Total (N=31)	Total (N=45)
Disease Duration since Symptoms Started (years)					
n	14	15	16	31	45
Mean (SD)	30.248 (11.4091)	30.410 (16.2001)	23.053 (9.7770)	26.613 (13.5734)	27.744 (12.9217)
Median	30.038	27.885	23.604	25.864	27.121
Min, Max	5.37, 44.81	6.36, 50.20	7.15, 44.29	6.36, 50.20	5.37, 50.20
Duration between Symptoms and Diagnosis (years)					
n	14	15	16	31	45
Mean (SD)	8.378 (15.2635)	5.222 (11.3201)	2.697 (6.8012)	3.919 (9.1964)	5.306 (11.4393)
Median	0.000	0.000	0.000	0.000	0.000
Min, Max	0.00, 43.75	0.00, 38.56	0.00, 23.00	0.00, 38.56	0.00, 43.75

Note: vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-; anxiety; HADS-D = Hospital Anxiety and Depression Scale-depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.
Percentages calculated on non-missing values.

Program Source Code: [redacted]

相互参照：M16-045 試験 W52 Japan Study Data Table 14.1　4.1 J

表 2.7.3.6-79.　被験者の内訳（盲検継続投与期）（ITT_M 集団，日本人部分集団）：M16-045 試験（投与 52 週時データカットオフ）

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
All					
Entered BE Period	5 (100)	3 (100)	15 (100)	15 (93.8)	38 (97.4)
Never Received Any Study Drug in BE Period	0	0	0	1 (6.3)	1 (2.6)
Received Study Drug in BE Period	5 (100)	3 (100)	15 (100)	14 (87.5)	37 (94.9)
Initiated Rescue Medication in BE Period	0	0	1 (6.7)	1 (6.3)	2 (5.1)
Completed Study	0	0	0	0	0
Discontinued Study in BE Period	1 (20.0)	0	2 (13.3)	2 (12.5)	5 (12.8)
All Reasons for Discontinuation$					
Adverse Event	0	0	1 (6.7)	0	1 (2.6)
Withdrawal Consent	1 (20.0)	0	2 (13.3)	2 (12.5)	5 (12.8)
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	0	0	0	0	0
Withdrawal Consent	1 (20.0)	0	2 (13.3)	2 (12.5)	5 (12.8)
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
All (Cont.)					
Completed Study Drug in BE Period	0	0	0	0	0
Ongoing Study Drug in BE Period	3 (60.0)	3 (100)	13 (86.7)	12 (75.0)	31 (79.5)
Discontinued Study Drug in BE Period	2 (40.0)	0	2 (13.3)	2 (12.5)	6 (15.4)
All Reasons for Discontinuation$					
Adverse Event	1 (20.0)	0	2 (13.3)	2 (12.5)	5 (12.8)
Withdrawal Consent	1 (20.0)	0	1 (6.7)	1 (6.3)	3 (7.7)
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	1 (6.7)	0	1 (2.6)
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
All (Cont.)					
Primary Reason for Discontinuation					
Adverse Event	1 (20.0)	0	1 (6.7)	1 (6.3)	3 (7.7)
Withdrawal Consent	1 (20.0)	0	0	1 (6.3)	2 (5.1)
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	1 (6.7)	0	1 (2.6)
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.

Program Source Code: [redacted]

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
Age Group: Adolescent					
Entered BE Period	1 (20.0)	0	1 (6.7)	2 (12.5)	4 (10.3)
Never Received Any Study Drug in BE Period	0	0	0	0	0
Received Study Drug in BE Period	1 (20.0)	0	1 (6.7)	2 (12.5)	4 (10.3)
Initiated Rescue Medication in BE Period	0	0	0	0	0
Completed Study	0	0	0	0	0
Discontinued Study in BE Period	0	0	0	0	0
All Reasons for Discontinuation$					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
Age Group: Adolescent (Cont.)					
Completed Study Drug in BE Period	0	0	0	0	0
Ongoing Study Drug in BE Period	1 (20.0)	0	1 (6.7)	2 (12.5)	4 (10.3)
Discontinued Study Drug in BE Period	0	0	0	0	0
All Reasons for Discontinuation$					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
Age Group: Adolescent (Cont.)					
Primary Reason for Discontinuation					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.

Program Source Code: [redacted]

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
Age Group: Adult					
Entered BE Period	4 (80.0)	3 (100)	14 (93.3)	13 (81.3)	34 (87.2)
Never Received Any Study Drug in BE Period	0	0	0	1 (6.3)	1 (2.6)
Received Study Drug in BE Period	4 (80.0)	3 (100)	14 (93.3)	12 (75.0)	33 (84.6)
Initiated Rescue Medication in BE Period	0	0	1 (6.7)	1 (6.3)	2 (5.1)
Completed Study	0	0	0	0	0
Discontinued Study in BE Period	1 (20.0)	0	2 (13.3)	2 (12.5)	5 (12.8)
All Reasons for Discontinuation$					
Adverse Event	0	0	1 (6.7)	0	1 (2.6)
Withdrawal Consent	1 (20.0)	0	2 (13.3)	2 (12.5)	5 (12.8)
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	0	0	0	0	0
Withdrawal Consent	1 (20.0)	0	2 (13.3)	2 (12.5)	5 (12.8)
Lost to Follow-Up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
Age Group: Adult (Cont.)					
Completed Study Drug in BE Period	0	0	0	0	0
Ongoing Study Drug in BE Period	2 (40.0)	3 (100)	12 (80.0)	10 (62.5)	27 (69.2)
Discontinued Study Drug in BE Period	2 (40.0)	0	2 (13.3)	2 (12.5)	6 (15.4)
All Reasons for Discontinuation$					
Adverse Event	1 (20.0)	0	2 (13.3)	2 (12.5)	5 (12.8)
Withdrawal Consent	1 (20.0)	0	1 (6.7)	1 (6.3)	3 (7.7)
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	1 (6.7)	0	1 (2.6)
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Strata Status	Placebo/ UPA 15 mg QD (N=5) n (%)	Placebo/ UPA 30 mg QD (N=3) n (%)	UPA 15 mg QD (N=15) n (%)	UPA 30 mg QD (N=16) n (%)	Total (N=39) n (%)
Age Group: Adult (Cont.)					
Primary Reason for Discontinuation					
Adverse Event	1 (20.0)	0	1 (6.7)	1 (6.3)	3 (7.7)
Withdrawal Consent	1 (20.0)	0	0	1 (6.3)	2 (5.1)
Lost to Follow-Up	0	0	0	0	0
Lack of Efficacy	0	0	1 (6.7)	0	1 (2.6)
EASI Score - Worsening of 25% Criteria Was Met	0	0	0	0	0
Protocol-Mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.

Program Source Code: [redacted]

相互参照：M16-045 試験 W52 Japan Study Data Table 14.1__2.1_J

表 2.7.3.6-80.　人口統計学的特性の要約（ITT_M 集団，日本人部分集団）：M16-047 試験

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Sex - n (%)					
Female	3 (16.7)	4 (25.0)	2 (11.8)	6 (18.2)	9 (17.6)
Male	15 (83.3)	12 (75.0)	15 (88.2)	27 (81.8)	42 (82.4)
Age Group 1 (years) - n (%)					
< 18	0	0	0	0	0
>= 18	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)
Age Group 2 (years) - n (%)					
< 18	0	0	0	0	0
18 - < 40	7 (38.9)	9 (56.3)	10 (58.8)	19 (57.6)	26 (51.0)
40 - < 65	11 (61.1)	7 (43.8)	7 (41.2)	14 (42.4)	25 (49.0)
>= 65	0	0	0	0	0
Age (years)					
n	18	16	17	33	51
Mean (SD)	39.9 (10.99)	37.4 (10.68)	36.5 (10.25)	36.9 (10.31)	38.0 (10.54)
Median	43.5	35.5	34.0	35.0	39.0
Min, Max	21, 55	20, 57	23, 53	20, 57	20, 57

Note: Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Weight (kg)					
n	18	16	17	33	51
Mean (SD)	69.14 (12.041)	66.36 (10.660)	68.36 (13.326)	67.39 (11.962)	68.01 (11.899)
Median	68.80	65.35	69.90	65.80	65.80
Min, Max	48.6, 88.2	48.5, 91.6	48.5, 103.4	48.5, 103.4	48.5, 103.4
Height (cm)					
n	18	16	17	33	51
Mean (SD)	169.23 (8.340)	164.66 (7.693)	170.16 (6.002)	167.49 (7.318)	168.11 (7.657)
Median	172.35	163.75	170.30	169.00	169.80
Min, Max	154.5, 178.5	152.8, 176.3	158.0, 179.5	152.8, 179.5	152.8, 179.5
Body Mass Index (kg/m^2)					
n	18	16	17	33	51
Mean (SD)	24.05 (3.374)	24.48 (3.529)	23.68 (4.856)	24.07 (4.219)	24.06 (3.906)
Median	24.95	23.60	22.80	22.80	23.30
Min, Max	19.4, 31.3	19.9, 30.3	17.0, 35.5	17.0, 35.5	17.0, 35.5
Body Mass Index (kg/m^2) - n (%)					
< 25	9 (50.0)	9 (56.3)	11 (64.7)	20 (60.6)	29 (56.9)
25 - < 30	8 (44.4)	6 (37.5)	4 (23.5)	10 (30.3)	18 (35.3)
>= 30	1 (5.6)	1 (6.3)	2 (11.8)	3 (9.1)	4 (7.8)

Note: Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Tobacco$ - n (%)					
Current	5 (27.8)	4 (25.0)	5 (29.4)	9 (27.3)	14 (27.5)
Former	4 (22.2)	2 (12.5)	2 (11.8)	4 (12.1)	8 (15.7)
Never	9 (50.0)	10 (62.5)	10 (58.8)	20 (60.6)	29 (56.9)
Unknown	0	0	0	0	0
Alcohol$ - n (%)					
Current	16 (88.9)	12 (75.0)	16 (94.1)	28 (84.8)	44 (86.3)
Former	0	2 (12.5)	0	2 (6.1)	2 (3.9)
Never	2 (11.1)	2 (12.5)	1 (5.9)	3 (9.1)	5 (9.8)
Unknown	0	0	0	0	0

Note: Percentages calculated on non-missing values.
$ Percentages calculated on non-missing/non-unknown values. A subject may be a current user of one type of tobacco, a former user of another type of tobacco and never used another type of tobacco. A subject will be counted in the category closest to user.

Program Source Code: [redacted]

相互参照：M16-047 試験 W16 Japan Study Data Table 14.1　4.1 J

表 2.7.3.6-81. ベースラインのその他の基準値の特性の要約（ITT_M 集団，日本人部分集団）：M16-047 試験

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Baseline vIGA-AD - n (%)					
3 (Moderate)	5 (27.8)	4 (25.0)	4 (23.5)	8 (24.2)	13 (25.5)
4 (Severe)	13 (72.2)	12 (75.0)	13 (76.5)	25 (75.8)	38 (74.5)
Baseline EASI - n (%)					
< Median (25.8)	7 (38.9)	6 (37.5)	4 (23.5)	10 (30.3)	17 (33.3)
>= Median (25.8)	11 (61.1)	10 (62.5)	13 (76.5)	23 (69.7)	34 (66.7)
hsCRP - n (%)					
< Median (1.41)	10 (55.6)	10 (62.5)	10 (58.8)	20 (60.6)	30 (58.8)
>= Median (1.41)	8 (44.4)	6 (37.5)	7 (41.2)	13 (39.4)	21 (41.2)
Previous Systemic Therapy - n (%)					
With	7 (38.9)	10 (62.5)	10 (58.8)	20 (60.6)	27 (52.9)
Without	11 (61.1)	6 (37.5)	7 (41.2)	13 (39.4)	24 (47.1)

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
EASI					
n	18	16	17	33	51
Mean (SD)	33.94 (12.512)	30.71 (13.177)	36.54 (12.114)	33.71 (12.788)	33.79 (12.566)
Median	33.35	26.60	37.20	34.20	34.20
Min, Max	16.3, 60.0	16.1, 63.5	18.2, 60.6	16.1, 63.5	16.1, 63.5
EASI Head/Neck					
n	18	16	17	33	51
Mean (SD)	3.42 (2.016)	3.31 (1.740)	3.87 (1.609)	3.60 (1.672)	3.54 (1.783)
Median	3.80	3.00	3.20	3.20	3.20
Min, Max	0.0, 6.0	0.5, 7.2	1.6, 6.6	0.5, 7.2	0.0, 7.2
EASI Lower Limbs					
n	18	16	17	33	51
Mean (SD)	13.16 (5.593)	10.83 (6.525)	14.61 (6.614)	12.78 (6.747)	12.91 (6.309)
Median	11.60	8.40	14.40	12.80	12.80
Min, Max	5.6, 24.0	0.8, 24.0	2.0, 28.8	0.8, 28.8	0.8, 28.8

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
EASI Trunk					
n	18	16	17	33	51
Mean (SD)	10.97 (4.852)	10.28 (5.175)	11.33 (4.625)	10.82 (4.851)	10.87 (4.803)
Median	11.40	10.50	12.00	12.00	12.00
Min, Max	0.3, 18.0	2.4, 21.6	3.6, 18.0	2.4, 21.6	0.3, 21.6
EASI Upper Limbs					
n	18	16	17	33	51
Mean (SD)	6.40 (2.810)	6.30 (3.733)	6.73 (2.557)	6.52 (3.138)	6.48 (2.999)
Median	6.00	5.50	6.40	6.00	6.00
Min, Max	2.0, 12.0	1.2, 14.4	3.2, 13.2	1.2, 14.4	1.2, 14.4
BSA in Percentage					
n	18	16	17	33	51
Mean (SD)	66.61 (17.191)	59.47 (19.719)	66.29 (18.213)	62.98 (18.977)	64.26 (18.276)
Median	68.50	58.50	70.00	63.00	65.00
Min, Max	36.0, 94.0	28.0, 92.0	38.0, 92.0	28.0, 92.0	28.0, 94.0

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Overall SCORAD Score					
n	18	16	17	33	51
Mean (SD)	68.108 (14.6800)	66.170 (15.4773)	73.993 (9.6419)	70.200 (13.2111)	69.462 (13.6379)
Median	67.800	66.050	71.940	70.000	69.100
Min, Max	40.70, 89.30	41.50, 94.40	55.70, 88.00	41.50, 94.40	40.70, 94.40
Objective SCORAD					
n	18	16	17	33	51
Mean (SD)	52.663 (14.7820)	52.358 (14.0048)	58.758 (7.9911)	55.655 (11.5939)	54.599 (12.7438)
Median	49.800	50.050	58.000	55.900	54.300
Min, Max	31.70, 77.60	31.50, 81.40	46.10, 71.00	31.50, 81.40	31.50, 81.40
SCORAD Itch					
n	18	16	17	33	51
Mean (SD)	7.9 (1.80)	7.9 (1.24)	8.2 (1.19)	8.1 (1.20)	8.0 (1.42)
Median	8.5	8.0	8.0	8.0	8.0
Min, Max	4, 10	6, 10	6, 10	6, 10	4, 10

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
SCORAD Sleep					
n	18	16	17	33	51
Mean (SD)	7.5 (2.57)	5.9 (2.45)	7.1 (2.08)	6.5 (2.31)	6.8 (2.43)
Median	8.0	7.0	7.0	7.0	7.0
Min, Max	1, 10	0, 9	1, 10	0, 10	0, 10
DLQI					
n	18	16	17	33	51
Mean (SD)	14.9 (6.45)	11.8 (5.58)	14.2 (7.22)	13.0 (6.50)	13.7 (6.48)
Median	14.5	12.5	14.0	13.0	14.0
Min, Max	6, 28	0, 21	2, 25	0, 25	0, 28
HADS Total Score					
n	18	16	17	33	51
Mean (SD)	14.2 (8.41)	11.8 (8.14)	12.8 (8.62)	12.3 (8.27)	13.0 (8.29)
Median	13.0	12.0	11.0	11.0	12.0
Min, Max	4, 33	1, 28	1, 30	1, 30	1, 33

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
HADS-A Total Score					
n	18	16	17	33	51
Mean (SD)	7.3 (4.90)	5.9 (4.37)	6.8 (4.46)	6.4 (4.37)	6.7 (4.54)
Median	6.0	5.0	7.0	5.0	6.0
Min, Max	2, 19	0, 14	1, 15	0, 15	0, 19
HADS-D Total Score					
n	18	16	17	33	51
Mean (SD)	6.9 (4.20)	5.9 (4.26)	5.9 (4.51)	5.9 (4.32)	6.3 (4.26)
Median	6.5	6.0	5.0	5.0	6.0
Min, Max	1, 14	0, 14	0, 17	0, 17	0, 17
WPAI: AD: Absenteeism (%)					
n	4	3	3	6	10
Mean (SD)	1.362 (1.6802)	11.111 (19.2450)	24.119 (21.0808)	17.615 (19.4080)	11.114 (16.7525)
Median	1.000	0.000	33.333	16.667	1.000
Min, Max	0.00, 3.45	0.00, 33.33	0.00, 39.02	0.00, 39.02	0.00, 39.02

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
WPAI: AD: Presenteeism (%)					
n	4	3	3	6	10
Mean (SD)	62.5 (17.08)	56.7 (28.87)	70.0 (17.32)	63.3 (22.51)	63.0 (19.47)
Median	65.0	40.0	80.0	65.0	65.0
Min, Max	40, 80	40, 90	50, 80	40, 90	40, 90
WPAI: AD: Work Productivity Loss (%)					
n	4	3	3	6	10
Mean (SD)	62.822 (17.4027)	63.333 (25.1661)	78.157 (10.6889)	70.745 (19.1039)	67.576 (17.9010)
Median	65.300	60.000	80.000	73.333	68.633
Min, Max	40.00, 80.69	40.00, 90.00	66.67, 87.80	40.00, 90.00	40.00, 90.00
WPAI: AD: Activity Impairment (%)					
n	18	16	17	33	51
Mean (SD)	69.4 (18.62)	51.3 (25.79)	68.8 (19.00)	60.3 (23.91)	63.5 (22.43)
Median	65.0	55.0	70.0	70.0	70.0
Min, Max	30, 100	0, 80	30, 100	0, 100	0, 100

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
EQ-5D-5L Index					
n	18	16	17	33	51
Mean (SD)	0.6106 (0.34800)	0.7534 (0.19625)	0.6323 (0.30095)	0.6910 (0.25907)	0.6626 (0.29264)
Median	0.6875	0.8495	0.7400	0.8030	0.7400
Min, Max	-0.153, 1.000	0.414, 1.000	0.070, 1.000	0.070, 1.000	-0.153, 1.000
EQ-5D-5L VAS Score					
n	18	16	17	33	51
Mean (SD)	45.4 (28.23)	56.1 (24.02)	50.5 (21.77)	53.2 (22.71)	50.4 (24.80)
Median	42.5	53.5	50.0	50.0	50.0
Min, Max	5, 95	20, 95	9, 91	9, 95	5, 95
Worst Pruritus NRS (Weekly Average)					
n	18	16	17	33	51
Mean (SD)	6.996 (1.8311)	7.069 (1.4138)	7.905 (1.5300)	7.500 (1.5124)	7.322 (1.6319)
Median	7.357	7.043	7.429	7.286	7.286
Min, Max	4.25, 10.00	4.71, 9.86	5.71, 10.00	4.71, 10.00	4.25, 10.00

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
PGIS					
n	18	16	17	33	51
Mean (SD)	4.9 (0.90)	4.3 (1.00)	4.2 (1.03)	4.2 (1.00)	4.5 (1.01)
Median	5.0	4.0	4.0	4.0	4.0
Min, Max	3, 6	3, 6	3, 6	3, 6	3, 6
PGIS - n (%)					
Absent	0	0	0	0	0
Minimal	0	0	0	0	0
Mild	0	0	0	0	0
Moderate	1 (5.6)	4 (25.0)	5 (29.4)	9 (27.3)	10 (19.6)
Moderately Severe	5 (27.8)	6 (37.5)	5 (29.4)	11 (33.3)	16 (31.4)
Severe	7 (38.9)	4 (25.0)	5 (29.4)	9 (27.3)	16 (31.4)
Very Severe	5 (27.8)	2 (12.5)	2 (11.8)	4 (12.1)	9 (17.6)

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
PGIT - n (%)					
Extremely Dissatisfied	3 (16.7)	2 (12.5)	2 (11.8)	4 (12.1)	7 (13.7)
Very Dissatisfied	0	1 (6.3)	3 (17.6)	4 (12.1)	4 (7.8)
Somewhat Dissatisfied	2 (11.1)	1 (6.3)	6 (35.3)	7 (21.2)	9 (17.6)
Neither Dissatisfied nor Satisfied	8 (44.4)	5 (31.3)	4 (23.5)	9 (27.3)	17 (33.3)
Somewhat Satisfied	4 (22.2)	7 (43.8)	2 (11.8)	9 (27.3)	13 (25.5)
Very Satisfied	1 (5.6)	0	0	0	1 (2.0)
Extremely Satisfied	0	0	0	0	0
ADerm-SS Skin Pain					
n	18	16	17	33	51
Mean (SD)	6.420 (1.8550)	5.169 (2.2523)	6.768 (2.4121)	5.992 (2.4383)	6.144 (2.2400)
Median	5.536	4.786	6.571	6.143	6.143
Min, Max	3.14, 10.00	1.71, 8.43	0.43, 10.00	0.43, 10.00	0.43, 10.00
ADerm-SS TSS-7					
n	18	16	17	33	51
Mean (SD)	42.9 (13.99)	40.3 (13.45)	48.9 (13.49)	44.8 (13.96)	44.1 (13.86)
Median	41.0	37.5	46.0	43.0	43.0
Min, Max	15, 70	17, 62	19, 70	17, 70	15, 70

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
ADerm-SS TSS-11					
n	18	16	17	33	51
Mean (SD)	65.4 (22.03)	60.8 (21.18)	73.7 (22.72)	67.4 (22.62)	66.7 (22.21)
Median	62.5	55.5	72.0	64.0	64.0
Min, Max	20, 110	28, 96	19, 110	19, 110	19, 110
ADerm-IS Sleep Domain Score					
n	18	16	17	33	51
Mean (SD)	18.160 (5.7716)	16.160 (8.9905)	21.815 (5.5275)	19.073 (7.8360)	18.751 (7.1287)
Median	16.786	20.214	21.714	21.143	20.286
Min, Max	5.00, 30.00	2.67, 29.29	9.00, 30.00	2.67, 30.00	2.67, 30.00
ADerm-IS Daily Activities Domain Score					
n	18	16	17	33	51
Mean (SD)	21.6 (8.68)	17.8 (11.51)	25.2 (7.80)	21.6 (10.33)	21.6 (9.69)
Median	23.0	20.0	23.0	21.0	22.0
Min, Max	5, 37	0, 35	12, 38	0, 38	0, 38

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
ADerm-IS Emotional State Domain Score					
n	18	16	17	33	51
Mean (SD)	18.9 (7.08)	15.6 (10.70)	19.9 (7.32)	17.8 (9.23)	18.2 (8.48)
Median	18.5	17.5	19.0	18.0	18.0
Min, Max	3, 30	0, 30	7, 30	0, 30	0, 30
POEM					
n	18	16	17	33	51
Mean (SD)	19.8 (5.48)	19.4 (4.96)	21.1 (5.73)	20.3 (5.36)	20.1 (5.36)
Median	20.0	19.5	21.0	20.0	20.0
Min, Max	9, 28	11, 27	10, 28	10, 28	9, 28
DIS					
n	18	16	17	33	51
Mean (SD)	29.6 (18.07)	24.9 (18.98)	22.9 (17.99)	23.8 (18.21)	25.9 (18.19)
Median	25.5	26.0	17.0	18.0	25.0
Min, Max	4, 68	0, 51	0, 58	0, 58	0, 68

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Disease Duration since Diagnosis (years)					
n	18	16	17	33	51
Mean (SD)	26.965 (16.7120)	29.777 (14.3166)	23.320 (15.6601)	26.450 (15.1471)	26.632 (15.5518)
Median	29.955	29.023	19.337	24.912	28.903
Min, Max	0.08, 50.95	4.13, 57.89	0.06, 53.39	0.06, 57.89	0.06, 57.89
Disease Duration since Symptoms Started (years)					
n	18	16	17	33	51
Mean (SD)	31.637 (15.5317)	30.970 (14.6667)	30.166 (12.1761)	30.555 (13.2336)	30.937 (13.9418)
Median	34.511	30.597	26.973	29.153	30.048
Min, Max	4.09, 51.72	4.13, 57.89	7.05, 53.39	4.13, 57.89	4.09, 57.89
Duration between Symptoms and Diagnosis (years)					
n	18	16	17	33	51
Mean (SD)	4.672 (8.2968)	1.193 (4.4892)	6.846 (12.4618)	4.105 (9.7635)	4.305 (9.1917)
Median	0.000	0.000	0.000	0.000	0.000
Min, Max	0.00, 22.00	0.00, 18.00	0.00, 46.86	0.00, 46.86	0.00, 46.86

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale.

Program Source Code: [redacted]

相互参照：M16-047 試験 W16 Japan Study Data Table 14.1　5.1_J

表 2.7.3.6-82.　疾患歴（ITT_M 集団，日本人部分集団）：M16-047 試験

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=18) n (%)	Active UPA 15 mg QD + TCS (N=16) n (%)	Active UPA 30 mg QD + TCS (N=17) n (%)	Active Total (N=33) n (%)	Total (N=51) n (%)
Blood and lymphatic system disorders	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Anaemia	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Cardiac disorders	2 (11.1)	1 (6.3)	1 (5.9)	2 (6.1)	4 (7.8)
Acute myocardial infarction	1 (5.6)	0	0	0	1 (2.0)
Atrioventricular block second degree	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Cardiac hypertrophy	1 (5.6)	0	0	0	1 (2.0)
Cardiac valve disease	1 (5.6)	0	0	0	1 (2.0)
Sinus tachycardia	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Congenital, familial and genetic disorders	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Congenital hepatobiliary anomaly	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Ear and labyrinth disorders	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Sudden hearing loss	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Eye disorders	3 (16.7)	5 (31.3)	3 (17.6)	8 (24.2)	11 (21.6)
Atopic cataract	1 (5.6)	0	0	0	1 (2.0)
Cataract	1 (5.6)	1 (6.3)	1 (5.9)	2 (6.1)	3 (5.9)
Conjunctivitis allergic	1 (5.6)	3 (18.8)	2 (11.8)	5 (15.2)	6 (11.8)
Dry eye	0	1 (6.3)	0	1 (3.0)	1 (2.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=18) n (%)	Active UPA 15 mg QD + TCS (N=16) n (%)	Active UPA 30 mg QD + TCS (N=17) n (%)	Active Total (N=33) n (%)	Total (N=51) n (%)
Eye disorders (Cont.)					
Retinal detachment	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Retinal tear	1 (5.6)	0	0	0	1 (2.0)
Rhegmatogenous retinal detachment	1 (5.6)	0	0	0	1 (2.0)
Uveitis	1 (5.6)	0	0	0	1 (2.0)
Vernal keratoconjunctivitis	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Gastrointestinal disorders	2 (11.1)	2 (12.5)	2 (11.8)	4 (12.1)	6 (11.8)
Chronic gastritis	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Gastric polyps	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Gastrooesophageal reflux disease	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
Haemorrhoids	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Periodontal disease	1 (5.6)	0	0	0	1 (2.0)
Stomatitis	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Hepatobiliary disorders	1 (5.6)	1 (6.3)	1 (5.9)	2 (6.1)	3 (5.9)
Hepatic cyst	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Hepatic steatosis	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
Immune system disorders	5 (27.8)	9 (56.3)	7 (41.2)	16 (48.5)	21 (41.2)
Allergy to metals	0	2 (12.5)	0	2 (6.1)	2 (3.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=18) n (%)	Active UPA 15 mg QD + TCS (N=16) n (%)	Active UPA 30 mg QD + TCS (N=17) n (%)	Active Total (N=33) n (%)	Total (N=51) n (%)
Immune system disorders (Cont.)					
Drug hypersensitivity	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Food allergy	3 (16.7)	5 (31.3)	4 (23.5)	9 (27.3)	12 (23.5)
Seasonal allergy	3 (16.7)	5 (31.3)	3 (17.6)	8 (24.2)	11 (21.6)
Infections and infestations	9 (50.0)	8 (50.0)	4 (23.5)	12 (36.4)	21 (41.2)
Acne pustular	0	1 (6.3)	1 (5.9)	2 (6.1)	2 (3.9)
Appendicitis	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Cellulitis	2 (11.1)	3 (18.8)	1 (5.9)	4 (12.1)	6 (11.8)
Cystitis	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Enterocolitis viral	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Folliculitis	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Genital herpes	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Herpes ophthalmic	1 (5.6)	0	0	0	1 (2.0)
Herpes zoster	2 (11.1)	2 (12.5)	2 (11.8)	4 (12.1)	6 (11.8)
Impetigo	1 (5.6)	0	0	0	1 (2.0)
Infectious mononucleosis	1 (5.6)	0	0	0	1 (2.0)
Influenza	1 (5.6)	0	0	0	1 (2.0)
Latent tuberculosis	2 (11.1)	0	0	0	2 (3.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=18) n (%)	Active UPA 15 mg QD + TCS (N=16) n (%)	Active UPA 30 mg QD + TCS (N=17) n (%)	Active Total (N=33) n (%)	Total (N=51) n (%)
Infections and infestations (Cont.)					
Malassezia infection	1 (5.6)	0	0	0	1 (2.0)
Nasopharyngitis	1 (5.6)	0	0	0	1 (2.0)
Oral herpes	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Pyelonephritis	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Tinea pedis	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
Varicella	1 (5.6)	1 (6.3)	1 (5.9)	2 (6.1)	3 (5.9)
Injury, poisoning and procedural complications	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
Contusion	1 (5.6)	0	0	0	1 (2.0)
Ligament sprain	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Investigations	1 (5.6)	0	0	0	1 (2.0)
Electrocardiogram low voltage	1 (5.6)	0	0	0	1 (2.0)
Liver function test abnormal	1 (5.6)	0	0	0	1 (2.0)
QRS axis abnormal	1 (5.6)	0	0	0	1 (2.0)
Metabolism and nutrition disorders	3 (16.7)	3 (18.8)	2 (11.8)	5 (15.2)	8 (15.7)
Diabetes mellitus	0	1 (6.3)	1 (5.9)	2 (6.1)	2 (3.9)
Dyslipidaemia	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Hyperlipidaemia	2 (11.1)	2 (12.5)	0	2 (6.1)	4 (7.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=18) n (%)	Active UPA 15 mg QD + TCS (N=16) n (%)	Active UPA 30 mg QD + TCS (N=17) n (%)	Active Total (N=33) n (%)	Total (N=51) n (%)
Metabolism and nutrition disorders (Cont.)					
Hyperuricaemia	2 (11.1)	0	1 (5.9)	1 (3.0)	3 (5.9)
Musculoskeletal and connective tissue disorders	4 (22.2)	3 (18.8)	2 (11.8)	5 (15.2)	9 (17.6)
Arthralgia	1 (5.6)	0	0	0	1 (2.0)
Back pain	3 (16.7)	1 (6.3)	0	1 (3.0)	4 (7.8)
Intervertebral disc protrusion	0	1 (6.3)	2 (11.8)	3 (9.1)	3 (5.9)
Musculoskeletal stiffness	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (11.1)	1 (6.3)	2 (11.8)	3 (9.1)	5 (9.8)
Cholesteatoma	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Skin papilloma	2 (11.1)	1 (6.3)	1 (5.9)	2 (6.1)	4 (7.8)
Nervous system disorders	2 (11.1)	2 (12.5)	4 (23.5)	6 (18.2)	8 (15.7)
Cluster headache	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Headache	2 (11.1)	1 (6.3)	3 (17.6)	4 (12.1)	6 (11.8)
Hypoaesthesia	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Psychiatric disorders	0	2 (12.5)	0	2 (6.1)	2 (3.9)
Depression	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Insomnia	0	2 (12.5)	0	2 (6.1)	2 (3.9)
Renal and urinary disorders	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=18) n (%)	Active UPA 15 mg QD + TCS (N=16) n (%)	Active UPA 30 mg QD + TCS (N=17) n (%)	Active Total (N=33) n (%)	Total (N=51) n (%)
Renal and urinary disorders (Cont.)					
Nephrotic syndrome	1 (5.6)	0	0	0	1 (2.0)
Ureterolithiasis	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Respiratory, thoracic and mediastinal disorders	10 (55.6)	8 (50.0)	11 (64.7)	19 (57.6)	29 (56.9)
Asthma	5 (27.8)	3 (18.8)	5 (29.4)	8 (24.2)	13 (25.5)
Childhood asthma	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
Rhinitis allergic	9 (50.0)	6 (37.5)	9 (52.9)	15 (45.5)	24 (47.1)
Skin and subcutaneous tissue disorders	6 (33.3)	6 (37.5)	5 (29.4)	11 (33.3)	17 (33.3)
Acne	6 (33.3)	3 (18.8)	4 (23.5)	7 (21.2)	13 (25.5)
Alopecia areata	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Alopecia universalis	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Dermatitis contact	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Hyperhidrosis	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Milia	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Nail bed tenderness	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Pityriasis alba	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Toxic skin eruption	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Xeroderma	1 (5.6)	0	0	0	1 (2.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=18) n (%)	Active UPA 15 mg QD + TCS (N=16) n (%)	Active UPA 30 mg QD + TCS (N=17) n (%)	Active Total (N=33) n (%)	Total (N=51) n (%)
Social circumstances	3 (16.7)	3 (18.8)	2 (11.8)	5 (15.2)	8 (15.7)
Menopause	0	0	1 (5.9)	1 (3.0)	1 (2.0)
Non-consummation	3 (16.7)	2 (12.5)	1 (5.9)	3 (9.1)	6 (11.8)
Postmenopause	0	1 (6.3)	0	1 (3.0)	1 (2.0)
Vascular disorders	5 (27.8)	1 (6.3)	3 (17.6)	4 (12.1)	9 (17.6)
Hypertension	4 (22.2)	1 (6.3)	3 (17.6)	4 (12.1)	8 (15.7)
Varicose vein	1 (5.6)	0	0	0	1 (2.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 W16 Japan Study Data Table 14.1　6_J

表 2.7.3.6-83.　前治療歴（ITT_M 集団，日本人部分集団）：M16-047 試験

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
Any Prior Medications	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)
ACETYLSALICYLIC ACID	1 (5.6)	0	0	0	1 (2.0)
ALCLOMETASONE	0	1 (6.3)	3 (17.6)	4 (12.1)	4 (7.8)
ALENDRONIC ACID	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 (5.6)	2 (12.5)	4 (23.5)	6 (18.2)	7 (13.7)
ALLOPURINOL	1 (5.6)	0	0	0	1 (2.0)
AMLODIPINE	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
ARIPIPRAZOLE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ATORVASTATIN	1 (5.6)	1 (6.3)	1 (5.9)	2 (6.1)	3 (5.9)
ATROPINE	1 (5.6)	0	0	0	1 (2.0)
AZATHIOPRINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
AZILSARTAN	1 (5.6)	0	0	0	1 (2.0)
BACTERIA NOS W/HYDROCORTISONE	0	1 (6.3)	1 (5.9)	2 (6.1)	2 (3.9)
BECLOMETASONE	0	2 (12.5)	3 (17.6)	5 (15.2)	5 (9.8)
BENZOYL PEROXIDE	1 (5.6)	0	0	0	1 (2.0)
BEPOTASTINE	4 (22.2)	3 (18.8)	5 (29.4)	8 (24.2)	12 (23.5)
BETAMETHASONE	16 (88.9)	13 (81.3)	14 (82.4)	27 (81.8)	43 (84.3)
BETNESOL-N	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
BILASTINE	5 (27.8)	5 (31.3)	4 (23.5)	9 (27.3)	14 (27.5)
BIOTIN	1 (5.6)	2 (12.5)	0	2 (6.1)	3 (5.9)
BISOPROLOL	1 (5.6)	0	0	0	1 (2.0)
BROMFENAC	1 (5.6)	0	0	0	1 (2.0)
BROTIZOLAM	0	1 (6.3)	0	1 (3.0)	1 (2.0)
BUDESONIDE W/FORMOTEROL FUMARATE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
BUFEXAMAC	0	0	1 (5.9)	1 (3.0)	1 (2.0)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
BUFFERIN A	1 (5.6)	0	0	0	1 (2.0)
BUTENAFINE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
CANDESARTAN	1 (5.6)	0	0	0	1 (2.0)
CARBOCISTEINE	1 (5.6)	0	0	0	1 (2.0)
CARVEDILOL	1 (5.6)	0	0	0	1 (2.0)
CEFDITOREN	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
CELESTAMINE	1 (5.6)	5 (31.3)	2 (11.8)	7 (21.2)	8 (15.7)
CETIRIZINE	2 (11.1)	2 (12.5)	0	2 (6.1)	4 (7.8)
CICLOSPORIN	5 (27.8)	5 (31.3)	7 (41.2)	12 (36.4)	17 (33.3)
CLOBETASOL	8 (44.4)	10 (62.5)	8 (47.1)	18 (54.5)	26 (51.0)
CLOBETASONE	2 (11.1)	0	6 (35.3)	6 (18.2)	8 (15.7)
CLOSTRIDIUM BUTYRICUM	0	1 (6.3)	0	1 (3.0)	1 (2.0)
CORDRAN-N	0	0	1 (5.9)	1 (3.0)	1 (2.0)
COSOPT	1 (5.6)	0	0	0	1 (2.0)
CROTAMITON	0	0	1 (5.9)	1 (3.0)	1 (2.0)
DAPSONE	2 (11.1)	0	0	0	2 (3.9)
DEPRODONE	0	1 (6.3)	3 (17.6)	4 (12.1)	4 (7.8)
DESLORATADINE	2 (11.1)	2 (12.5)	1 (5.9)	3 (9.1)	5 (9.8)
DEXAMETHASONE	4 (22.2)	3 (18.8)	6 (35.3)	9 (27.3)	13 (25.5)
DEXCHLORPHENIRAMINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
DEXTROMETHORPHAN	1 (5.6)	0	0	0	1 (2.0)
DIFLORASONE	7 (38.9)	4 (25.0)	6 (35.3)	10 (30.3)	17 (33.3)
DIFLUCORTOLONE	6 (33.3)	5 (31.3)	4 (23.5)	9 (27.3)	15 (29.4)
DIFLUPREDNATE	7 (38.9)	7 (43.8)	7 (41.2)	14 (42.4)	21 (41.2)
DIPHENHYDRAMINE	2 (11.1)	0	0	0	2 (3.9)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
DIPHENHYDRAMINE HYDROCHLORIDE;LIDOCAINE;UREA	0	0	1 (5.9)	1 (3.0)	1 (2.0)
DOXYCYCLINE	0	1 (6.3)	1 (5.9)	2 (6.1)	2 (3.9)
EBASTINE	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
ENOXOLONE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
EPINASTINE	3 (16.7)	2 (12.5)	1 (5.9)	3 (9.1)	6 (11.8)
ESCITALOPRAM	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ESOMEPRAZOLE	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
ETIZOLAM	0	1 (6.3)	0	1 (3.0)	1 (2.0)
EVE A	0	0	1 (5.9)	1 (3.0)	1 (2.0)
FAMOTIDINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
FELBINAC	0	1 (6.3)	0	1 (3.0)	1 (2.0)
FENOFIBRATE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
FEXOFENADINE	6 (33.3)	6 (37.5)	5 (29.4)	11 (33.3)	17 (33.3)
FLUDROXYCORTIDE	3 (16.7)	2 (12.5)	0	2 (6.1)	5 (9.8)
FLUMETASONE	1 (5.6)	0	0	0	1 (2.0)
FLUOCINOLONE ACETONIDE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
FLUOCINONIDE	2 (11.1)	3 (18.8)	0	3 (9.1)	5 (9.8)
FLUTICASONE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
FUSIDIC ACID	0	0	1 (5.9)	1 (3.0)	1 (2.0)
GUAIAZULENE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
HACHIMIJIOGAN	1 (5.6)	0	0	0	1 (2.0)
HEPARIN	1 (5.6)	0	0	0	1 (2.0)
HEPARINOID	9 (50.0)	12 (75.0)	9 (52.9)	21 (63.6)	30 (58.8)
HYDROCORTISONE	8 (44.4)	9 (56.3)	10 (58.8)	19 (57.6)	27 (52.9)
HYDROPHILIC	0	1 (6.3)	3 (17.6)	4 (12.1)	4 (7.8)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
HYDROXYZINE	4 (22.2)	1 (6.3)	3 (17.6)	4 (12.1)	8 (15.7)
HYZAAR	0	1 (6.3)	0	1 (3.0)	1 (2.0)
IBUPROFEN	0	1 (6.3)	1 (5.9)	2 (6.1)	2 (3.9)
INFLUENZA VACCINE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
IRON	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ISONIAZID	2 (11.1)	0	0	0	2 (3.9)
KETOCONAZOLE	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
KETOTIFEN	2 (11.1)	0	0	0	2 (3.9)
LANOCONAZOLE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
LEVOCETIRIZINE	5 (27.8)	1 (6.3)	2 (11.8)	3 (9.1)	8 (15.7)
LEVOFLOXACIN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
LORATADINE	2 (11.1)	0	1 (5.9)	1 (3.0)	3 (5.9)
LOXOPROFEN	1 (5.6)	1 (6.3)	2 (11.8)	3 (9.1)	4 (7.8)
LUSEOGLIFLOZIN	0	0	1 (5.9)	1 (3.0)	1 (2.0)
MAXACALCITOL	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
MEQUITAZINE	0	1 (6.3)	2 (11.8)	3 (9.1)	3 (5.9)
METFORMIN	0	1 (6.3)	1 (5.9)	2 (6.1)	2 (3.9)
METHYLPREDNISOLONE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
MINOCYCLINE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
MOMETASONE	3 (16.7)	1 (6.3)	3 (17.6)	4 (12.1)	7 (13.7)
MONTELUKAST	1 (5.6)	1 (6.3)	1 (5.9)	2 (6.1)	3 (5.9)
MOSAPRIDE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
MOXIFLOXACIN	1 (5.6)	0	0	0	1 (2.0)
MYDRIN P	1 (5.6)	0	0	0	1 (2.0)
NADIFLOXACIN	0	0	1 (5.9)	1 (3.0)	1 (2.0)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
NEO-MEDROL EYE-EAR	0	1 (6.3)	1 (5.9)	2 (6.1)	2 (3.9)
NIFEDIPINE	1 (5.6)	0	0	0	1 (2.0)
OFLOXACIN	1 (5.6)	0	0	0	1 (2.0)
OGIKENCHUTO	1 (5.6)	0	0	0	1 (2.0)
OLOPATADINE	7 (38.9)	8 (50.0)	7 (41.2)	15 (45.5)	22 (43.1)
ORENGEDOKUTO	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
OSMOTAN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
OTHER DERMATOLOGICAL PREPARATIONS	1 (5.6)	0	0	0	1 (2.0)
PARACETAMOL	1 (5.6)	1 (6.3)	1 (5.9)	2 (6.1)	3 (5.9)
PARAFFIN SOFT	0	0	1 (5.9)	1 (3.0)	1 (2.0)
PETROLATUM	0	1 (6.3)	0	1 (3.0)	1 (2.0)
PITAVASTATIN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
POLAPREZINC	0	0	1 (5.9)	1 (3.0)	1 (2.0)
POVIDONE-IODINE	1 (5.6)	0	0	0	1 (2.0)
PRANLUKAST	1 (5.6)	1 (6.3)	1 (5.9)	2 (6.1)	3 (5.9)
PREDNISOLONE	10 (55.6)	7 (43.8)	11 (64.7)	18 (54.5)	28 (54.9)
PROCATEROL	1 (5.6)	0	0	0	1 (2.0)
REBAMIPIDE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
RESERPINE	1 (5.6)	0	0	0	1 (2.0)
RILMAZAFONE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ROSUVASTATIN	1 (5.6)	0	0	0	1 (2.0)
RUPATADINE	1 (5.6)	2 (12.5)	1 (5.9)	3 (9.1)	4 (7.8)
SALICYLIC ACID	1 (5.6)	4 (25.0)	0	4 (12.1)	5 (9.8)
SERETIDE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
STELAMIN	0	1 (6.3)	2 (11.8)	3 (9.1)	3 (5.9)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
SUPLATAST TOSILATE	1 (5.6)	0	3 (17.6)	3 (9.1)	4 (7.8)
TACALCITOL	0	0	1 (5.9)	1 (3.0)	1 (2.0)
TACROLIMUS	12 (66.7)	10 (62.5)	8 (47.1)	18 (54.5)	30 (58.8)
TELMISARTAN	1 (5.6)	0	0	0	1 (2.0)
TENELIGLIPTIN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
TERRA-CORTRIL	1 (5.6)	0	0	0	1 (2.0)
TOKIINSHI	0	1 (6.3)	0	1 (3.0)	1 (2.0)
TRALOKINUMAB	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
TRANEXAMIC ACID	0	0	1 (5.9)	1 (3.0)	1 (2.0)
TRANILAST	2 (11.1)	0	0	0	2 (3.9)
UFENAMATE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
UREA	3 (16.7)	2 (12.5)	4 (23.5)	6 (18.2)	9 (17.6)
VALISONE-G	1 (5.6)	3 (18.8)	5 (29.4)	8 (24.2)	9 (17.6)
VONOPRAZAN	0	0	1 (5.9)	1 (3.0)	1 (2.0)
WHITE SOFT PARAFFIN	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)
ZINC	2 (11.1)	5 (31.3)	3 (17.6)	8 (24.2)	10 (19.6)
ZOLMITRIPTAN	0	0	1 (5.9)	1 (3.0)	1 (2.0)
ZOLPIDEM	0	1 (6.3)	0	1 (3.0)	1 (2.0)

Note: All medications with a start date prior to the first study drug dose are included. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

相互参照：M16-047 試験 W16 Japan Study Data Table 14.1　7.1_J

表 2.7.3.6-84.　　併用薬（二重盲検投与期）（ITT_M 集団，日本人部分集団）：M16-047 試験

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
Any Concomitant Medications	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)
ACETAZOLAMIDE	1 (5.6)	0	0	0	1 (2.0)
ACETYLSALICYLIC ACID	1 (5.6)	0	0	0	1 (2.0)
ALENDRONIC ACID	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ALLOPURINOL	1 (5.6)	0	0	0	1 (2.0)
ALUMINIUM HYDROXIDE GEL, DRIED W/CAFFEINE/IBU	1 (5.6)	0	0	0	1 (2.0)
AMLODIPINE	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
AMOXICILLIN	2 (11.1)	0	0	0	2 (3.9)
ANTIVIRALS FOR SYSTEMIC USE	0	3 (18.8)	0	3 (9.1)	3 (5.9)
ARIPIPRAZOLE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ATORVASTATIN	1 (5.6)	1 (6.3)	1 (5.9)	2 (6.1)	3 (5.9)
ATROPINE	1 (5.6)	0	0	0	1 (2.0)
AUGMENTIN	1 (5.6)	0	0	0	1 (2.0)
AZILSARTAN	1 (5.6)	0	0	0	1 (2.0)
AZITHROMYCIN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
BACTRIM	0	0	1 (5.9)	1 (3.0)	1 (2.0)
BENFOTIAMINE;CAFFEINE;CLEMASTINE FUMARATE;DIH	0	1 (6.3)	0	1 (3.0)	1 (2.0)
BENPROPERINE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
BENZOYL PEROXIDE	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
BEPOTASTINE	0	1 (6.3)	2 (11.8)	3 (9.1)	3 (5.9)
BETAMETHASONE	2 (11.1)	1 (6.3)	0	1 (3.0)	3 (5.9)
BILASTINE	4 (22.2)	4 (25.0)	3 (17.6)	7 (21.2)	11 (21.6)
BIOTIN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
BISOPROLOL	1 (5.6)	0	0	0	1 (2.0)
BREO ELLIPTA	0	1 (6.3)	0	1 (3.0)	1 (2.0)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
BROMFENAC	1 (5.6)	0	0	0	1 (2.0)
BROMHEXINE HYDROCHLORIDE;CLEMASTINE FUMARATE;	0	1 (6.3)	0	1 (3.0)	1 (2.0)
BROTIZOLAM	0	1 (6.3)	0	1 (3.0)	1 (2.0)
BUDESONIDE W/FORMOTEROL FUMARATE	0	2 (12.5)	0	2 (6.1)	2 (3.9)
BUFFERIN A	1 (5.6)	0	0	0	1 (2.0)
CANDESARTAN	1 (5.6)	0	0	0	1 (2.0)
CARBOCISTEINE	2 (11.1)	1 (6.3)	1 (5.9)	2 (6.1)	4 (7.8)
CARVEDILOL	1 (5.6)	0	0	0	1 (2.0)
CEFACLOR	1 (5.6)	0	0	0	1 (2.0)
CEFDITOREN	1 (5.6)	2 (12.5)	0	2 (6.1)	3 (5.9)
CLARITHROMYCIN	0	0	1 (5.9)	1 (3.0)	1 (2.0)
CLOBETASOL	4 (22.2)	0	0	0	4 (7.8)
CLOSTRIDIUM BUTYRICUM	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
CODEINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
COSOPT	1 (5.6)	0	0	0	1 (2.0)
DESLORATADINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
DESOXIMETASONE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
DEXAMETHASONE	4 (22.2)	0	0	0	4 (7.8)
DEXTROMETHORPHAN	1 (5.6)	2 (12.5)	1 (5.9)	3 (9.1)	4 (7.8)
DIFLORASONE	1 (5.6)	0	0	0	1 (2.0)
DIPHENHYDRAMINE	1 (5.6)	0	0	0	1 (2.0)
DIPHENHYDRAMINE HYDROCHLORIDE;LIDOCAINE;UREA	0	0	1 (5.9)	1 (3.0)	1 (2.0)
DOXYCYCLINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
EBASTINE	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
ENTEROCOCCUS FAECALIS	0	1 (6.3)	0	1 (3.0)	1 (2.0)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
EPINASTINE	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
ESCITALOPRAM	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ESOMEPRAZOLE	2 (11.1)	0	1 (5.9)	1 (3.0)	3 (5.9)
ETIZOLAM	0	1 (6.3)	0	1 (3.0)	1 (2.0)
EVE A	0	0	1 (5.9)	1 (3.0)	1 (2.0)
FAMOTIDINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
FELBINAC	0	1 (6.3)	0	1 (3.0)	1 (2.0)
FENOFIBRATE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
FEXOFENADINE	3 (16.7)	4 (25.0)	4 (23.5)	8 (24.2)	11 (21.6)
FLUOCINOLONE ACETONIDE	9 (50.0)	8 (50.0)	7 (41.2)	15 (45.5)	24 (47.1)
FLUOROMETHOLONE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
FLUTICASONE	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
FOSFOMYCIN	1 (5.6)	0	0	0	1 (2.0)
HEPARINOID	4 (22.2)	8 (50.0)	5 (29.4)	13 (39.4)	17 (33.3)
HUSCODE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
HYDROCORTISONE	1 (5.6)	0	0	0	1 (2.0)
HYDROXYZINE	2 (11.1)	0	1 (5.9)	1 (3.0)	3 (5.9)
HYZAAR	0	1 (6.3)	0	1 (3.0)	1 (2.0)
IRON	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ISONIAZID	2 (11.1)	0	0	0	2 (3.9)
KETOCONAZOLE	1 (5.6)	0	0	0	1 (2.0)
KIKYOTO	1 (5.6)	0	0	0	1 (2.0)
LANINAMIVIR	1 (5.6)	0	0	0	1 (2.0)
LANSOPRAZOLE	0	0	2 (11.8)	2 (6.1)	2 (3.9)
LATANOPROST	1 (5.6)	0	0	0	1 (2.0)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
LEVOCETIRIZINE	3 (16.7)	1 (6.3)	1 (5.9)	2 (6.1)	5 (9.8)
LEVOFLOXACIN	0	1 (6.3)	2 (11.8)	3 (9.1)	3 (5.9)
LORATADINE	1 (5.6)	0	0	0	1 (2.0)
LOXOPROFEN	1 (5.6)	2 (12.5)	4 (23.5)	6 (18.2)	7 (13.7)
LUSEOGLIFLOZIN	0	0	1 (5.9)	1 (3.0)	1 (2.0)
METFORMIN	0	1 (6.3)	1 (5.9)	2 (6.1)	2 (3.9)
MINOCYCLINE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
MOMETASONE	5 (27.8)	3 (18.8)	2 (11.8)	5 (15.2)	10 (19.6)
MONTELUKAST	1 (5.6)	2 (12.5)	1 (5.9)	3 (9.1)	4 (7.8)
MOSAPRIDE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
MOXIFLOXACIN	1 (5.6)	0	0	0	1 (2.0)
MUBEN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
MYDRIN P	1 (5.6)	0	0	0	1 (2.0)
NADIFLOXACIN	2 (11.1)	0	2 (11.8)	2 (6.1)	4 (7.8)
NIFEDIPINE	1 (5.6)	0	0	0	1 (2.0)
OLOPATADINE	3 (16.7)	7 (43.8)	5 (29.4)	12 (36.4)	15 (29.4)
OSELTAMIVIR	0	0	1 (5.9)	1 (3.0)	1 (2.0)
OSMOTAN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
OTHER DERMATOLOGICAL PREPARATIONS	1 (5.6)	0	0	0	1 (2.0)
PA	1 (5.6)	0	1 (5.9)	1 (3.0)	2 (3.9)
PABRON GOLD A	0	0	1 (5.9)	1 (3.0)	1 (2.0)
PARACETAMOL	2 (11.1)	2 (12.5)	1 (5.9)	3 (9.1)	5 (9.8)
PENCICLOVIR	0	1 (6.3)	0	1 (3.0)	1 (2.0)
PITAVASTATIN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
POLAPREZINC	0	0	1 (5.9)	1 (3.0)	1 (2.0)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
POVIDONE-IODINE	1 (5.6)	0	0	0	1 (2.0)
PRANLUKAST	1 (5.6)	1 (6.3)	2 (11.8)	3 (9.1)	4 (7.8)
PREDNICARBATE	1 (5.6)	0	0	0	1 (2.0)
PREDNISOLONE	14 (77.8)	16 (100)	16 (94.1)	32 (97.0)	46 (90.2)
PROCATEROL	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
PYRIDOXAL	1 (5.6)	0	0	0	1 (2.0)
REBAMIPIDE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
RILMAZAFONE	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ROSUVASTATIN	1 (5.6)	0	0	0	1 (2.0)
RUPATADINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
SCHWEFEL-DIASPORAL	1 (5.6)	0	0	0	1 (2.0)
SENNA ALEXANDRINA	0	1 (6.3)	0	1 (3.0)	1 (2.0)
SERETIDE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
SQUARIC ACID	0	0	1 (5.9)	1 (3.0)	1 (2.0)
TACROLIMUS	2 (11.1)	3 (18.8)	4 (23.5)	7 (21.2)	9 (17.6)
TAISHO KAMPO ICHOYAKU	0	1 (6.3)	0	1 (3.0)	1 (2.0)
TELMISARTAN	1 (5.6)	0	0	0	1 (2.0)
TENELIGLIPTIN	0	1 (6.3)	0	1 (3.0)	1 (2.0)
THEOPHYLLINE	0	0	1 (5.9)	1 (3.0)	1 (2.0)
TIARAMIDE	1 (5.6)	1 (6.3)	0	1 (3.0)	2 (3.9)
TRANEXAMIC ACID	0	0	2 (11.8)	2 (6.1)	2 (3.9)
TRIAMCINOLONE	8 (44.4)	7 (43.8)	8 (47.1)	15 (45.5)	23 (45.1)
UREA	0	0	1 (5.9)	1 (3.0)	1 (2.0)
VONOPRAZAN	0	0	1 (5.9)	1 (3.0)	1 (2.0)
WHITE SOFT PARAFFIN	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

Generic Name (WHO Q1_2018)	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
ZANAMIVIR	0	1 (6.3)	0	1 (3.0)	1 (2.0)
ZINC	2 (11.1)	2 (12.5)	1 (5.9)	3 (9.1)	5 (9.8)
ZOLMITRIPTAN	0	0	1 (5.9)	1 (3.0)	1 (2.0)
ZOLPIDEM	0	1 (6.3)	0	1 (3.0)	1 (2.0)

Note: This table includes all medications administered during DB Period (i.e., first study drug dose through the final study drug dose in DB Period). Thus all medications with an end date prior to the first study drug dose are excluded. Subjects are counted once in each row, regardless of the number of medications they may have taken.

Program Source Code: [redacted]

相互参照：M16-047 試験 W16 Japan Study Data Table 14.1　7.2.1_J

表 2.7.3.6-85.　被験者の内訳（二重盲検投与期）（ITT_M 集団，日本人部分集団）：M16-047 試験

Status	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
Randomized	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)
Never Received Any Study Drug	0	0	0	0	0
Received Randomized Study Drug	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)
Received Rescue Medication	7 (38.9)	1 (6.3)	1 (5.9)	2 (6.1)	9 (17.6)
Completed DB Period	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)
Discontinued Study in DB Period	0	0	0	0	0
All Reasons for Discontinuation$					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	0	0	0
Lost to Follow-up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Status	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
Completed Study Drug in DB Period	17 (94.4)	16 (100)	17 (100)	33 (100)	50 (98.0)
Ongoing Study Drug in DB Period	0	0	0	0	0
Discontinued Study Drug in DB Period	1 (5.6)	0	0	0	1 (2.0)
All Reasons for Discontinuation$					
Adverse Event	1 (5.6)	0	0	0	1 (2.0)
Withdrawal Consent	1 (5.6)	0	0	0	1 (2.0)
Lost to Follow-up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria was Met	0	0	0	0	0
Protocol-mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Status	Placebo + TCS (N=18) n (%)	Active: UPA 15 mg QD + TCS (N=16) n (%)	Active: UPA 30 mg QD + TCS (N=17) n (%)	Active: Total (N=33) n (%)	Total (N=51) n (%)
Primary Reason for Discontinuation					
Adverse Event	1 (5.6)	0	0	0	1 (2.0)
Withdrawal Consent	0	0	0	0	0
Lost to Follow-up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria was Met	0	0	0	0	0
Protocol-mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

相互参照：M16-047 試験 W16 Japan Study Data Table 14.1　3.1.1_J

表 2.7.3.6-86.　人口統計学的特性の要約（ITT_M 集団，日本人部分集団）：M16-047 試験（投与 52 週時データカットオフ）

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Sex - n (%)					
Female	3 (16.7)	4 (25.0)	2 (11.8)	6 (18.2)	9 (17.6)
Male	15 (83.3)	12 (75.0)	15 (88.2)	27 (81.8)	42 (82.4)
Age Group 1 (years) - n (%)					
< 18	0	0	0	0	0
>= 18	18 (100)	16 (100)	17 (100)	33 (100)	51 (100)
Age Group 2 (years) - n (%)					
< 18	0	0	0	0	0
18 - < 40	7 (38.9)	9 (56.3)	10 (58.8)	19 (57.6)	26 (51.0)
40 - < 65	11 (61.1)	7 (43.8)	7 (41.2)	14 (42.4)	25 (49.0)
>= 65	0	0	0	0	0
Age (years)					
n	18	16	17	33	51
Mean (SD)	39.9 (10.99)	37.4 (10.68)	36.5 (10.25)	36.9 (10.31)	38.0 (10.54)
Median	43.5	35.5	34.0	35.0	39.0
Min, Max	21, 55	20, 57	23, 53	20, 57	20, 57

Note: Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Weight (kg)					
n	18	16	17	33	51
Mean (SD)	69.14 (12.041)	66.36 (10.660)	68.36 (13.326)	67.39 (11.962)	68.01 (11.899)
Median	68.80	65.35	69.90	65.80	65.80
Min, Max	48.6, 88.2	48.5, 91.6	48.5, 103.4	48.5, 103.4	48.5, 103.4
Height (cm)					
n	18	16	17	33	51
Mean (SD)	169.23 (8.340)	164.66 (7.693)	170.16 (6.002)	167.49 (7.318)	168.11 (7.657)
Median	172.35	163.75	170.30	169.00	169.80
Min, Max	154.5, 178.5	152.8, 176.3	158.0, 179.5	152.8, 179.5	152.8, 179.5
Body Mass Index (kg/m^2)					
n	18	16	17	33	51
Mean (SD)	24.05 (3.374)	24.48 (3.529)	23.68 (4.856)	24.07 (4.219)	24.06 (3.906)
Median	24.95	23.60	22.80	22.80	23.30
Min, Max	19.4, 31.3	19.9, 30.3	17.0, 35.5	17.0, 35.5	17.0, 35.5
Body Mass Index (kg/m^2) - n (%)					
< 25	9 (50.0)	9 (56.3)	11 (64.7)	20 (60.6)	29 (56.9)
25 - < 30	8 (44.4)	6 (37.5)	4 (23.5)	10 (30.3)	18 (35.3)
>= 30	1 (5.6)	1 (6.3)	2 (11.8)	3 (9.1)	4 (7.8)

Note: Percentages calculated on non-missing values.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Tobacco$ - n (%)					
Current	5 (27.8)	4 (25.0)	5 (29.4)	9 (27.3)	14 (27.5)
Former	4 (22.2)	2 (12.5)	2 (11.8)	4 (12.1)	8 (15.7)
Never	9 (50.0)	10 (62.5)	10 (58.8)	20 (60.6)	29 (56.9)
Unknown	0	0	0	0	0
Alcohol$ - n (%)					
Current	16 (88.9)	12 (75.0)	16 (94.1)	28 (84.8)	44 (86.3)
Former	0	2 (12.5)	0	2 (6.1)	2 (3.9)
Never	2 (11.1)	2 (12.5)	1 (5.9)	3 (9.1)	5 (9.8)
Unknown	0	0	0	0	0

Note: Percentages calculated on non-missing values.
$ Percentages calculated on non-missing/non-unknown values. A subject may be a current user of one type of tobacco, a former user of another type of tobacco and never used another type of tobacco. A subject will be counted in the category closest to user.

Program Source Code: [redacted]

相互参照：M16-047 試験 W52 Japan Study Data Table 14.1__3.1_J

表 2.7.3.6-87.　ベースラインのその他の基準値の特性の要約（ITT_M 集団，日本人部分集団）：M16-047 試験（投与 52 週時データカットオフ）

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Baseline vIGA-AD - n (%)					
3 (Moderate)	5 (27.8)	4 (25.0)	4 (23.5)	8 (24.2)	13 (25.5)
4 (Severe)	13 (72.2)	12 (75.0)	13 (76.5)	25 (75.8)	38 (74.5)
Baseline EASI - n (%)					
< Median (25.8)	7 (38.9)	6 (37.5)	4 (23.5)	10 (30.3)	17 (33.3)
>= Median (25.8)	11 (61.1)	10 (62.5)	13 (76.5)	23 (69.7)	34 (66.7)
hsCRP - n (%)					
< Median (1.41)	10 (55.6)	10 (62.5)	10 (58.8)	20 (60.6)	30 (58.8)
>= Median (1.41)	8 (44.4)	6 (37.5)	7 (41.2)	13 (39.4)	21 (41.2)
Previous Systemic Therapy - n (%)					
With	7 (38.9)	10 (62.5)	10 (58.8)	20 (60.6)	27 (52.9)
Without	11 (61.1)	6 (37.5)	7 (41.2)	13 (39.4)	24 (47.1)

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
EASI					
n	18	16	17	33	51
Mean (SD)	33.94 (12.512)	30.71 (13.177)	36.54 (12.114)	33.71 (12.788)	33.79 (12.566)
Median	33.35	26.60	37.20	34.20	34.20
Min, Max	16.3, 60.0	16.1, 63.5	18.2, 60.6	16.1, 63.5	16.1, 63.5
EASI Head/Neck					
n	18	16	17	33	51
Mean (SD)	3.42 (2.016)	3.31 (1.740)	3.87 (1.609)	3.60 (1.672)	3.54 (1.783)
Median	3.80	3.00	3.20	3.20	3.20
Min, Max	0.0, 6.0	0.5, 7.2	1.6, 6.6	0.5, 7.2	0.0, 7.2
EASI Lower Limbs					
n	18	16	17	33	51
Mean (SD)	13.16 (5.593)	10.83 (6.525)	14.61 (6.614)	12.78 (6.747)	12.91 (6.309)
Median	11.60	8.40	14.40	12.80	12.80
Min, Max	5.6, 24.0	0.8, 24.0	2.0, 28.8	0.8, 28.8	0.8, 28.8

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
EASI Trunk					
n	18	16	17	33	51
Mean (SD)	10.97 (4.852)	10.28 (5.175)	11.33 (4.625)	10.82 (4.851)	10.87 (4.803)
Median	11.40	10.50	12.00	12.00	12.00
Min, Max	0.3, 18.0	2.4, 21.6	3.6, 18.0	2.4, 21.6	0.3, 21.6
EASI Upper Limbs					
n	18	16	17	33	51
Mean (SD)	6.40 (2.810)	6.30 (3.733)	6.73 (2.557)	6.52 (3.138)	6.48 (2.999)
Median	6.00	5.50	6.40	6.00	6.00
Min, Max	2.0, 12.0	1.2, 14.4	3.2, 13.2	1.2, 14.4	1.2, 14.4
BSA in Percentage					
n	18	16	17	33	51
Mean (SD)	66.61 (17.191)	59.47 (19.719)	66.29 (18.213)	62.98 (18.977)	64.26 (18.276)
Median	68.50	58.50	70.00	63.00	65.00
Min, Max	36.0, 94.0	28.0, 92.0	38.0, 92.0	28.0, 92.0	28.0, 94.0

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Overall SCORAD Score					
n	18	16	17	33	51
Mean (SD)	68.108 (14.6800)	66.170 (15.4773)	73.993 (9.6419)	70.200 (13.2111)	69.462 (13.6379)
Median	67.800	66.050	71.940	70.000	69.100
Min, Max	40.70, 89.30	41.50, 94.40	55.70, 88.00	41.50, 94.40	40.70, 94.40
Objective SCORAD					
n	18	16	17	33	51
Mean (SD)	52.663 (14.7820)	52.358 (14.0048)	58.758 (7.9911)	55.655 (11.5939)	54.599 (12.7438)
Median	49.800	50.050	58.000	55.900	54.300
Min, Max	31.70, 77.60	31.50, 81.40	46.10, 71.00	31.50, 81.40	31.50, 81.40
SCORAD Itch					
n	18	16	17	33	51
Mean (SD)	7.9 (1.80)	7.9 (1.24)	8.2 (1.19)	8.1 (1.20)	8.0 (1.42)
Median	8.5	8.0	8.0	8.0	8.0
Min, Max	4, 10	6, 10	6, 10	6, 10	4, 10

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
SCORAD Sleep					
n	18	16	17	33	51
Mean (SD)	7.5 (2.57)	5.9 (2.45)	7.1 (2.08)	6.5 (2.31)	6.8 (2.43)
Median	8.0	7.0	7.0	7.0	7.0
Min, Max	1, 10	0, 9	1, 10	0, 10	0, 10
DLQI					
n	18	16	17	33	51
Mean (SD)	14.9 (6.45)	11.8 (5.58)	14.2 (7.22)	13.0 (6.50)	13.7 (6.48)
Median	14.5	12.5	14.0	13.0	14.0
Min, Max	6, 28	0, 21	2, 25	0, 25	0, 28
HADS Total Score					
n	18	16	17	33	51
Mean (SD)	14.2 (8.41)	11.8 (8.14)	12.8 (8.62)	12.3 (8.27)	13.0 (8.29)
Median	13.0	12.0	11.0	11.0	12.0
Min, Max	4, 33	1, 28	1, 30	1, 30	1, 33

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
HADS-A Total Score					
n	18	16	17	33	51
Mean (SD)	7.3 (4.90)	5.9 (4.37)	6.8 (4.46)	6.4 (4.37)	6.7 (4.54)
Median	6.0	5.0	7.0	5.0	6.0
Min, Max	2, 19	0, 14	1, 15	0, 15	0, 19
HADS-D Total Score					
n	18	16	17	33	51
Mean (SD)	6.9 (4.20)	5.9 (4.26)	5.9 (4.51)	5.9 (4.32)	6.3 (4.26)
Median	6.5	6.0	5.0	5.0	6.0
Min, Max	1, 14	0, 14	0, 17	0, 17	0, 17
WPAI: AD: Absenteeism (%)					
n	4	3	3	6	10
Mean (SD)	1.362 (1.6802)	11.111 (19.2450)	24.119 (21.0808)	17.615 (19.4080)	11.114 (16.7525)
Median	1.000	0.000	33.333	16.667	1.000
Min, Max	0.00, 3.45	0.00, 33.33	0.00, 39.02	0.00, 39.02	0.00, 39.02

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
WPAI: AD: Presenteeism (%)					
n	4	3	3	6	10
Mean (SD)	62.5 (17.08)	56.7 (28.87)	70.0 (17.32)	63.3 (22.51)	63.0 (19.47)
Median	65.0	40.0	80.0	65.0	65.0
Min, Max	40, 80	40, 90	50, 80	40, 90	40, 90
WPAI: AD: Work Productivity Loss (%)					
n	4	3	3	6	10
Mean (SD)	62.822 (17.4027)	63.333 (25.1661)	78.157 (10.6889)	70.745 (19.1039)	67.576 (17.9010)
Median	65.300	60.000	80.000	73.333	68.633
Min, Max	40.00, 80.69	40.00, 90.00	66.67, 87.80	40.00, 90.00	40.00, 90.00
WPAI: AD: Activity Impairment (%)					
n	18	16	17	33	51
Mean (SD)	69.4 (18.62)	51.3 (25.79)	68.8 (19.00)	60.3 (23.91)	63.5 (22.43)
Median	65.0	55.0	70.0	70.0	70.0
Min, Max	30, 100	0, 80	30, 100	0, 100	0, 100

Note: Percentages calculated on non-missing values.
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Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
EQ-5D-5L Index					
n	18	16	17	33	51
Mean (SD)	0.6106 (0.34800)	0.7534 (0.19625)	0.6323 (0.30095)	0.6910 (0.25907)	0.6626 (0.29264)
Median	0.6875	0.8495	0.7400	0.8030	0.7400
Min, Max	-0.153, 1.000	0.414, 1.000	0.070, 1.000	0.070, 1.000	-0.153, 1.000
EQ-5D-5L VAS Score					
n	18	16	17	33	51
Mean (SD)	45.4 (28.23)	56.1 (24.02)	50.5 (21.77)	53.2 (22.71)	50.4 (24.80)
Median	42.5	53.5	50.0	50.0	50.0
Min, Max	5, 95	20, 95	9, 91	9, 95	5, 95
Worst Pruritus NRS (Weekly Average)					
n	18	16	17	33	51
Mean (SD)	6.996 (1.8311)	7.069 (1.4138)	7.905 (1.5300)	7.500 (1.5124)	7.322 (1.6319)
Median	7.357	7.043	7.429	7.286	7.286
Min, Max	4.25, 10.00	4.71, 9.86	5.71, 10.00	4.71, 10.00	4.25, 10.00

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
PGIS					
n	18	16	17	33	51
Mean (SD)	4.9 (0.90)	4.3 (1.00)	4.2 (1.03)	4.2 (1.00)	4.5 (1.01)
Median	5.0	4.0	4.0	4.0	4.0
Min, Max	3, 6	3, 6	3, 6	3, 6	3, 6
PGIS - n (%)					
Absent	0	0	0	0	0
Minimal	0	0	0	0	0
Mild	0	0	0	0	0
Moderate	1 (5.6)	4 (25.0)	5 (29.4)	9 (27.3)	10 (19.6)
Moderately Severe	5 (27.8)	6 (37.5)	5 (29.4)	11 (33.3)	16 (31.4)
Severe	7 (38.9)	4 (25.0)	5 (29.4)	9 (27.3)	16 (31.4)
Very Severe	5 (27.8)	2 (12.5)	2 (11.8)	4 (12.1)	9 (17.6)

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
PGIT - n (%)					
Extremely Dissatisfied	3 (16.7)	2 (12.5)	2 (11.8)	4 (12.1)	7 (13.7)
Very Dissatisfied	0	1 (6.3)	3 (17.6)	4 (12.1)	4 (7.8)
Somewhat Dissatisfied	2 (11.1)	1 (6.3)	6 (35.3)	7 (21.2)	9 (17.6)
Neither Dissatisfied nor Satisfied	8 (44.4)	5 (31.3)	4 (23.5)	9 (27.3)	17 (33.3)
Somewhat Satisfied	4 (22.2)	7 (43.8)	2 (11.8)	9 (27.3)	13 (25.5)
Very Satisfied	1 (5.6)	0	0	0	1 (2.0)
Extremely Satisfied	0	0	0	0	0
ADerm-SS Skin Pain					
n	18	16	17	33	51
Mean (SD)	6.420 (1.8550)	5.169 (2.2523)	6.768 (2.4121)	5.992 (2.4383)	6.144 (2.2400)
Median	5.536	4.786	6.571	6.143	6.143
Min, Max	3.14, 10.00	1.71, 8.43	0.43, 10.00	0.43, 10.00	0.43, 10.00
ADerm-SS TSS-7					
n	18	16	17	33	51
Mean (SD)	42.9 (13.99)	40.3 (13.45)	48.9 (13.49)	44.8 (13.96)	44.1 (13.86)
Median	41.0	37.5	46.0	43.0	43.0
Min, Max	15, 70	17, 62	19, 70	17, 70	15, 70

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
ADerm-SS TSS-11					
n	18	16	17	33	51
Mean (SD)	65.4 (22.03)	60.8 (21.18)	73.7 (22.72)	67.4 (22.62)	66.7 (22.21)
Median	62.5	55.5	72.0	64.0	64.0
Min, Max	20, 110	28, 96	19, 110	19, 110	19, 110
ADerm-IS Sleep Domain Score					
n	18	16	17	33	51
Mean (SD)	18.160 (5.7716)	16.160 (8.9905)	21.815 (5.5275)	19.073 (7.8360)	18.751 (7.1287)
Median	16.786	20.214	21.714	21.143	20.286
Min, Max	5.00, 30.00	2.67, 29.29	9.00, 30.00	2.67, 30.00	2.67, 30.00
ADerm-IS Daily Activities Domain Score					
n	18	16	17	33	51
Mean (SD)	21.6 (8.68)	17.8 (11.51)	25.2 (7.80)	21.6 (10.33)	21.6 (9.69)
Median	23.0	20.0	23.0	21.0	22.0
Min, Max	5, 37	0, 35	12, 38	0, 38	0, 38

Note: Percentages calculated on non-missing values.
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Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
ADerm-IS Emotional State Domain Score					
n	18	16	17	33	51
Mean (SD)	18.9 (7.08)	15.6 (10.70)	19.9 (7.32)	17.8 (9.23)	18.2 (8.48)
Median	18.5	17.5	19.0	18.0	18.0
Min, Max	3, 30	0, 30	7, 30	0, 30	0, 30
POEM					
n	18	16	17	33	51
Mean (SD)	19.8 (5.48)	19.4 (4.96)	21.1 (5.73)	20.3 (5.36)	20.1 (5.36)
Median	20.0	19.5	21.0	20.0	20.0
Min, Max	9, 28	11, 27	10, 28	10, 28	9, 28
DIS					
n	18	16	17	33	51
Mean (SD)	29.6 (18.07)	24.9 (18.98)	22.9 (17.99)	23.8 (18.21)	25.9 (18.19)
Median	25.5	26.0	17.0	18.0	25.0
Min, Max	4, 68	0, 51	0, 58	0, 58	0, 68

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

	Placebo + TCS (N=18)	Active: UPA 15 mg QD + TCS (N=16)	Active: UPA 30 mg QD + TCS (N=17)	Active: Total (N=33)	Total (N=51)
Disease Duration since Diagnosis (years)					
n	18	16	17	33	51
Mean (SD)	26.965 (16.7120)	29.777 (14.3166)	23.320 (15.6601)	26.450 (15.1471)	26.632 (15.5518)
Median	29.955	29.023	19.337	24.912	28.903
Min, Max	0.08, 50.95	4.13, 57.89	0.06, 53.39	0.06, 57.89	0.06, 57.89
Disease Duration since Symptoms Started (years)					
n	18	16	17	33	51
Mean (SD)	31.637 (15.5317)	30.970 (14.6667)	30.166 (12.1761)	30.555 (13.2336)	30.937 (13.9418)
Median	34.511	30.597	26.973	29.153	30.048
Min, Max	4.09, 51.72	4.13, 57.89	7.05, 53.39	4.13, 57.89	4.09, 57.89
Duration between Symptoms and Diagnosis (years)					
n	18	16	17	33	51
Mean (SD)	4.672 (8.2968)	1.193 (4.4892)	6.846 (12.4618)	4.105 (9.7635)	4.305 (9.1917)
Median	0.000	0.000	0.000	0.000	0.000
Min, Max	0.00, 22.00	0.00, 18.00	0.00, 46.86	0.00, 46.86	0.00, 46.86

Note: Percentages calculated on non-missing values.
vIGA-AD = validated Investigator Global Assessment for Atopic Dermatitis; POEM = Patient Oriented Eczema Measure; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression; WPAI: AD = Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis; PGIS = Patient Global Impression of Severity; PGIT = Patient Global Impression of Treatment; ADerm-SS = Atopic Dermatitis Symptom Scale; ADerm-IS = Atopic Dermatitis Impact Scale; DIS=Derm. Intimacy Scale.

Program Source Code: [redacted]

相互参照：M16-047 試験 W52 Japan Study Data Table 14.1　4.1_J

表 2.7.3.6-88.　被験者の内訳（盲検継続投与期）（ITT_M 集団，日本人部分集団）：M16-047 試験（投与 52 週時データカットオフ）

Status	Placebo + TCS/ UPA 15 mg QD + TCS (N=9) n (%)	Placebo + TCS/ UPA 30 mg QD + TCS (N=9) n (%)	UPA 15 mg QD + TCS (N=16) n (%)	UPA 30 mg QD + TCS (N=17) n (%)	Total (N=51) n (%)
Entered BE Period	9 (100)	9 (100)	16 (100)	17 (100)	51 (100)
Never Received Any Study Drug in BE Period	1 (11.1)	0	0	0	1 (2.0)
Received Study Drug in BE Period	8 (88.9)	9 (100)	16 (100)	17 (100)	50 (98.0)
Received Rescue Medication in BE Period	1 (11.1)	1 (11.1)	3 (18.8)	0	5 (9.8)
Completed Study	0	0	0	0	0
Discontinued Study in BE Period	1 (11.1)	0	2 (12.5)	0	3 (5.9)
All Reasons for Discontinuation$					
Adverse Event	1 (11.1)	0	0	0	1 (2.0)
Withdrawal Consent	1 (11.1)	0	2 (12.5)	0	3 (5.9)
Lost to Follow-up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0
Primary Reason for Discontinuation					
Adverse Event	1 (11.1)	0	0	0	1 (2.0)
Withdrawal Consent	0	0	2 (12.5)	0	2 (3.9)
Lost to Follow-up	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Status	Placebo + TCS/ UPA 15 mg QD + TCS (N=9) n (%)	Placebo + TCS/ UPA 30 mg QD + TCS (N=9) n (%)	UPA 15 mg QD + TCS (N=16) n (%)	UPA 30 mg QD + TCS (N=17) n (%)	Total (N=51) n (%)
Completed Study Drug in BE Period	0	0	0	0	0
Ongoing Study Drug in BE Period	8 (88.9)	9 (100)	14 (87.5)	17 (100)	48 (94.1)
Discontinued Study Drug in BE Period	0	0	2 (12.5)	0	2 (3.9)
All Reasons for Discontinuation$					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	2 (12.5)	0	2 (3.9)
Lost to Follow-up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria was Met	0	0	0	0	0
Protocol-mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

Status	Placebo + TCS/ UPA 15 mg QD + TCS (N=9) n (%)	Placebo + TCS/ UPA 30 mg QD + TCS (N=9) n (%)	UPA 15 mg QD + TCS (N=16) n (%)	UPA 30 mg QD + TCS (N=17) n (%)	Total (N=51) n (%)
Primary Reason for Discontinuation					
Adverse Event	0	0	0	0	0
Withdrawal Consent	0	0	2 (12.5)	0	2 (3.9)
Lost to Follow-up	0	0	0	0	0
Lack of Efficacy	0	0	0	0	0
EASI Score - Worsening of 25% Criteria was Met	0	0	0	0	0
Protocol-mandated Discontinuation Due to Systemic Rescue	0	0	0	0	0
COVID-19 Infection	0	0	0	0	0
COVID-19 Logistical Restrictions	0	0	0	0	0
Other	0	0	0	0	0

Note: Percentages calculated based on 'N' in each treatment group.
$ Subjects who discontinued study or study drug are counted under each reason given for discontinuation, therefore, the sum of the counts given for the reasons may be greater than the overall number of discontinuations.

Program Source Code: [redacted]

相互参照：M16-047 試験 W52 Japan Study Data Table 14.1　2.1_J

表 2.7.3.6-89. 部分集団別の投与 16 週時の EASI スコアのベースラインからの変化率（%）（LOCF，第 1 ピリオドの ITT 集団）：M16-048 試験

						WITHIN GROUP -PERCENT CHANGE FORM BASELINE-		BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ----------			
SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	LSMEAN	SE	LSMEAN DIFF	95% CI	SE	P-VALUE [A]
AGE (YEARS)											
	<40										
		UPA 30 MG QD	22	28.8	6.4	-76.8	7.43	-55.7	(-76.3, -35.1)	10.36	<0.001***
		UPA 15 MG QD	25	33.9	14.6	-60.7	6.92	-39.7	(-59.5, -19.8)	9.99	<0.001***
		UPA 7.5 MG QD	22	34.6	24.1	-34.5	7.39	-13.4	(-33.9, 7.1)	10.32	0.197
		PLACEBO	23	32.8	26.4	-21.1	7.21				
	40-64										
		UPA 30 MG QD	17	27.1	6.0	-77.3	7.97	-24.6	(-50.9, 1.6)	13.09	0.065
		UPA 15 MG QD	14	27.6	9.1	-67.2	8.77	-14.5	(-41.7, 12.7)	13.55	0.290
		UPA 7.5 MG QD	16	27.7	12.8	-51.9	8.20	0.7	(-25.7, 27.2)	13.18	0.956
		PLACEBO	11	36.1	21.1	-52.7	10.20				
	>=65										
		UPA 30 MG QD	3	29.4	0.5	-99.0	17.19	-97.5	(-147.5, -47.5)	22.44	0.001**
		UPA 15 MG QD	3	28.4	0.0	-101.2	17.11	-99.7	(-149.3, -50.1)	22.25	0.001**
		UPA 7.5 MG QD	4	28.5	14.3	-61.1	14.85	-59.6	(-105.5, -13.8)	20.58	0.016*
		PLACEBO	5	20.0	18.8	-1 5	13.75				
TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.055											
SEX											
	MALE										
		UPA 30 MG QD	22	25.3	7.5	-69.5	7.41	-48.1	(-68.4, -27.8)	10.23	<0.001***
		UPA 15 MG QD	30	33.9	13.0	-65.6	6.21	-44.1	(-62.8, -25.4)	9.41	<0.001***
		UPA 7.5 MG QD	28	34.7	23.2	-36.7	6.45	-15.3	(-34.2, 3.7)	9.57	0.114
		PLACEBO	23	31.6	24.2	-21.4	7.07				
	FEMALE										
		UPA 30 MG QD	20	31.3	4.0	-89.5	7.70	-52.9	(-75.9, -29.9)	11.50	<0.001***

SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FORM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
		UPA 15 MG QD	12	25.2	8.6	-65.5	9.98	-28.9	(-55.6, -2.2)	13.35	0.035*
		UPA 7.5 MG QD	14	24.9	10.1	-56.5	9.27	-19.9	(-45.7, 5.8)	12.84	0.126
		PLACEBO	16	32.8	23.6	-36.6	8.66				
TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.568											
BMI (KG/M^2)											
	< 25										
		UPA 30 MG QD	20	26.8	3.6	-85.1	7.84	-68.0	(-89.7, -46.3)	10.90	<0.001***
		UPA 15 MG QD	18	31.8	12.5	-63.0	8.17	-45.9	(-68.1, -23.7)	11.13	<0.001***
		UPA 7.5 MG QD	16	35.2	24.3	-40.5	8.75	-23.5	(-46.5, -0.4)	11.56	0.046*
		PLACEBO	21	31.1	26.5	-17.0	7.56				
	25 -< 30										
		UPA 30 MG QD	11	31.0	11.4	-66.1	9.60	-39.8	(-68.0, -11.6)	13.96	0.007**
		UPA 15 MG QD	11	30.3	7.9	-75.6	9.61	-49.2	(-77.6, -20.9)	14.02	0.001**
		UPA 7.5 MG QD	13	26.1	16.2	-34.2	9.07	-7.9	(-36.2, 20.4)	14.02	0.575
		PLACEBO	11	39.3	28.4	-26.3	10.08				
	30 -< 40										
		UPA 30 MG QD	9	26.4	4.7	-76.6	11.11	-38.3	(-76.5, -0.1)	18.75	0.049*
		UPA 15 MG QD	12	30.2	13.1	-63.1	9.58	-24.8	(-62.1, 12.5)	18.31	0.185
		UPA 7.5 MG QD	11	34.0	16.0	-63.8	10.26	-25.6	(-64.5, 13.2)	19.07	0.189
		PLACEBO	5	19.4	11.0	-38.2	15.44				
	>= 40										
		UPA 30 MG QD	2	34.6	3.2	-80.4	29.69	6.9	(-173.5, 187.3)	41.93	0.885
		UPA 15 MG QD	1	52.1	25.0	-33.3	48.71	54.1	(-189.6, 297.7)	56.63	0.441
		UPA 7.5 MG QD	2	22.0	8.0	-63.8	33.20	23.6	(-169.3, 216.4)	44.82	0.652
		PLACEBO	2	34.0	4.7	-87.3	29.66				
TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.144											

SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FORM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
RACE											
	WHITE										
		UPA 30 MG QD	23	29.4	5.9	-80.3	6.87	-58.9	(-77.5, -40.3)	9.37	<0.001***
		UPA 15 MG QD	21	26.7	10.1	-65.2	7.25	-43.8	(-63.0, -24.5)	9.69	<0.001***
		UPA 7.5 MG QD	24	32.6	18.9	-45.6	6.75	-24.2	(-42.6, -5.9)	9.23	0.010**
		PLACEBO	27	32.3	26.3	-21.4	6.35				
	ASIAN										
		UPA 30 MG QD	13	24.6	6.2	-80.2	10.10	-49.1	(-84.5, -13.8)	17.36	0.008**
		UPA 15 MG QD	9	37.8	15.9	-51.0	11.84	-19.8	(-57.5, 17.9)	18.51	0.292
		UPA 7.5 MG QD	9	36.9	28.2	-17.8	11.77	13.3	(-24.3, 50.9)	18.46	0.475
		PLACEBO	6	31.2	18.7	-31.1	14.18				
	OTHER										
		UPA 30 MG QD	6	31.3	4.6	-82.1	14.02	-28.6	(-69.2, 12.0)	19.83	0.160
		UPA 15 MG QD	12	34.8	11.6	-75.0	10.11	-21.5	(-56.7, 13.8)	17.21	0.223
		UPA 7.5 MG QD	9	22.7	9.4	-57.7	11.94	-4.2	(-42.2, 33.8)	18.56	0.824
		PLACEBO	6	32.0	18.4	-53.5	14.04				
TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.564											
WEIGHT											
	< MEDIAN (76.5 KG)										
		UPA 30 MG QD	21	27.8	4.5	-83.4	7.71	-69.3	(-90.5, -48.0)	10.67	<0.001***
		UPA 15 MG QD	18	32.3	13.0	-62.1	8.26	-48.0	(-69.9, -26.0)	11.03	<0.001***
		UPA 7.5 MG QD	19	32.8	22.0	-40.2	8.05	-26.1	(-47.7, -4.5)	10.86	0.019*
		PLACEBO	23	33.0	29.0	-14.1	7.32				
	>= MEDIAN (76.5 KG)										
		UPA 30 MG QD	21	28.5	7.2	-73.7	7.09	-27.1	(-48.6, -5.7)	10.77	0.014*
		UPA 15 MG QD	24	30.8	10.8	-68.6	6.62	-22.0	(-42.9, -1.2)	10.46	0.038*
		UPA 7.5 MG QD	23	30.2	16.2	-46.5	6.76	0.1	(-20.9, 21.1)	10.55	0.995
		PLACEBO	16	30.8	16.6	-46.6	8.11				

SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FORM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.045*											

[A] P-VALUES WERE CALCULATED FROM ANCOVA WITH BASELINE VALUE AND THE TREATMENT IN THE MODEL.
@ P-VALUES WERE CALCULATED FROM ANCOVA WITH SUBGROUP CATEGORIES, BASELINE VALUE, TREATMENT, INTERACTION OF SUBGROUP AND TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2　1.1.3

表 2.7.3.6-90. 部分集団別の投与 16 週時に EASI 75 を達成した被験者の割合（NRI，第 1 ピリオドの ITT 集団）：M16-048 試験

SUBGROUP CATEGORY	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	95 % CI [A]	P-VALUE [B]
AGE (YEARS)											
< 40											
	UPA 30 MG QD	22	15	(68.2)	6	(27.3)	1	(4.5)	64.2	(43.3, 85 1)	<0.001***
	UPA 15 MG QD	25	10	(40.0)	12	(48.0)	3	(12.0)	36.0	(15.3, 56.7)	0.002**
	UPA 7.5 MG QD	22	5	(22.7)	13	(59.1)	4	(18.2)	18.7	(-0.4, 37.8)	0.085
	PLACEBO	25	1	(4.0)	14	(56.0)	10	(40.0)			
40 - 64											
	UPA 30 MG QD	17	11	(64.7)	5	(29.4)	1	(5.9)	37.4	(2.7, 72.2)	0.053
	UPA 15 MG QD	14	9	(64.3)	4	(28.6)	1	(7.1)	37.0	(0.6, 73.4)	0.066
	UPA 7.5 MG QD	16	5	(31.3)	7	(43.8)	4	(25.0)	4.0	(-30.8, 38.7)	1.000
	PLACEBO	11	3	(27.3)	5	(45.5)	3	(27.3)			
>= 65											
	UPA 30 MG QD	3	3	(100)	0		0		100.0	(100.0, 100.0)	0.018*
	UPA 15 MG QD	3	3	(100)	0		0		100.0	(100.0, 100.0)	0.018*
	UPA 7.5 MG QD	4	2	(50.0)	2	(50.0)	0		50.0	(1.0, 99.0)	0.167
	PLACEBO	5	0		2	(40.0)	3	(60.0)			
SEX											
MALE											
	UPA 30 MG QD	22	12	(54.5)	8	(36.4)	2	(9.1)	42.0	(17.4, 66.7)	0.002**
	UPA 15 MG QD	30	14	(46.7)	15	(50.0)	1	(3.3)	34.2	(11.9, 56.4)	0.007**
	UPA 7.5 MG QD	28	5	(17.9)	19	(67.9)	4	(14.3)	5.4	(-14.0, 24.8)	0.711
	PLACEBO	24	3	(12.5)	12	(50.0)	9	(37.5)			
FEMALE											
	UPA 30 MG QD	20	17	(85.0)	3	(15.0)	0		79.1	(59.9, 98.4)	<0.001***
	UPA 15 MG QD	12	8	(66.7)	1	(8.3)	3	(25.0)	60.8	(31.9, 89.7)	<0.001***
	UPA 7.5 MG QD	14	7	(50.0)	3	(21.4)	4	(28.6)	44.1	(15.6, 72.6)	0.011*
	PLACEBO	17	1	(5.9)	9	(52.9)	7	(41.2)			
BMI (KG/M^2)											
< 25											
	UPA 30 MG QD	20	17	(85.0)	2	(10.0)	1	(5.0)	85.0	(69.4, 100.0)	<0.001***
	UPA 15 MG QD	18	9	(50.0)	6	(33.3)	3	(16.7)	50.0	(26.9, 73 1)	<0.001***
	UPA 7.5 MG QD	16	4	(25.0)	8	(50.0)	4	(25.0)	25.0	(3.8, 46.2)	0.025*
	PLACEBO	22	0		10	(45.5)	12	(54.5)			

SUBGROUP CATEGORY	TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
	25 -< 30							
	UPA 30 MG QD	11	4 (36.4)	6 (54.5)	1 (9.1)	27.3	(-5.8, 60.4)	0.311
	UPA 15 MG QD	11	7 (63.6)	4 (36.4)	0	54.5	(21.4, 87.7)	0.024*
	UPA 7.5 MG QD	13	1 (7.7)	9 (69.2)	3 (23.1)	-1.4	(-23.7, 20.9)	1.000
	PLACEBO	11	1 (9.1)	8 (72.7)	2 (18.2)			
	30 -< 40							
	UPA 30 MG QD	9	7 (77.8)	2 (22.2)	0	61.1	(20.8, 100.0)	0.041*
	UPA 15 MG QD	12	6 (50.0)	5 (41.7)	1 (8.3)	33.3	(-7.8, 74.4)	0.316
	UPA 7.5 MG QD	11	6 (54.5)	5 (45.5)	0	37.9	(-4.0, 79.8)	0.304
	PLACEBO	6	1 (16.7)	3 (50.0)	2 (33.3)			
	>= 40							
	UPA 30 MG QD	2	1 (50.0)	1 (50.0)	0	-50.0	(-100.0, 19.3)	1.000
	UPA 15 MG QD	1	0	1 (100)	0	-100.0	(-100.0, -100.0)	0.333
	UPA 7.5 MG QD	2	1 (50.0)	0	1 (50.0)	-50.0	(-100.0, 19.3)	1.000
	PLACEBO	2	2 (100)	0	0			
RACE								
	WHITE							
	UPA 30 MG QD	23	17 (73.9)	4 (17.4)	2 (8.7)	66.8	(46.4, 87 1)	<0.001***
	UPA 15 MG QD	21	13 (61.9)	6 (28.6)	2 (9.5)	54.8	(31.9, 77.6)	<0.001***
	UPA 7.5 MG QD	24	5 (20.8)	12 (50.0)	7 (29.2)	13.7	(-5.2, 32.5)	0.227
	PLACEBO	28	2 (7.1)	12 (42.9)	14 (50.0)			
	ASIAN							
	UPA 30 MG QD	13	8 (61.5)	5 (38.5)	0	47.3	(10.2, 84 3)	0.070
	UPA 15 MG QD	9	1 (11.1)	7 (77.8)	1 (11.1)	-3 2	(-36.2, 29.9)	1.000
	UPA 7.5 MG QD	9	2 (22.2)	7 (77.8)	0	7.9	(-29.6, 45.5)	1.000
	PLACEBO	7	1 (14.3)	5 (71.4)	1 (14.3)			
	OTHER							
	UPA 30 MG QD	6	4 (66.7)	2 (33.3)	0	50.0	(1.9, 98.1)	0.242
	UPA 15 MG QD	12	8 (66.7)	3 (25.0)	1 (8.3)	50.0	(10.0, 90.0)	0.131
	UPA 7.5 MG QD	9	5 (55.6)	3 (33.3)	1 (11.1)	38.9	(-5.2, 83.0)	0.287
	PLACEBO	6	1 (16.7)	4 (66.7)	1 (16.7)			
WEIGHT								
	< MEDIAN (76.5 KG)							
	UPA 30 MG QD	21	17 (81.0)	4 (19.0)	0	81.0	(64.2, 97.7)	<0.001***
	UPA 15 MG QD	18	8 (44.4)	7 (38.9)	3 (16.7)	44.4	(21.5, 67.4)	<0.001***

SUBGROUP CATEGORY TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
UPA 7.5 MG QD	19	5 (26.3)	9 (47.4)	5 (26.3)	26.3	(6.5, 46.1)	0.011*
PLACEBO	25	0	13 (52.0)	12 (48.0)			
>= MEDIAN (76.5 KG)							
UPA 30 MG QD	21	12 (57.1)	7 (33.3)	2 (9.5)	32.1	(2.2, 62.1)	0.051
UPA 15 MG QD	24	14 (58.3)	9 (37.5)	1 (4.2)	33.3	(4.4, 62 3)	0.038*
UPA 7.5 MG QD	23	7 (30.4)	13 (56.5)	3 (13.0)	5.4	(-22.9, 33.8)	1.000
PLACEBO	16	4 (25.0)	8 (50.0)	4 (25.0)			

[A]: 95% CI FOR DIFFERENCE WAS CALCULATED BASED ON NORMAL APPROXIMATION TO THE BINOMIAL DISTRIBUTION.
[B]: P-VALUE WAS CALCULATED BASED ON CHI-SQUARE TEST (OR FISHER'S EXACT TEST IF >= 25% OF THE CELLS HAVE EXPECTED CELL COUNT < 5).
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.2.3

表 2.7.3.6-91. 部分集団別の投与 16 週時に IGA スコアが 0 又は 1 を達成した被験者の割合（NRI，第 1 ピリオドの ITT 集団）：M16-048 試験

SUBGROUP CATEGORY	TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
AGE (YEARS)								
< 40								
	UPA 30 MG QD	22	10 (45.5)	11 (50.0)	1 (4.5)	45.5	(24.6, 66 3)	<0.001***
	UPA 15 MG QD	25	7 (28.0)	15 (60.0)	3 (12.0)	28.0	(10.4, 45.6)	0.010**
	UPA 7.5 MG QD	22	2 (9.1)	16 (72.7)	4 (18.2)	9.1	(-2.9, 21.1)	0.214
	PLACEBO	25	0	15 (60.0)	10 (40.0)			
40 - 64								
	UPA 30 MG QD	17	9 (52.9)	7 (41.2)	1 (5.9)	43.9	(14.7, 73.0)	0.041*
	UPA 15 MG QD	14	3 (21.4)	10 (71.4)	1 (7.1)	12.3	(-15.1, 39.7)	0.604
	UPA 7.5 MG QD	16	3 (18.8)	9 (56.3)	4 (25.0)	9.7	(-15.9, 35.2)	0.624
	PLACEBO	11	1 (9.1)	7 (63.6)	3 (27.3)			
>= 65								
	UPA 30 MG QD	3	2 (66.7)	1 (33.3)	0	66.7	(13.3, 100.0)	0.107
	UPA 15 MG QD	3	3 (100)	0	0	100.0	(100.0, 100.0)	0.018*
	UPA 7.5 MG QD	4	1 (25.0)	3 (75.0)	0	25.0	(-17.4, 67.4)	0.444
	PLACEBO	5	0	2 (40.0)	3 (60.0)			
SEX								
MALE								
	UPA 30 MG QD	22	7 (31.8)	13 (59.1)	2 (9.1)	27.7	(6.6, 48.7)	0.020*
	UPA 15 MG QD	30	8 (26.7)	21 (70.0)	1 (3.3)	22.5	(4.8, 40.2)	0.033*
	UPA 7.5 MG QD	28	2 (7.1)	22 (78.6)	4 (14.3)	3.0	(-9.5, 15.4)	1.000
	PLACEBO	24	1 (4.2)	14 (58.3)	9 (37.5)			
FEMALE								
	UPA 30 MG QD	20	14 (70.0)	6 (30.0)	0	70.0	(49.9, 90 1)	<0.001***
	UPA 15 MG QD	12	5 (41.7)	4 (33.3)	3 (25.0)	41.7	(13.8, 69.6)	0.007**
	UPA 7.5 MG QD	14	4 (28.6)	6 (42.9)	4 (28.6)	28.6	(4.9, 52.2)	0.032*
	PLACEBO	17	0	10 (58.8)	7 (41.2)			
BMI (KG/M^2)								
< 25								
	UPA 30 MG QD	20	11 (55.0)	8 (40.0)	1 (5.0)	55.0	(33.2, 76.8)	<0.001***
	UPA 15 MG QD	18	4 (22.2)	11 (61.1)	3 (16.7)	22.2	(3.0, 41.4)	0.033*
	UPA 7.5 MG QD	16	3 (18.8)	9 (56.3)	4 (25.0)	18.8	(-0.4, 37.9)	0.066
	PLACEBO	22	0	10 (45.5)	12 (54.5)			

SUBGROUP CATEGORY	TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
	25 -< 30							
	UPA 30 MG QD	11	3 (27.3)	7 (63.6)	1 (9.1)	27.3	(1.0, 53.6)	0.214
	UPA 15 MG QD	11	5 (45.5)	6 (54.5)	0	45.5	(16.0, 74 9)	0.035*
	UPA 7.5 MG QD	13	1 (7.7)	9 (69.2)	3 (23.1)	7.7	(-6.8, 22.2)	1.000
	PLACEBO	11	0	9 (81.8)	2 (18.2)			
	30 -< 40							
	UPA 30 MG QD	9	6 (66.7)	3 (33.3)	0	66.7	(35.9, 97 5)	0.028*
	UPA 15 MG QD	12	4 (33.3)	7 (58.3)	1 (8.3)	33.3	(6.7, 60.0)	0.245
	UPA 7.5 MG QD	11	2 (18.2)	9 (81.8)	0	18.2	(-4.6, 41.0)	0.515
	PLACEBO	6	0	4 (66.7)	2 (33.3)			
	>= 40							
	UPA 30 MG QD	2	1 (50.0)	1 (50.0)	0	0.0	(-98.0, 98.0)	1.000
	UPA 15 MG QD	1	0	1 (100)	0	-50.0	(-100.0, 19.3)	1.000
	UPA 7.5 MG QD	2	0	1 (50.0)	1 (50.0)	-50.0	(-100.0, 19.3)	1.000
	PLACEBO	2	1 (50.0)	1 (50.0)	0			
RACE								
	WHITE							
	UPA 30 MG QD	23	12 (52.2)	9 (39.1)	2 (8.7)	52.2	(31.8, 72.6)	<0.001***
	UPA 15 MG QD	21	8 (38.1)	11 (52.4)	2 (9.5)	38.1	(17.3, 58 9)	<0.001***
	UPA 7.5 MG QD	24	1 (4.2)	16 (66.7)	7 (29.2)	4.2	(-3.8, 12.2)	0.462
	PLACEBO	28	0	14 (50.0)	14 (50.0)			
	ASIAN							
	UPA 30 MG QD	13	6 (46.2)	7 (53.8)	0	46.2	(19.1, 73 3)	0.051
	UPA 15 MG QD	9	1 (11.1)	7 (77.8)	1 (11.1)	11.1	(-9.4, 31.6)	1.000
	UPA 7.5 MG QD	9	1 (11.1)	8 (88.9)	0	11.1	(-9.4, 31.6)	1.000
	PLACEBO	7	0	6 (85.7)	1 (14.3)			
	OTHER							
	UPA 30 MG QD	6	3 (50.0)	3 (50.0)	0	33.3	(-16.6, 83.2)	0.545
	UPA 15 MG QD	12	4 (33.3)	7 (58.3)	1 (8.3)	16.7	(-23.3, 56.7)	0.615
	UPA 7.5 MG QD	9	4 (44.4)	4 (44.4)	1 (11.1)	27.8	(-16.3, 71.9)	0.580
	PLACEBO	6	1 (16.7)	4 (66.7)	1 (16.7)			
WEIGHT								
	< MEDIAN (76.5 KG)							
	UPA 30 MG QD	21	11 (52.4)	10 (47.6)	0	52.4	(31.0, 73.7)	<0.001***
	UPA 15 MG QD	18	3 (16.7)	12 (66.7)	3 (16.7)	16.7	(-0.5, 33.9)	0.066

SUBGROUP CATEGORY TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
UPA 7.5 MG QD	19	3 (15.8)	11 (57.9)	5 (26.3)	15.8	(-0.6, 32.2)	0.073
PLACEBO	25	0	13 (52.0)	12 (48.0)			
>= MEDIAN (76.5 KG)							
UPA 30 MG QD	21	10 (47.6)	9 (42.9)	2 (9.5)	41.4	(16.9, 65.8)	0.010**
UPA 15 MG QD	24	10 (41.7)	13 (54.2)	1 (4.2)	35.4	(12.4, 58.4)	0.027*
UPA 7.5 MG QD	23	3 (13.0)	17 (73.9)	3 (13.0)	6.8	(-11.4, 25.0)	0.631
PLACEBO	16	1 (6.3)	11 (68.8)	4 (25.0)			

[A]: 95% CI FOR DIFFERENCE WAS CALCULATED BASED ON NORMAL APPROXIMATION TO THE BINOMIAL DISTRIBUTION.
[B]: P-VALUE WAS CALCULATED BASED ON CHI-SQUARE TEST (OR FISHER'S EXACT TEST IF >= 25% OF THE CELLS HAVE EXPECTED CELL COUNT < 5).
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.3.3

表 2.7.3.6-92. 部分集団別の投与 16 週時の移動平均に基づくかゆみの NRS のベースラインからの変化率（%）（第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION SUBGROUP CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----COMPARED TO PLACEBO---- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF										
AGE (YEARS)										
<40										
	UPA 30 MG QD	22	6.3	2.6	-61.5	8.35	-56.0	(-78.9, -33.1)	11.53	<0.001***
	UPA 15 MG QD	21	6.4	3.0	-50.9	8.53	-45.4	(-68.6, -22.2)	11.67	<0.001***
	UPA 7.5 MG QD	20	7.2	4.8	-28.1	8.86	-22.6	(-46.4, 1.2)	11.97	0.062
	PLACEBO	24	6.4	5.8	-5.5	7.98				
40-64										
	UPA 30 MG QD	17	6.5	1.8	-74.9	11.99	-61.3	(-99.8, -22.7)	19.20	0.002**
	UPA 15 MG QD	13	6.2	3.1	-37.7	13.76	-24.0	(-65.0, 17.0)	20.44	0.245
	UPA 7.5 MG QD	16	6.6	3.4	-43.4	12.36	-29.7	(-68.7, 9.2)	19.41	0.132
	PLACEBO	11	6.9	5.8	-13.7	14.98				
>=65										
	UPA 30 MG QD	3	5.1	0.7	-88.8	11.57	-59.6	(-102.5, -16.7)	18.13	0.013*
	UPA 15 MG QD	3	7.1	1.1	-84.1	12.15	-55.0	(-100.3, -9.6)	19.16	0.024*
	UPA 7.5 MG QD	4	5.4	1.0	-80.8	9.95	-51.6	(-92.4, -10.8)	17.25	0.020*
	PLACEBO	2	4.9	3.6	-29.2	14.20				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.776

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
SEX											
	MALE										
		UPA 30 MG QD	22	6.0	3.0	-57.6	9.62	-43.6	(-70.8, -16.3)	13.72	0.002**
		UPA 15 MG QD	27	6.5	3.0	-46.4	8.60	-32.3	(-58.1, -6.5)	13.00	0.015*
		UPA 7.5 MG QD	27	6.9	4.2	-35.3	8.65	-21.2	(-47.1, 4.7)	13.02	0.107
		PLACEBO	21	6.6	5.6	-14.1	9.75				
	FEMALE										
		UPA 30 MG QD	20	6.6	1.2	-81.2	8.99	-77.3	(-104.3, -50.3)	13.48	<0.001***
		UPA 15 MG QD	10	5.9	2.7	-52.9	12.75	-49.0	(-81.5, -16.5)	16.21	0.004**
		UPA 7.5 MG QD	13	6.5	3.1	-49.2	11.14	-45.2	(-75.3, -15.2)	15.00	0.004**
		PLACEBO	16	6.3	5.8	-3.9	10.04				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.374

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
BMI (KG/M^2)											
	< 25										
		UPA 30 MG QD	20	6.2	2.5	-63.3	9.14	-61.3	(-87.1, -35.6)	12.90	<0.001***
		UPA 15 MG QD	16	6.4	3.2	-46.3	10.17	-44.3	(-71.5, -17.0)	13.65	0.002**
		UPA 7.5 MG QD	14	7.1	4.5	-34.3	10.98	-32.3	(-60.7, -3.9)	14.24	0.027*
		PLACEBO	20	6.6	6.2	-2.0	9.09				
	25 -< 30										
		UPA 30 MG QD	11	5.9	1.9	-76.9	12.01	-67.9	(-102.9, -32.9)	17.31	<0.001***
		UPA 15 MG QD	10	6.8	1.8	-65.8	12.58	-56.8	(-93.1, -20.6)	17.94	0.003**
		UPA 7.5 MG QD	13	6.8	3.9	-33.1	11.07	-24.2	(-58.4, 10.0)	16.92	0.161
		PLACEBO	10	5.8	5.2	-8.9	12.63				
	30 -< 40										
		UPA 30 MG QD	9	6.7	1.9	-69.7	18.21	-41.1	(-102.7, 20.6)	30.18	0.184
		UPA 15 MG QD	10	5.9	3.5	-32.1	17.19	-3.4	(-64.3, 57.4)	29.79	0.909
		UPA 7.5 MG QD	11	6.0	2.4	-58.5	16.35	-29.8	(-89.6, 30.0)	29.29	0.317
		PLACEBO	5	6.5	5.0	-28.6	24.23				
	>= 40										
		UPA 30 MG QD	2	7.0	1.7	-54.5	24.72	18.3	(-157.2, 193.7)	40.78	0.698
		UPA 15 MG QD	1	6.9	3.3	-26.2	33.25	46.5	(-157.5, 250.5)	47.41	0.430
		UPA 7.5 MG QD	2	8.1	6.9	-31.1	21.71	41.7	(-82.4, 165.7)	28.84	0.285
		PLACEBO	2	8.4	4.1	-72.7	24.84				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.516

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF											
RACE											
	WHITE										
		UPA 30 MG QD	23	6.2	2.0	-71.7	9.83	-66.5	(-93.9, -39.2)	13.75	<0.001***
		UPA 15 MG QD	19	6.2	2.5	-50.3	10.81	-45.1	(-73.9, -16.4)	14.46	0.002**
		UPA 7.5 MG QD	23	6.7	3.5	-41.0	9.86	-35.8	(-63.2, -8.4)	13.78	0.011*
		PLACEBO	24	6.3	5.8	-5.2	9.62				
	ASIAN										
		UPA 30 MG QD	13	7.0	2.6	-60.6	9.94	-33.2	(-67.5, 1.1)	16.86	0.057
		UPA 15 MG QD	9	6.4	4.2	-27.0	11.85	0.4	(-35.9, 36.7)	17.86	0.982
		UPA 7.5 MG QD	9	6.6	5.3	-23.2	11.81	4.2	(-32.2, 40.6)	17.90	0.815
		PLACEBO	7	6.2	4.6	-27.4	13.46				
	OTHER										
		UPA 30 MG QD	6	5.2	2.1	-67.7	15.70	-55.0	(-101.3, -8.7)	22.41	0.022*
		UPA 15 MG QD	9	6.7	2.5	-65.8	12.11	-53.1	(-93.1, -13.2)	19.35	0.011*
		UPA 7.5 MG QD	8	7.3	3.3	-56.1	12.97	-43.5	(-84.0, -2.9)	19.65	0.037*
		PLACEBO	6	7.6	6.4	-12.7	15.09				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.566

IMPUTATION SUBGROUP CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF										
WEIGHT										
< MEDIAN (76.5 KG)										
	UPA 30 MG QD	21	6.5	2.6	-62.8	8.99	-64.6	(-89.9, -39.3)	12.70	<0.001***
	UPA 15 MG QD	15	6.9	3.4	-43.5	10.67	-45.4	(-73.2, -17.5)	13.97	0.002**
	UPA 7.5 MG QD	17	6.6	4.3	-32.2	9.98	-34.0	(-60.8, -7.2)	13.44	0.014*
	PLACEBO	21	6.5	6.5	1.8	8.99				
>= MEDIAN (76.5 KG)										
	UPA 30 MG QD	21	6.1	1.8	-75.3	9.68	-50.0	(-79.4, -20.7)	14.72	0.001**
	UPA 15 MG QD	22	6.0	2.6	-50.7	9.49	-25.5	(-54.6, 3.6)	14.60	0.085
	UPA 7.5 MG QD	23	6.8	3.5	-45.3	9.32	-20.1	(-48.9, 8.7)	14.45	0.169
	PLACEBO	16	6.5	4.6	-25.3	11.08				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.782

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
AGE (YEARS)											
	<40										
		UPA 30 MG QD	18	6.6	2.9	-56.8	8.03	-56.5	(-80.3, -32.7)	11.91	<0.001***
		UPA 15 MG QD	19	6.3	2.6	-55.9	7.84	-55.6	(-79.2, -32.1)	11.79	<0.001***
		UPA 7.5 MG QD	15	6.9	4.9	-27.1	8.84	-26.8	(-51.7, -1.8)	12.47	0.036*
		PLACEBO	15	6.6	6.3	-0.3	8.79				
	40-64										
		UPA 30 MG QD	15	6.4	2.0	-73.0	12.59	-44.1	(-89.6, 1.3)	22.46	0.057
		UPA 15 MG QD	11	6.2	2.8	-41.9	14.75	-13.0	(-61.2, 35.2)	23.82	0.587
		UPA 7.5 MG QD	11	6.5	2.2	-64.4	14.70	-35.5	(-83.3, 12.4)	23.66	0.142
		PLACEBO	7	7.0	5.0	-28.9	18.56				
	>=65										
		UPA 30 MG QD	3	5.1	0.7	-89.1	11.96	-48.5	(-107.6, 10.5)	24.13	0.091
		UPA 15 MG QD	3	7.1	1.1	-83.3	12.67	-42.8	(-106.2, 20.6)	25.91	0.150
		UPA 7.5 MG QD	4	5.4	1.0	-80.9	10.29	-40.4	(-98.1, 17.3)	23.57	0.137
		PLACEBO	1	3.7	2.2	-40.6	21.39				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.360

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
SEX											
	MALE										
		UPA 30 MG QD	18	6.1	3.3	-52.9	10.64	-33.3	(-65.3, -1.2)	16.09	0.042*
		UPA 15 MG QD	26	6.4	2.9	-46.8	8.82	-27.2	(-56.9, 2.5)	14.91	0.072
		UPA 7.5 MG QD	20	6.6	4.3	-34.9	10.07	-15.2	(-46.4, 16.0)	15.66	0.334
		PLACEBO	14	6.6	5.4	-19.7	12.02				
	FEMALE										
		UPA 30 MG QD	18	6.7	1.3	-79.8	5.93	-81.9	(-102.6, -61.1)	10.26	<0.001***
		UPA 15 MG QD	7	6.0	1.4	-75.8	9.55	-77.9	(-103.7, -52.2)	12.72	<0.001***
		UPA 7.5 MG QD	10	6.5	1.6	-75.4	7.95	-77.5	(-100.8, -54.1)	11.55	<0.001***
		PLACEBO	9	6.6	6.3	2.1	8.38				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.039*

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE											
BMI (KG/M^2)											
	< 25										
		UPA 30 MG QD	16	6.2	2.7	-58.5	8.81	-61.4	(-90.3, -32.6)	14.29	<0.001***
		UPA 15 MG QD	12	6.3	2.3	-58.8	10.12	-61.7	(-92.2, -31.2)	15.11	<0.001***
		UPA 7.5 MG QD	10	7.1	4.8	-34.5	11.15	-37.5	(-69.0, -6.0)	15.63	0.021*
		PLACEBO	10	7.0	7.1	2.9	11.12				
	25 -< 30										
		UPA 30 MG QD	9	6.3	2.1	-72.0	11.35	-63.4	(-97.2, -29.7)	16.57	<0.001***
		UPA 15 MG QD	10	6.8	1.8	-66.8	10.80	-58.2	(-91.5, -24.9)	16.34	0.001**
		UPA 7.5 MG QD	9	6.8	3.2	-51.2	11.38	-42.6	(-76.7, -8.5)	16.73	0.016*
		PLACEBO	8	5.9	5.3	-8.6	12.14				
	30 -< 40										
		UPA 30 MG QD	9	6.7	1.9	-68.6	18.82	-22.8	(-99.4, 53.9)	37.35	0.547
		UPA 15 MG QD	10	5.9	3.5	-32.0	17.65	13.9	(-61.3, 89.1)	36.64	0.707
		UPA 7.5 MG QD	10	5.9	2.1	-61.4	17.64	-15.5	(-90.7, 59.7)	36.64	0.676
		PLACEBO	3	5.9	3.8	-45.9	32.15				
	>= 40										
		UPA 30 MG QD	2	7.0	1.7	-70.5	55.46	-8.9	(-1872.7, 1854.8)	146.68	0.961
		UPA 15 MG QD	1	6.9	3.3	-45.0	73.78	16.5	(-2055.3, 2088.4)	163.06	0.936
		UPA 7.5 MG QD	1	7.2	3.8	-44.8	47.93	16.8	(-1637.4, 1670.9)	130.19	0.918
		PLACEBO	2	8.4	4.1	-61.5	97.29				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.391

IMPUTATION SUBGROUP CATEGORY	TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE										
RACE										
WHITE										
	UPA 30 MG QD	18	6.2	2.1	-69.0	10.67	-65.2	(-98.2, -32.2)	16.48	<0.001***
	UPA 15 MG QD	17	6.3	2.3	-54.5	10.98	-50.7	(-84.2, -17.3)	16.69	0.004**
	UPA 7.5 MG QD	15	6.2	2.7	-55.2	11.69	-51.4	(-85.7, -17.0)	17.16	0.004**
	PLACEBO	13	6.0	5.9	-3.8	12.56				
ASIAN										
	UPA 30 MG QD	13	7.0	2.6	-60.4	9.78	-37.7	(-73.0, -2.3)	17.35	0.038*
	UPA 15 MG QD	8	6.3	3.7	-33.4	12.43	-10.7	(-49.2, 27.8)	18.87	0.576
	UPA 7.5 MG QD	9	6.6	5.3	-23.4	11.64	-0.7	(-38.2, 36.9)	18.41	0.972
	PLACEBO	6	6.5	4.9	-22.8	14.27				
OTHER										
	UPA 30 MG QD	5	5.5	2.5	-58.8	14.29	-27.7	(-75.2, 19.8)	22.62	0.237
	UPA 15 MG QD	8	6.4	2.0	-67.3	10.87	-36.2	(-77.9, 5.6)	19.87	0.085
	UPA 7.5 MG QD	6	7.5	2.3	-73.7	12.59	-42.6	(-84.5, -0.6)	19.96	0.047*
	PLACEBO	4	8.5	6.6	-31.1	16.16				

TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.512

IMPUTATION SUBGROUP CATEGORY TREATMENT	N	BASELINE MEAN	VISIT MEAN	-WITHIN GROUP PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ----------COMPARED TO PLACEBO---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE									
WEIGHT									
< MEDIAN (76.5 KG)									
UPA 30 MG QD	19	6.5	2.8	-58.4	8.12	-63.6	(-89.1, -38.0)	12.73	<0.001***
UPA 15 MG QD	11	7.0	2.5	-58.9	10.70	-64.2	(-93.3, -35.0)	14.52	<0.001***
UPA 7.5 MG QD	12	6.7	4.3	-39.9	10.21	-45.1	(-73.5, -16.7)	14.15	0.002**
PLACEBO	13	6.6	6.8	5.2	9.81				
>= MEDIAN (76.5 KG)									
UPA 30 MG QD	17	6.2	1.7	-75.1	10.67	-42.9	(-78.0, -7.8)	17.56	0.017*
UPA 15 MG QD	22	6.0	2.6	-50.6	9.42	-18.4	(-52.1, 15.3)	16.85	0.279
UPA 7.5 MG QD	18	6.5	2.8	-53.6	10.40	-21.4	(-56.1, 13.3)	17.35	0.222
PLACEBO	10	6.5	4.4	-32.2	13.93				
TEST OF INTERACTION BETWEEN SUBGROUP AND TREATMENT: P-VALUE @ = 0.252									

[A] P-VALUES WERE CALCULATED FROM ANCOVA WITH BASELINE VALUE AND THE TREATMENT IN THE MODEL.
@ P-VALUES WERE CALCULATED FROM ANCOVA WITH SUBGROUP CATEGORIES, BASELINE VALUE, TREATMENT, INTERACTION OF SUBGROUP AND TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2　1.4.3

表 2.7.3.6-93. 部分集団別のかゆみの NRS がベースラインで 4 以上であった被験者のうち，投与 16 週時にかゆみの NRS がベースラインから 4 以上改善した被験者の割合（NRI，LOCF，第 1 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
NRI									
AGE (YEARS)									
	< 40								
		UPA 30 MG QD	19	8 (42.1)	9 (47.4)	2 (10.5)	37.6	(13.7, 61.4)	0.006**
		UPA 15 MG QD	19	9 (47.4)	8 (42.1)	2 (10.5)	42.8	(18.7, 66.9)	0.002**
		UPA 7.5 MG QD	19	1 (5.3)	13 (68.4)	5 (26.3)	0.7	(-12.6, 14.0)	1.000
		PLACEBO	22	1 (4.5)	12 (54.5)	9 (40.9)			
	40 - 64								
		UPA 30 MG QD	15	9 (60.0)	4 (26.7)	2 (13.3)	50.9	(20.9, 81.0)	0.014*
		UPA 15 MG QD	10	7 (70.0)	2 (20.0)	1 (10.0)	60.9	(27.8, 94.0)	0.008**
		UPA 7.5 MG QD	15	6 (40.0)	5 (33.3)	4 (26.7)	30.9	(0.9, 61.0)	0.178
		PLACEBO	11	1 (9.1)	6 (54.5)	4 (36.4)			
	>= 65								
		UPA 30 MG QD	2	2 (100)	0	0	100.0	(100.0, 100.0)	0.333
		UPA 15 MG QD	3	3 (100)	0	0	100.0	(100.0, 100.0)	0.100
		UPA 7.5 MG QD	3	2 (66.7)	1 (33.3)	0	66.7	(13.3, 100.0)	0.400
		PLACEBO	2	0	0	2 (100)			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
NRI									
SEX									
	MALE								
		UPA 30 MG QD	18	6 (33.3)	9 (50.0)	3 (16.7)	23.3	(-2.1, 48.8)	0.117
		UPA 15 MG QD	25	15 (60.0)	9 (36.0)	1 (4.0)	50.0	(26.7, 73.3)	<0.001***
		UPA 7.5 MG QD	26	3 (11.5)	16 (61.5)	7 (26.9)	1.5	(-16.5, 19.5)	1.000
		PLACEBO	20	2 (10.0)	10 (50.0)	8 (40.0)			
	FEMALE								
		UPA 30 MG QD	18	13 (72.2)	4 (22.2)	1 (5.6)	72.2	(51.5, 92.9)	<0.001***
		UPA 15 MG QD	7	4 (57.1)	1 (14.3)	2 (28.6)	57.1	(20.5, 93.8)	0.005**
		UPA 7.5 MG QD	11	6 (54.5)	3 (27.3)	2 (18.2)	54.5	(25.1, 84.0)	0.002**
		PLACEBO	15	0	8 (53.3)	7 (46.7)			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
NRI									
BMI (KG/M^2)									
	< 25								
		UPA 30 MG QD	17	6 (35.3)	8 (47.1)	3 (17.6)	29.7	(4.7, 54.8)	0.041*
		UPA 15 MG QD	14	7 (50.0)	4 (28.6)	3 (21.4)	44.4	(16.2, 72.7)	0.010**
		UPA 7.5 MG QD	14	3 (21.4)	7 (50.0)	4 (28.6)	15.9	(-8.1, 39.8)	0.295
		PLACEBO	18	1 (5.6)	8 (44.4)	9 (50.0)			
	25 -< 30								
		UPA 30 MG QD	8	5 (62.5)	2 (25.0)	1 (12.5)	62.5	(29.0, 96.0)	0.007**
		UPA 15 MG QD	9	7 (77.8)	2 (22.2)	0	77.8	(50.6, 100.0)	<0.001***
		UPA 7.5 MG QD	12	2 (16.7)	7 (58.3)	3 (25.0)	16.7	(-4.4, 37.8)	0.481
		PLACEBO	10	0	7 (70.0)	3 (30.0)			
	30 -< 40								
		UPA 30 MG QD	9	6 (66.7)	3 (33.3)	0	66.7	(35.9, 97.5)	0.031*
		UPA 15 MG QD	8	5 (62.5)	3 (37.5)	0	62.5	(29.0, 96.0)	0.075
		UPA 7.5 MG QD	9	4 (44.4)	4 (44.4)	1 (11.1)	44.4	(12.0, 76.9)	0.221
		PLACEBO	5	0	2 (40.0)	3 (60.0)			
	>= 40								
		UPA 30 MG QD	2	2 (100)	0	0	50.0	(-19.3, 100.0)	1.000
		UPA 15 MG QD	1	0	1 (100)	0	-50.0	(-100.0, 19.3)	1.000
		UPA 7.5 MG QD	2	0	1 (50.0)	1 (50.0)	-50.0	(-100.0, 19.3)	1.000
		PLACEBO	2	1 (50.0)	1 (50.0)	0			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n %	NO n %	MISSING n %	DIFF %	95 % CI [A]	P-VALUE [B]
NRI									
RACE									
	WHITE								
		UPA 30 MG QD	19	10 (52.6)	5 (26.3)	4 (21.1)	48.3	(24.3, 72.2)	<0.001***
		UPA 15 MG QD	16	11 (68.8)	4 (25.0)	1 (6.3)	64.4	(40.2, 88.6)	<0.001***
		UPA 7.5 MG QD	22	5 (22.7)	10 (45.5)	7 (31.8)	18.4	(-1.0, 37.8)	0.096
		PLACEBO	23	1 (4.3)	10 (43.5)	12 (52.2)			
	ASIAN								
		UPA 30 MG QD	13	7 (53.8)	6 (46.2)	0	53.8	(26.7, 80.9)	0.044*
		UPA 15 MG QD	8	3 (37.5)	4 (50.0)	1 (12.5)	37.5	(4.0, 71.0)	0.209
		UPA 7.5 MG QD	8	1 (12.5)	7 (87.5)	0	12.5	(-10.4, 35.4)	1.000
		PLACEBO	6	0	5 (83.3)	1 (16.7)			
	OTHER								
		UPA 30 MG QD	4	2 (50.0)	2 (50.0)	0	33.3	(-24.0, 90.7)	0.500
		UPA 15 MG QD	8	5 (62.5)	2 (25.0)	1 (12.5)	45.8	(0.9, 90.7)	0.138
		UPA 7.5 MG QD	7	3 (42.9)	2 (28.6)	2 (28.6)	26.2	(-21.1, 73.4)	0.559
		PLACEBO	6	1 (16.7)	3 (50.0)	2 (33.3)			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n	YES %	NO n	NO %	MISSING n	MISSING %	DIFF %	95 % CI [A]	P-VALUE [B]
NRI												
WEIGHT												
	< MEDIAN (76.5 KG)											
		UPA 30 MG QD	18	8	(44.4)	9	(50.0)	1	(5.6)	39.9	(15.3, 64.4)	0.006**
		UPA 15 MG QD	14	7	(50.0)	4	(28.6)	3	(21.4)	45.5	(17.9, 73.1)	0.003**
		UPA 7.5 MG QD	16	3	(18.8)	9	(56.3)	4	(25.0)	14.2	(-6.8, 35.2)	0.291
		PLACEBO	22	1	(4.5)	11	(50.0)	10	(45.5)			
	>= MEDIAN (76.5 KG)											
		UPA 30 MG QD	18	11	(61.1)	4	(22.2)	3	(16.7)	53.4	(26.6, 80.2)	0.003**
		UPA 15 MG QD	18	12	(66.7)	6	(33.3)	0		59.0	(32.8, 85.1)	0.001**
		UPA 7.5 MG QD	21	6	(28.6)	10	(47.6)	5	(23.8)	20.9	(-3.3, 45.0)	0.210
		PLACEBO	13	1	(7.7)	7	(53.8)	5	(38.5)			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n %	NO n %	DIFF %	95 % CI [A]	P-VALUE [B]
LOCF								
AGE (YEARS)								
	< 40							
		UPA 30 MG QD	19	9 (47.4)	10 (52.6)	33.1	(6.1, 60.1)	0.023*
		UPA 15 MG QD	19	9 (47.4)	10 (52.6)	33.1	(6.1, 60.1)	0.023*
		UPA 7.5 MG QD	19	4 (21.1)	15 (78.9)	6.8	(-16.9, 30.4)	0.689
		PLACEBO	21	3 (14.3)	18 (85.7)			
	40 - 64							
		UPA 30 MG QD	15	11 (73.3)	4 (26.7)	64.2	(36.1, 92 3)	0.001**
		UPA 15 MG QD	10	7 (70.0)	3 (30.0)	60.9	(27.8, 94.0)	0.008**
		UPA 7.5 MG QD	15	7 (46.7)	8 (53.3)	37.6	(7.1, 68.0)	0.084
		PLACEBO	11	1 (9.1)	10 (90.9)			
	>= 65							
		UPA 30 MG QD	2	2 (100)	0	100.0	(100.0, 100.0)	0.333
		UPA 15 MG QD	3	3 (100)	0	100.0	(100.0, 100.0)	0.250
		UPA 7.5 MG QD	3	2 (66.7)	1 (33.3)	66.7	(13.3, 100.0)	1.000
		PLACEBO	1	0	1 (100)			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n %	NO n %	DIFF %	95 % CI [A]	P-VALUE [B]
LOCF								
SEX								
	MALE							
		UPA 30 MG QD	18	8 (44.4)	10 (55.6)	27.8	(-0.9, 56.5)	0.070
		UPA 15 MG QD	25	15 (60.0)	10 (40.0)	43.3	(17.5, 69 1)	0.004**
		UPA 7.5 MG QD	26	7 (26.9)	19 (73.1)	10.3	(-14.0, 34.5)	0.489
		PLACEBO	18	3 (16.7)	15 (83.3)			
	FEMALE							
		UPA 30 MG QD	18	14 (77.8)	4 (22.2)	71.1	(48.1, 94 1)	<0.001***
		UPA 15 MG QD	7	4 (57.1)	3 (42.9)	50.5	(11.7, 89 2)	0.021*
		UPA 7.5 MG QD	11	6 (54.5)	5 (45.5)	47.9	(15.9, 79 9)	0.021*
		PLACEBO	15	1 (6.7)	14 (93.3)			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n %	NO n %	DIFF %	95 % CI [A]	P-VALUE [B]
LOCF								
BMI (KG/M^2)								
	< 25							
		UPA 30 MG QD	17	8 (47.1)	9 (52.9)	30.4	(1.1, 59.7)	0.053
		UPA 15 MG QD	14	7 (50.0)	7 (50.0)	33.3	(2.0, 64.7)	0.062
		UPA 7.5 MG QD	14	6 (42.9)	8 (57.1)	26.2	(-4.9, 57.3)	0.132
		PLACEBO	18	3 (16.7)	15 (83.3)			
	25 -< 30							
		UPA 30 MG QD	8	6 (75.0)	2 (25.0)	75.0	(45.0, 100.0)	0.002**
		UPA 15 MG QD	9	7 (77.8)	2 (22.2)	77.8	(50.6, 100.0)	0.002**
		UPA 7.5 MG QD	12	3 (25.0)	9 (75.0)	25.0	(0.5, 49.5)	0.229
		PLACEBO	9	0	9 (100)			
	30 -< 40							
		UPA 30 MG QD	9	6 (66.7)	3 (33.3)	66.7	(35.9, 97 5)	0.070
		UPA 15 MG QD	8	5 (62.5)	3 (37.5)	62.5	(29.0, 96.0)	0.081
		UPA 7.5 MG QD	9	4 (44.4)	5 (55.6)	44.4	(12.0, 76 9)	0.228
		PLACEBO	4	0	4 (100)			
	>= 40							
		UPA 30 MG QD	2	2 (100)	0	50.0	(-19.3, 100.0)	1.000
		UPA 15 MG QD	1	0	1 (100)	-50.0	(-100.0, 19.3)	1.000
		UPA 7.5 MG QD	2	0	2 (100)	-50.0	(-100.0, 19.3)	1.000
		PLACEBO	2	1 (50.0)	1 (50.0)			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n %	NO n %	DIFF %	95 % CI [A]	P-VALUE [B]
LOCF								
RACE								
	WHITE							
		UPA 30 MG QD	19	13 (68.4)	6 (31.6)	54.1	(28.4, 79.8)	<0.001***
		UPA 15 MG QD	16	11 (68.8)	5 (31.3)	54.5	(27.3, 81.7)	<0.001***
		UPA 7.5 MG QD	22	9 (40.9)	13 (59.1)	26.6	(1.2, 52.0)	0.052
		PLACEBO	21	3 (14.3)	18 (85.7)			
	ASIAN							
		UPA 30 MG QD	13	7 (53.8)	6 (46.2)	53.8	(26.7, 80 9)	0.044*
		UPA 15 MG QD	8	3 (37.5)	5 (62.5)	37.5	(4.0, 71.0)	0.209
		UPA 7.5 MG QD	8	1 (12.5)	7 (87.5)	12.5	(-10.4, 35.4)	1.000
		PLACEBO	6	0	6 (100)			
	OTHER							
		UPA 30 MG QD	4	2 (50.0)	2 (50.0)	33.3	(-24.0, 90.7)	0.500
		UPA 15 MG QD	8	5 (62.5)	3 (37.5)	45.8	(0.9, 90.7)	0.138
		UPA 7.5 MG QD	7	3 (42.9)	4 (57.1)	26.2	(-21.1, 73.4)	0.559
		PLACEBO	6	1 (16.7)	5 (83.3)			

IMPUTATION SUBGROUP	CATEGORY	TREATMENT	N	YES n	YES %	NO n	NO %	DIFF %	95 % CI [A]	P-VALUE [B]
LOCF										
WEIGHT										
	< MEDIAN (76.5 KG)									
		UPA 30 MG QD	18	9	(50.0)	9	(50.0)	40.0	(13.4, 66.6)	0.007**
		UPA 15 MG QD	14	7	(50.0)	7	(50.0)	40.0	(10.7, 69 3)	0.017*
		UPA 7.5 MG QD	16	6	(37.5)	10	(62.5)	27.5	(0.4, 54.6)	0.103
		PLACEBO	20	2	(10.0)	18	(90.0)			
	>= MEDIAN (76.5 KG)									
		UPA 30 MG QD	18	13	(72.2)	5	(27.8)	56.8	(28.3, 85 3)	0.002**
		UPA 15 MG QD	18	12	(66.7)	6	(33.3)	51.3	(22.0, 80.6)	0.005**
		UPA 7.5 MG QD	21	7	(33.3)	14	(66.7)	17.9	(-10.2, 46.1)	0.427
		PLACEBO	13	2	(15.4)	11	(84.6)			

[A]: 95% CI FOR DIFFERENCE WAS CALCULATED BASED ON NORMAL APPROXIMATION TO THE BINOMIAL DISTRIBUTION.
[B]: P-VALUE WAS CALCULATED BASED ON CHI-SQUARE TEST (OR FISHER'S EXACT TEST IF >= 25% OF THE CELLS HAVE EXPECTED CELL COUNT < 5).
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2 1.4.4

表 2.7.3.6-94.　第 2 ピリオドの来院時別の EASI スコアの再ランダム化からの変化率（%）（LOCF，OC，第 2 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF										
WEEK 20										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	3.7	5.0	-73.8	215.54	-865.3	(-1506.0, -224.6)	312.26	0.010**
	PLACEBO	13	7.8	20.1	791.5	262.34				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	14.0	15.9	65.7	178.24	-516.6	(-1024.6, -8.7)	248.37	0.046*
	PLACEBO	17	9.9	29.9	582.3	172.19				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	21.5	79.1	48.42	-106.8	(-236.4, 22.8)	63.05	0.102
	PLACEBO	15	19.4	31.5	186.0	46.53				
	PLACEBO/									
	UPA 30 MG QD	10	23.8	10.0	11.8	30.59	-38.8	(-114.6, 36.9)	35.75	0.293
	PLACEBO	10	25.7	28.5	50.7	33.50				
LOCF										
WEEK 24										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	3.5	5.7	-69.6	200.01	-968.0	(-1564.1, -371.9)	291.00	0.002**
	PLACEBO	13	7.8	21.0	898.5	248.78				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	14.0	16.6	72.6	175.44	-534.7	(-1034.7, -34.7)	244.46	0.037*
	PLACEBO	17	9.9	30.3	607.3	169.49				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	21.8	59.0	45.97	-130.6	(-253.6, -7 5)	59.86	0.038*
	PLACEBO	15	19.4	31.7	189.6	44.17				
	PLACEBO/									
	UPA 30 MG QD	10	23.8	4.4	-67.5	15.64	-81.0	(-119.8, -42 3)	18.28	<0.001***
	PLACEBO	10	25.7	28.2	13.5	17.13				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF										
WEEK 32										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	3.5	6.2	-28.8	210.78	-800.2	(-1402.2, -198.3)	294.31	0.011*
	PLACEBO	14	7.3	19.1	771.5	252.90				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	14.0	19.5	151.7	175.59	-461.7	(-962.1, 38.7)	244.67	0.069
	PLACEBO	17	9.9	29.8	613.3	169.63				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	23.1	63.5	46.56	-118.0	(-242.6, 6.6)	60.62	0.063
	PLACEBO	15	19.4	31.6	181.5	44.74				
	PLACEBO/									
	UPA 30 MG QD	10	23.8	4.3	-83.1	13.83	-80.7	(-115.0, -46.4)	16.17	<0.001***
	PLACEBO	10	25.7	28.0	-2.3	15.15				
LOCF										
WEEK 40										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	3.7	6.8	140.6	293.17	-638.4	(-1474.4, 197.7)	408.15	0.129
	PLACEBO	14	7.3	19.2	778.9	344.45				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	14.0	19.6	154.1	175.92	-454.7	(-956.1, 46.6)	245.13	0.074
	PLACEBO	17	9.9	29.3	608.8	169.95				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	23.2	77.6	43.27	-123.4	(-239.2, -7.6)	56.34	0.038*
	PLACEBO	15	19.4	31.8	200.9	41.58				
	PLACEBO/									
	UPA 30 MG QD	10	23.8	4.5	-92.0	16.58	-60.7	(-101.8, -19.6)	19.38	0.006**
	PLACEBO	10	25.7	27.0	-31.2	18.16				
LOCF										
WEEK 52										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	18	3.7	6.3	-13.3	216.44	-812.9	(-1430.1, -195.6)	301.33	0.012*
	PLACEBO	14	7.3	19.4	799.5	254.30				
	UPA 15 MG QD/									
	UPA 15 MG QD	18	12.5	17.3	104.1	164.05	-509.7	(-983.4, -36.0)	232.25	0.036*
	PLACEBO	17	9.9	29.0	613.8	166.85				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	23.2	74.4	45.42	-114.7	(-236.3, 6.9)	59.15	0.063
	PLACEBO	15	19.4	31.8	189.1	43.65				
	PLACEBO/									
	UPA 30 MG QD	10	23.8	5.2	-90.1	16.20	-60.3	(-100.4, -20 2)	18.93	0.006**
	PLACEBO	10	25.7	27.1	-29.8	17.74				
LOCF WEEK 64										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	3.7	7.0	63.6	237.26	-738.4	(-1415.1, -61.8)	330.32	0.034*
	PLACEBO	14	7.3	19.4	802.1	278.76				
	UPA 15 MG QD/									
	UPA 15 MG QD	18	12.5	17.4	104.1	163.78	-510.5	(-983.4, -37.6)	231.87	0.035*
	PLACEBO	17	9.9	29.3	614.6	166.57				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	23.2	71.8	46.74	-108.2	(-233.3, 16.9)	60.86	0.087
	PLACEBO	15	19.4	31.5	179.9	44.91				
	PLACEBO/									
	UPA 30 MG QD	10	23.8	6.1	-91.4	15.83	-55.6	(-94.8, -16.4)	18.51	0.008**
	PLACEBO	10	25.7	27.2	-35.8	17.34				
LOCF WEEK 76										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	3.5	6.9	24.4	219.11	-763.5	(-1389.2, -137.7)	305.94	0.019*
	PLACEBO	14	7.3	19.3	787.8	262.89				
	UPA 15 MG QD/									
	UPA 15 MG QD	17	13.2	18.5	130.2	169.29	-483.8	(-969.6, 2.0)	237.88	0.051

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	17	9.9	29.7	614.0	168.03				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	23.2	77.7	43.60	-123.8	(-240.4, -7 1)	56.77	0.038*
	PLACEBO	15	19.4	31.8	201.4	41.89				
	PLACEBO/									
	UPA 30 MG QD	10	23.8	5.9	-90.3	17.43	-52.9	(-96.1, -9.7)	20.37	0.019*
	PLACEBO	10	25.7	27.0	-37.3	19.09				
LOCF										
WEEK 88										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	3.7	7.5	39.0	226.10	-730.8	(-1375.5, -86.0)	314.77	0.028*
	PLACEBO	14	7.3	19.2	769.7	265.64				
	UPA 15 MG QD/									
	UPA 15 MG QD	18	12.5	17.2	99.3	163.06	-518.1	(-988.9, -47 3)	230.86	0.032*
	PLACEBO	17	9.9	29.0	617.5	165.84				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	23.2	69.1	48.78	-101.6	(-232.2, 28.9)	63.52	0.122
	PLACEBO	15	19.4	31.3	170.7	46.87				
	PLACEBO/									
	UPA 30 MG QD	10	23.8	8.2	-84.6	17.51	-46.9	(-90.3, -3.5)	20.47	0.036*
	PLACEBO	10	25.7	26.9	-37.7	19.18				
OBSERVED CASE										
WEEK 20										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	3.7	5.0	-73.8	215.54	-865.3	(-1506.0, -224.6)	312.26	0.010**
	PLACEBO	13	7.8	20.1	791.5	262.34				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	14.0	15.9	65.7	178.24	-516.6	(-1024.6, -8.7)	248.37	0.046*
	PLACEBO	17	9.9	29.9	582.3	172.19				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	19.4	21.5	79.1	48.42	-106.8	(-236.4, 22.8)	63.05	0.102
	PLACEBO	15	19.4	31.5	186.0	46.53				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	10	23.8	10.0	11.8	30.59	-38.8	(-114.6, 36.9)	35.75	0.293
	PLACEBO	10	25.7	28.5	50.7	33.50				
OBSERVED CASE WEEK 24										
	UPA 30 MG QD/									
	UPA 30 MG QD	16	2.6	3.5	-29.0	81.09	-349.6	(-626.4, -72.7)	131.22	0.016*
	PLACEBO	5	6.3	10.5	320.6	124.59				
	UPA 15 MG QD/									
	UPA 15 MG QD	6	5.5	4.7	-8.0	92.10	-284.1	(-614.4, 46.2)	139.68	0.081
	PLACEBO	5	6.8	22.2	276.1	126.15				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	6	6.5	6.5	12.2	44.21	-13.2	(-276.0, 249.5)	94.63	0.896
	PLACEBO	2	2.4	4.3	25.4	91.23				
	PLACEBO/									
	UPA 30 MG QD	9	25.4	3.7	-67.6	16.14	-58.6	(-141.2, 24.1)	34.95	0.138
	PLACEBO	2	6.9	6.7	-9.0	31.91				
OBSERVED CASE WEEK 32										
	UPA 30 MG QD/									
	UPA 30 MG QD	14	2.0	2.6	18.1	86.49	82.3	(-143.8, 308.5)	105.46	0.448
	PLACEBO	4	4.4	2.4	-64.2	108.26				
	UPA 15 MG QD/									
	UPA 15 MG QD	6	5.5	12.5	170.7	192.18	1.4	(-896.0, 898.9)	349.12	0.997
	PLACEBO	3	8.7	16.5	169.2	310.58				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	4	6.4	10.6	34.7	50.23	-55.5	(-463.2, 352.3)	94.77	0.618
	PLACEBO	2	2.4	3.4	90.2	89.76				
	PLACEBO/									
	UPA 30 MG QD	8	27.0	3.8	-83.4	12.98	-59.8	(-129.0, 9.5)	28.28	0.079
	PLACEBO	2	6.9	5.4	-23.7	25.78				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 40										
	UPA 30 MG QD/									
	UPA 30 MG QD	13	2.2	3.2	622.0	680.91	415.8	(-1262.0, 2093.6)	770.05	0.599
	PLACEBO	3	2.6	2.9	206.2	778.50				
	UPA 15 MG QD/									
	UPA 15 MG QD	3	4.4	2.6	-16.8	23.59	40.3	(-518.3, 598.8)	43.96	0.528
	PLACEBO	2	11.8	13.2	-57.0	32.67				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	2	1.0	1.3	-35.2	166.10	-226.6	(-3800.2, 3347.1)	281.25	0.568
	PLACEBO	2	2.4	5.0	191.4	166.10				
	PLACEBO/									
	UPA 30 MG QD	8	27.0	4.1	-86.7	12.56	15.7	(-51.3, 82.7)	27.38	0.586
	PLACEBO	2	6.9	0.6	-102.4	24.96				
OBSERVED CASE WEEK 52										
	UPA 30 MG QD/									
	UPA 30 MG QD	13	2.2	2.5	117.4	200.14	39.7	(-488.2, 567.6)	239.84	0.872
	PLACEBO	2	0.6	1.6	77.8	269.67				
	UPA 15 MG QD/									
	UPA 15 MG QD	5	2.6	1.3	-12.7	26.11	35.3	(-152.8, 223.3)	59.08	0.592
	PLACEBO	2	11.8	10.8	-48.0	51.51				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	1	1.0	0.0	-1.6	0.00	-11.7		0.00	NA
	PLACEBO	2	2.4	4.5	10.2	0.00				
	PLACEBO/									
	UPA 30 MG QD	8	27.0	5.0	-85.1	13.81	9.7	(-64.0, 83.3)	30.10	0.759
	PLACEBO	2	6.9	1.1	-94.8	27.44				
OBSERVED CASE WEEK 64										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	12	1.7	2.9	329.3	538.58	218.7	(-1030.7, 1468.1)	560.74	0.705
	PLACEBO	2	0.6	1.8	110.7	678.68				
	UPA 15 MG QD/									
	UPA 15 MG QD	5	2.6	1.3	-14.0	28.12	50.4	(-152.1, 252.9)	63.63	0.486
	PLACEBO	2	11.8	12.7	-64.3	55.48				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	1	1.0	0.0	-65.4	0.00	-52.7		0.00	NA
	PLACEBO	2	2.4	2.8	-12.6	0.00				
	PLACEBO/									
	UPA 30 MG QD	7	24.8	3.3	-86.8	15.65	11.6	(-73.7, 97.0)	33.22	0.740
	PLACEBO	2	6.9	1.4	-98.5	29.61				
OBSERVED CASE WEEK 76										
	UPA 30 MG QD/									
	UPA 30 MG QD	13	1.5	3.1	38.5	361.89	135.0	(-694.2, 964.1)	376.71	0.727
	PLACEBO	2	0.6	1.2	-96.5	466.46				
	UPA 15 MG QD/									
	UPA 15 MG QD	4	3.3	2.3	4.7	37.80	66.2	(-276.4, 408.8)	79.62	0.493
	PLACEBO	2	11.8	16.2	-61.5	64.94				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	1	1.0	0.0	-220.3	0.00	-414.8		0.00	NA
	PLACEBO	2	2.4	4.8	194.5	0.00				
	PLACEBO/									
	UPA 30 MG QD	5	24.2	0.9	-98.8	1.91	-5.1	(-17.5, 7.3)	3.90	0.285
	PLACEBO	2	6.9	0.4	-93.7	3.28				
OBSERVED CASE WEEK 88										
	UPA 30 MG QD/									
	UPA 30 MG QD	10	1.7	1.7	-125.1	80.16	21.0	(-155.1, 197.0)	76.36	0.791
	PLACEBO	2	0.6	0.3	-146.1	95.65				
	UPA 15 MG QD/									
	UPA 15 MG QD	5	2.6	0.7	-49.8	22.29	-71.9	(-232.4, 88.6)	50.43	0.249

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	2	11.8	10.4	22.0	43.97				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	1	1.0	0.0	-158.3	0.00	-137.5		0.00	NA
	PLACEBO	2	2.4	0.8	-20.8	0.00				
	PLACEBO/									
	UPA 30 MG QD	4	17.0	0.5	-97.4	1.14	1.6	(-7.3, 10.5)	2.07	0.522
	PLACEBO	2	6.9	0.1	-99.0	1.65				

NA = NOT APPLICABLE.
STRATA IS DEFINED AS EASI 75 RESPONDER AT THE ENTRY OF PERIOD 2 (YES, NO).
[A] P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATA, BASELINE VALUE AND THE TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2　2.1.4

表 2.7.3.6-95. 第 1 ピリオド及び第 2 ピリオド全体の各週の移動平均に基づくかゆみの NRS のベースラインからの変化率（%）（LOCF，OC，第 2 ピリオドの ITT 集団）：M16-048 試験

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM LSMEAN	WITHIN GROUP -PERCENT CHANGE BASELINE-SE	BETWEEN GROUP COMPARISON COMPARED TO PLACEBO LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF WEEK 1										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	4.0	-38.6	6.48	-0.8	(-17.7, 16.2)	8.35	0.928
	PLACEBO	19	5.9	3.6	-37.9	6.33				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	4.5	-32.6	5.37	-2.9	(-17.8, 12.0)	7.30	0.698
	PLACEBO	18	6.4	4.4	-29.7	5.07				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	5.3	-18.0	6.12	1.8	(-15.2, 18.8)	8.27	0.831
	PLACEBO	14	6.7	5.8	-19.8	5.99				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	7.1	-0.4	5.44	1.3	(-13.3, 15.9)	6.87	0.852
	PLACEBO	10	6.2	6.2	-1.7	5.98				
LOCF WEEK 2										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.8	-59.5	7.35	4.3	(-15.0, 23.6)	9.48	0.653
	PLACEBO	19	5.9	2.3	-63.8	7.19				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.9	-54.0	5.97	-8.7	(-25.3, 7.8)	8.12	0.290
	PLACEBO	18	6.4	3.3	-45.3	5.64				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.7	-30.2	6.92	2.8	(-16.5, 22.0)	9.35	0.768
	PLACEBO	14	6.7	4.7	-33.0	6.78				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	6.5	-4.9	9.82	-18.3	(-44.5, 8.0)	12.39	0.160
	PLACEBO	10	6.2	6.9	13.4	10.79				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF WEEK 3										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.2	-65.1	7.82	6.4	(-14.1, 26.9)	10.07	0.531
	PLACEBO	19	5.9	1.9	-71.5	7.64				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.4	-60.0	6.00	-4.3	(-20.9, 12.4)	8.16	0.606
	PLACEBO	18	6.4	2.7	-55.7	5.67				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.4	-39.3	8.99	10.5	(-14.0, 35.0)	11.91	0.387
	PLACEBO	15	6.9	3.6	-49.7	8.54				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	6.0	-15.2	9.52	-16.7	(-42.2, 8.7)	12.01	0.183
	PLACEBO	10	6.2	6.3	1.5	10.46				
LOCF WEEK 4										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.2	-65.9	7.32	8.3	(-10.9, 27.5)	9.44	0.387
	PLACEBO	19	5.9	1.7	-74.1	7.16				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.6	-57.5	6.61	4.0	(-14.3, 22.4)	8.99	0.659
	PLACEBO	18	6.4	2.3	-61.5	6.24				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.3	-42.1	8.99	12.3	(-12.2, 36.8)	11.91	0.312
	PLACEBO	15	6.9	3.3	-54.4	8.54				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.8	-14.7	9.52	-24.8	(-50.3, 0.6)	12.01	0.055
	PLACEBO	10	6.2	6.6	10.1	10.46				
LOCF WEEK 5										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	19	6.5	1.9	-70.2	6.73	0.6	(-17.0, 18.2)	8.68	0.945
	PLACEBO	19	5.9	1.8	-70.8	6.58				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.5	-58.9	6.30	6.0	(-11.5, 23.5)	8.57	0.490
	PLACEBO	18	6.4	2.1	-64.9	5.95				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.2	-45.0	9.36	10.7	(-14.8, 36.2)	12.40	0.395
	PLACEBO	15	6.9	3.2	-55.7	8.89				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.7	-20.2	11.05	-22.7	(-52.3, 6.8)	13.94	0.123
	PLACEBO	10	6.2	6.3	2.5	12.14				
LOCF WEEK 6										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	1.8	-72.1	7.17	0.7	(-18.1, 19.5)	9.24	0.941
	PLACEBO	19	5.9	1.7	-72.8	7.01				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.1	-48.3	7.24	15.2	(-4.9, 35.3)	9.85	0.133
	PLACEBO	18	6.4	2.2	-63.5	6.84				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-46.5	8.74	10.2	(-13.6, 33.9)	11.57	0.388
	PLACEBO	15	6.9	3.2	-56.6	8.30				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.4	-24.8	11.43	-18.2	(-48.8, 12.3)	14.42	0.224
	PLACEBO	10	6.2	5.8	-6.6	12.56				
LOCF WEEK 7										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	1.6	-74.2	6.36	-0.6	(-17.2, 16.1)	8.19	0.945
	PLACEBO	19	5.9	1.6	-73.6	6.21				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.8	-51.2	9.42	7.9	(-18.3, 34.0)	12.81	0.543

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	18	6.4	2.5	-59.1	8.90				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.7	-49.3	9.97	12.9	(-14.3, 40.0)	13.21	0.338
	PLACEBO	15	6.9	2.8	-62.2	9.47				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.1	-32.7	10.00	-21.9	(-48.6, 4.9)	12.61	0.102
	PLACEBO	10	6.2	5.7	-10.8	10.99				
LOCF WEEK 8										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	1.6	-73.9	6.70	1.3	(-16.3, 18.8)	8.64	0.882
	PLACEBO	19	5.9	1.5	-75.2	6.55				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.8	-52.0	8.81	3.3	(-21.1, 27.8)	11.98	0.784
	PLACEBO	18	6.4	2.7	-55.3	8.32				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-49.5	9.52	11.3	(-14.6, 37.2)	12.60	0.378
	PLACEBO	15	6.9	2.9	-60.8	9.04				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.2	-33.7	11.79	-21.5	(-53.0, 10.0)	14.87	0.168
	PLACEBO	10	6.2	5.8	-12.3	12.96				
LOCF WEEK 9										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	1.5	-75.5	6.16	3.3	(-12.8, 19.5)	7.94	0.678
	PLACEBO	19	5.9	1.3	-78.9	6.02				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.7	-54.2	7.47	2.8	(-17.9, 23.6)	10.16	0.784
	PLACEBO	18	6.4	2.6	-57.0	7.06				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.8	-50.6	9.75	6.6	(-19.9, 33.2)	12.91	0.612
	PLACEBO	15	6.9	3.0	-57.3	9.26				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.1	-41.0	12.20	-30.1	(-62.8, 2.5)	15.39	0.068
	PLACEBO	10	6.2	6.1	-10.9	13.41				
LOCF WEEK 10										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.1	-68.6	6.82	8.7	(-9.2, 26.5)	8.79	0.331
	PLACEBO	19	5.9	1.4	-77.2	6.66				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.7	-52.1	6.26	6.4	(-11.0, 23.8)	8.51	0.458
	PLACEBO	18	6.4	2.5	-58.5	5.91				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.7	-53.2	9.24	6.6	(-18.6, 31.7)	12.23	0.595
	PLACEBO	15	6.9	3.0	-59.8	8.77				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	4.9	-47.4	13.33	-35.9	(-71.5, -0.2)	16.82	0.049*
	PLACEBO	10	6.2	6.1	-11.6	14.65				
LOCF WEEK 11										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.4	-65.1	7.01	13.9	(-4.4, 32.3)	9.03	0.132
	PLACEBO	19	5.9	1.3	-79.0	6.85				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.5	-55.2	7.10	6.6	(-13.1, 26.3)	9.66	0.499
	PLACEBO	18	6.4	2.3	-61.8	6.71				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.5	-56.1	8.52	4.5	(-18.7, 27.6)	11.28	0.696
	PLACEBO	15	6.9	3.0	-60.6	8.09				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.0	-44.9	13.87	-35.0	(-72.1, 2.1)	17.50	0.063
	PLACEBO	10	6.2	6.1	-9.9	15.24				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF										
WEEK 12										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.4	-61.7	8.11	14.9	(-6.4, 36.1)	10.45	0.164
	PLACEBO	19	5.9	1.4	-76.6	7.92				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.5	-53.6	7.26	9.0	(-11.2, 29.1)	9.87	0.372
	PLACEBO	18	6.4	2.2	-62.5	6.86				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.6	-54.2	8.96	-0.8	(-25.2, 23.6)	11.87	0.947
	PLACEBO	15	6.9	2.9	-53.5	8.51				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	4.7	-51.2	11.91	-33.6	(-65.5, -1.8)	15.03	0.040*
	PLACEBO	10	6.2	5.9	-17.5	13.09				
LOCF										
WEEK 13										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.4	-62.9	7.59	13.6	(-6.3, 33.5)	9.78	0.173
	PLACEBO	19	5.9	1.4	-76.5	7.42				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.6	-52.3	7.11	11.7	(-8.0, 31.5)	9.67	0.235
	PLACEBO	18	6.4	2.1	-64.0	6.71				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.6	-52.7	8.60	3.5	(-19.9, 26.9)	11.39	0.760
	PLACEBO	15	6.9	2.9	-56.2	8.17				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	4.9	-48.0	11.21	-34.2	(-64.2, -4.3)	14.14	0.028*
	PLACEBO	10	6.2	6.2	-13.8	12.32				
LOCF										
WEEK 14										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	19	6.5	2.3	-63.4	7.44	15.1	(-4.4, 34.6)	9.59	0.125
	PLACEBO	19	5.9	1.3	-78.5	7.27				
UPA 15 MG QD/										
	UPA 15 MG QD	16	6.7	2.6	-49.8	7.58	12.5	(-8.6, 33.5)	10.31	0.236
	PLACEBO	18	6.4	2.2	-62.3	7.16				
UPA 7.5 MG QD/										
	UPA 7.5 MG QD	15	6.3	3.9	-48.6	9.08	14.4	(-10.3, 39.1)	12.03	0.242
	PLACEBO	15	6.9	2.7	-63.0	8.63				
PLACEBO/										
	UPA 30 MG QD	10	7.4	5.1	-46.8	11.42	-36.1	(-66.6, -5.5)	14.41	0.023*
	PLACEBO	10	6.2	6.3	-10.7	12.56				
LOCF WEEK 15										
UPA 30 MG QD/										
	UPA 30 MG QD	19	6.5	2.4	-61.7	7.79	15.7	(-4.7, 36.1)	10.03	0.126
	PLACEBO	19	5.9	1.3	-77.4	7.61				
UPA 15 MG QD/										
	UPA 15 MG QD	16	6.7	2.5	-50.6	7.96	9.1	(-13.0, 31.2)	10.82	0.407
	PLACEBO	18	6.4	2.3	-59.7	7.52				
UPA 7.5 MG QD/										
	UPA 7.5 MG QD	15	6.3	3.7	-53.3	8.91	8.3	(-16.0, 32.5)	11.80	0.488
	PLACEBO	15	6.9	2.9	-61.6	8.46				
PLACEBO/										
	UPA 30 MG QD	10	7.4	5.0	-50.0	11.52	-40.2	(-71.0, -9.4)	14.53	0.014*
	PLACEBO	10	6.2	6.5	-9.9	12.66				
LOCF WEEK 16										
UPA 30 MG QD/										
	UPA 30 MG QD	19	6.5	2.4	-59.5	8.02	15.1	(-5.9, 36.1)	10.34	0.153
	PLACEBO	19	5.9	1.4	-74.6	7.84				
UPA 15 MG QD/										
	UPA 15 MG QD	16	6.7	2.5	-51.5	7.14	8.3	(-11.6, 28.1)	9.71	0.402

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	18	6.4	2.3	-59.7	6.75				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.6	-54.9	9.87	4.1	(-22.8, 31.0)	13.07	0.756
	PLACEBO	15	6.9	3.0	-59.0	9.37				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.1	-47.7	11.01	-38.5	(-68.0, -9.1)	13.89	0.014*
	PLACEBO	10	6.2	6.6	-9.1	12.10				
LOCF										
ENTRY OF PERIOD 2										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.4	-59.1	7.80	15.6	(-4.8, 36.0)	10.06	0.130
	PLACEBO	19	5.9	1.4	-74.7	7.62				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.5	-51.1	7.30	8.9	(-11.4, 29.2)	9.93	0.378
	PLACEBO	18	6.4	2.3	-60.0	6.90				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.7	-54.2	9.85	5.1	(-21.8, 31.9)	13.05	0.701
	PLACEBO	15	6.9	2.9	-59.3	9.36				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.1	-47.1	11.02	-38.8	(-68.3, -9.3)	13.90	0.013*
	PLACEBO	10	6.2	6.6	-8.3	12.11				
LOCF										
WEEK 17										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.4	-52.8	10.20	-17.7	(-43.2, 7.9)	12.54	0.168
	PLACEBO	18	5.7	3.1	-35.1	9.99				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.9	2.4	-54.1	8.50	-17.9	(-41.4, 5.5)	11.44	0.128
	PLACEBO	17	6.3	3.8	-36.2	8.00				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.1	-51.3	10.48	-12.2	(-40.8, 16.3)	13.87	0.386
	PLACEBO	15	6.9	4.3	-39.1	9.95				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	8	7.1	3.0	-60.2	10.20	-50.6	(-79.1, -22.1)	13.21	0.002**
	PLACEBO	9	5.8	6.0	-9.6	10.74				
LOCF WEEK 18										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.4	-59.7	10.39	-45.1	(-71.1, -19.1)	12.78	0.001**
	PLACEBO	18	5.7	4.7	-14.6	10.19				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.9	2.5	-52.3	10.33	-42.6	(-70.7, -14.5)	13.74	0.004**
	PLACEBO	18	6.4	5.6	-9.7	9.34				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-52.9	10.58	-22.2	(-51.0, 6.6)	14.02	0.126
	PLACEBO	15	6.9	4.9	-30.7	10.05				
	PLACEBO/									
	UPA 30 MG QD	8	7.1	1.8	-76.2	10.06	-84.4	(-111.5, -57 2)	12.65	<0.001***
	PLACEBO	10	6.2	6.9	8.2	10.49				
LOCF WEEK 19										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.5	-67.7	11.92	-59.7	(-89.6, -29.8)	14.66	<0.001***
	PLACEBO	18	5.7	5.5	-8.0	11.68				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.0	-44.6	9.91	-40.1	(-67.6, -12.6)	13.47	0.006**
	PLACEBO	18	6.4	5.9	-4.5	9.36				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-54.0	9.50	-38.2	(-64.0, -12.3)	12.58	0.005**
	PLACEBO	15	6.9	5.4	-15.9	9.02				
	PLACEBO/									
	UPA 30 MG QD	8	7.1	1.5	-79.8	13.36	-86.1	(-122.1, -50.0)	16.79	<0.001***
	PLACEBO	10	6.2	6.6	6.2	13.92				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF										
WEEK 20										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.6	-67.3	16.21	-69.6	(-110.2, -29.0)	19.93	0.001**
	PLACEBO	18	5.7	5.9	2.3	15.89				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.1	-45.2	8.62	-42.0	(-65.9, -18.1)	11.71	0.001**
	PLACEBO	18	6.4	6.0	-3.1	8.14				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.7	-58.6	10.75	-32.1	(-61.3, -2.8)	14.23	0.033*
	PLACEBO	15	6.9	5.2	-26.5	10.20				
	PLACEBO/									
	UPA 30 MG QD	9	7.3	1.7	-78.4	12.55	-89.8	(-123.6, -56 1)	15.82	<0.001***
	PLACEBO	10	6.2	6.9	11.4	13.46				
LOCF										
WEEK 21										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.7	-69.3	16.68	-69.2	(-111.0, -27.4)	20.51	0.002**
	PLACEBO	18	5.7	5.9	-0.2	16.35				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.0	-46.4	8.60	-42.9	(-66.8, -19.0)	11.70	<0.001***
	PLACEBO	18	6.4	6.0	-3.5	8.13				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.8	-58.0	10.19	-35.4	(-63.1, -7.6)	13.49	0.014*
	PLACEBO	15	6.9	5.3	-22.6	9.68				
	PLACEBO/									
	UPA 30 MG QD	9	7.3	1.6	-81.9	12.35	-90.7	(-123.8, -57 5)	15.57	<0.001***
	PLACEBO	10	6.2	6.8	8.8	13.24				
LOCF										
WEEK 22										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	18	6.4	2.8	-65.4	16.50	-66.7	(-108.1, -25.4)	20.30	0.002**
	PLACEBO	18	5.7	5.9	1.4	16.18				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.0	-46.3	8.54	-42.8	(-66.5, -19.1)	11.62	<0.001***
	PLACEBO	18	6.4	6.0	-3.5	8.07				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-56.0	12.43	-49.6	(-83.4, -15.8)	16.46	0.006**
	PLACEBO	15	6.9	5.7	-6.4	11.80				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.2	-89.0	11.46	-89.6	(-120.2, -58 9)	14.46	<0.001***
	PLACEBO	10	6.2	6.4	0.5	12.59				
LOCF WEEK 23										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.9	-64.1	16.97	-64.5	(-107.0, -22.0)	20.87	0.004**
	PLACEBO	18	5.7	5.8	0.4	16.63				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.9	-47.0	8.09	-44.4	(-66.9, -22.0)	10.99	<0.001***
	PLACEBO	18	6.4	6.1	-2.6	7.64				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-55.5	15.67	-58.4	(-101.1, -15.7)	20.76	0.009**
	PLACEBO	15	6.9	5.8	2.9	14.88				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.0	-91.3	11.74	-89.0	(-120.4, -57.6)	14.82	<0.001***
	PLACEBO	10	6.2	6.3	-2.2	12.91				
LOCF WEEK 24										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	3.0	-61.8	15.35	-66.2	(-106.8, -25 5)	19.98	0.002**
	PLACEBO	18	5.7	5.9	4.4	15.85				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.0	-46.5	8.29	-44.0	(-67.0, -20.9)	11.28	<0.001***

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	18	6.4	6.1	-2.6	7.83				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-55.6	13.89	-54.5	(-92.3, -16.7)	18.39	0.006**
	PLACEBO	15	6.9	5.8	-1.1	13.19				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.0	-90.7	10.98	-93.0	(-122.4, -63.6)	13.85	<0.001***
	PLACEBO	10	6.2	6.5	2.3	12.07				
LOCF WEEK 25										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.9	-62.1	15.30	-67.6	(-108.1, -27 1)	19.91	0.002**
	PLACEBO	18	5.7	5.9	5.5	15.80				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.9	-48.0	8.87	-46.0	(-70.6, -21.4)	12.06	<0.001***
	PLACEBO	18	6.4	6.1	-2.0	8.38				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-55.0	13.90	-54.6	(-92.4, -16.7)	18.42	0.006**
	PLACEBO	15	6.9	5.8	-0.4	13.20				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.8	-92.7	10.26	-96.8	(-124.2, -69 3)	12.94	<0.001***
	PLACEBO	10	6.2	6.6	4.1	11.28				
LOCF WEEK 26										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.8	-64.8	15.30	-69.5	(-110.0, -29.0)	19.91	0.001**
	PLACEBO	18	5.7	6.0	4.7	15.80				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.0	-46.6	8.85	-44.3	(-68.9, -19.7)	12.03	<0.001***
	PLACEBO	18	6.4	6.1	-2.3	8.35				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-55.3	13.88	-56.4	(-94.2, -18.6)	18.39	0.005**
	PLACEBO	15	6.9	5.9	1.1	13.18				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.8	-92.3	9.78	-96.1	(-122.3, -70.0)	12.33	<0.001***
	PLACEBO	10	6.2	6.6	3.8	10.74				
LOCF WEEK 27										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-69.2	15.99	-69.1	(-111.5, -26.8)	20.81	0.002**
	PLACEBO	18	5.7	5.9	-0.1	16.51				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.0	-46.5	8.65	-43.3	(-67.3, -19.3)	11.76	<0.001***
	PLACEBO	18	6.4	6.0	-3.2	8.17				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-55.0	13.60	-56.5	(-93.5, -19.5)	18.02	0.004**
	PLACEBO	15	6.9	5.9	1.5	12.92				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.6	-95.1	9.48	-99.2	(-124.5, -73.8)	11.96	<0.001***
	PLACEBO	10	6.2	6.6	4.1	10.42				
LOCF WEEK 28										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.8	-67.0	15.67	-70.4	(-111.9, -28 9)	20.39	0.002**
	PLACEBO	18	5.7	6.0	3.4	16.18				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.1	-44.5	8.73	-42.0	(-66.2, -17.7)	11.86	0.001**
	PLACEBO	18	6.4	6.1	-2.5	8.24				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.8	-55.4	13.62	-58.1	(-95.1, -21.0)	18.03	0.003**
	PLACEBO	15	6.9	6.0	2.7	12.93				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.6	-94.4	9.80	-100.6	(-126.8, -74.4)	12.36	<0.001***
	PLACEBO	10	6.2	6.8	6.2	10.77				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF										
WEEK 29										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-68.3	15.92	-69.0	(-111.2, -26 9)	20.72	0.002**
	PLACEBO	18	5.7	6.0	0.7	16.44				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-42.7	8.85	-39.6	(-64.2, -15.1)	12.03	0.003**
	PLACEBO	18	6.4	6.0	-3.1	8.36				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-54.4	14.64	-61.2	(-101.1, -21.4)	19.39	0.004**
	PLACEBO	15	6.9	6.1	6.8	13.90				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.8	-92.2	10.23	-98.7	(-126.1, -71.4)	12.90	<0.001***
	PLACEBO	10	6.2	6.8	6.5	11.24				
LOCF										
WEEK 30										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.9	-65.1	15.60	-67.5	(-108.8, -26 2)	20.30	0.002**
	PLACEBO	18	5.7	5.9	2.4	16.11				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-42.9	9.18	-40.3	(-65.8, -14.8)	12.48	0.003**
	PLACEBO	18	6.4	6.1	-2.6	8.67				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-52.8	15.37	-62.4	(-104.2, -20 5)	20.36	0.005**
	PLACEBO	15	6.9	6.2	9.6	14.60				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.7	-94.1	9.99	-100.6	(-127.3, -73 9)	12.60	<0.001***
	PLACEBO	10	6.2	6.8	6.5	10.98				
LOCF										
WEEK 31										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	19	6.5	2.9	-65.5	15.73	-66.9	(-108.6, -25 3)	20.47	0.003**
	PLACEBO	18	5.7	5.9	1.4	16.25				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-42.4	9.75	-40.5	(-67.5, -13.4)	13.25	0.005**
	PLACEBO	18	6.4	6.1	-1.9	9.20				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-52.1	14.97	-60.7	(-101.4, -19 9)	19.83	0.005**
	PLACEBO	15	6.9	6.2	8.5	14.22				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.7	-93.8	9.77	-98.7	(-124.8, -72.6)	12.32	<0.001***
	PLACEBO	10	6.2	6.7	4.9	10.73				
LOCF WEEK 32										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.8	-65.2	15.44	-68.7	(-109.5, -27.8)	20.09	0.002**
	PLACEBO	18	5.7	5.9	3.4	15.94				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-44.5	9.47	-41.6	(-67.9, -15.3)	12.88	0.003**
	PLACEBO	18	6.4	6.1	-2.9	8.94				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.1	-50.9	14.09	-56.3	(-94.6, -17.9)	18.66	0.006**
	PLACEBO	15	6.9	6.1	5.4	13.38				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.7	-93.8	9.81	-99.5	(-125.7, -73 3)	12.37	<0.001***
	PLACEBO	10	6.2	6.7	5.8	10.78				
LOCF WEEK 33										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.8	-67.4	15.92	-66.8	(-108.9, -24.6)	20.72	0.003**
	PLACEBO	18	5.7	5.9	-0.7	16.44				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-44.3	9.47	-41.4	(-67.6, -15.1)	12.87	0.003**

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	18	6.4	6.1	-2.9	8.94				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-52.7	14.02	-57.8	(-96.0, -19.6)	18.57	0.004**
	PLACEBO	15	6.9	6.1	5.1	13.31				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.7	-96.0	10.16	-94.9	(-122.1, -67.7)	12.82	<0.001***
	PLACEBO	10	6.2	6.5	-1.0	11.17				
LOCF WEEK 34										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.8	-68.5	16.08	-66.9	(-109.5, -24 3)	20.92	0.003**
	PLACEBO	18	5.7	5.9	-1.6	16.60				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-43.7	9.34	-41.2	(-67.2, -15.3)	12.70	0.003**
	PLACEBO	18	6.4	6.1	-2.5	8.82				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-53.6	14.29	-55.5	(-94.4, -16.6)	18.92	0.007**
	PLACEBO	15	6.9	5.9	2.0	13.57				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.7	-95.3	9.91	-95.9	(-122.4, -69.4)	12.50	<0.001***
	PLACEBO	10	6.2	6.5	0.6	10.90				
LOCF WEEK 35										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-69.5	16.09	-69.1	(-111.7, -26 5)	20.94	0.002**
	PLACEBO	18	5.7	5.9	-0.4	16.61				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-44.0	9.38	-41.0	(-67.0, -14.9)	12.75	0.003**
	PLACEBO	18	6.4	6.1	-3.1	8.86				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-52.4	13.99	-55.2	(-93.3, -17.1)	18.54	0.006**
	PLACEBO	15	6.9	6.0	2.8	13.29				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.8	-94.3	10.18	-92.4	(-119.6, -65 2)	12.84	<0.001***
	PLACEBO	10	6.2	6.5	-1.9	11.19				
LOCF WEEK 36										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-70.5	16.16	-68.0	(-110.8, -25 3)	21.02	0.003**
	PLACEBO	18	5.7	5.8	-2.5	16.68				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-44.5	9.57	-41.2	(-67.8, -14.6)	13.02	0.004**
	PLACEBO	18	6.4	6.1	-3.3	9.04				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-51.9	13.89	-56.0	(-93.8, -18.2)	18.40	0.005**
	PLACEBO	15	6.9	6.0	4.1	13.19				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.1	-91.2	10.30	-87.4	(-115.0, -59 9)	13.00	<0.001***
	PLACEBO	10	6.2	6.4	-3.8	11.32				
LOCF WEEK 37										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-69.1	16.02	-65.9	(-108.4, -23 5)	20.85	0.003**
	PLACEBO	18	5.7	5.8	-3.1	16.54				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-44.8	9.61	-41.8	(-68.5, -15.1)	13.07	0.003**
	PLACEBO	18	6.4	6.1	-3.0	9.08				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-52.1	16.01	-60.1	(-103.6, -16 5)	21.20	0.009**
	PLACEBO	15	6.9	6.1	7.9	15.20				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.0	-92.6	10.11	-88.1	(-115.1, -61.0)	12.75	<0.001***
	PLACEBO	10	6.2	6.4	-4.6	11.11				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
LOCF										
WEEK 38										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.8	-67.5	15.99	-65.5	(-107.8, -23 2)	20.81	0.003**
	PLACEBO	18	5.7	5.9	-2.0	16.51				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-44.3	9.67	-41.5	(-68.3, -14.6)	13.15	0.004**
	PLACEBO	18	6.4	6.1	-2.9	9.14				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-53.1	15.29	-57.7	(-99.3, -16.0)	20.25	0.008**
	PLACEBO	15	6.9	6.0	4.6	14.52				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	0.9	-94.6	9.95	-87.6	(-114.2, -61.0)	12.56	<0.001***
	PLACEBO	10	6.2	6.3	-7.0	10.94				
LOCF										
WEEK 39										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.8	-66.3	16.02	-65.0	(-107.5, -22.6)	20.85	0.004**
	PLACEBO	18	5.7	5.9	-1.2	16.55				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.2	-45.2	9.32	-42.6	(-68.4, -16.7)	12.68	0.002**
	PLACEBO	18	6.4	6.1	-2.6	8.81				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.2	-49.9	15.08	-52.5	(-93.6, -11.4)	19.98	0.014*
	PLACEBO	15	6.9	5.9	2.6	14.32				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.1	-93.5	10.40	-84.0	(-111.8, -56 2)	13.12	<0.001***
	PLACEBO	10	6.2	6.3	-9.5	11.43				
LOCF										
WEEK 40										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	19	6.5	2.8	-67.0	15.92	-65.4	(-107.5, -23 2)	20.72	0.003**
	PLACEBO	18	5.7	5.9	-1.7	16.44				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.2	-46.2	9.42	-43.4	(-69.5, -17.2)	12.81	0.002**
	PLACEBO	18	6.4	6.1	-2.8	8.90				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.2	-49.9	15.08	-52.5	(-93.6, -11.4)	19.98	0.014*
	PLACEBO	15	6.9	5.9	2.6	14.32				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.0	-94.7	10.27	-84.4	(-111.9, -57.0)	12.95	<0.001***
	PLACEBO	10	6.2	6.2	-10.3	11.28				
LOCF WEEK 52										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-69.6	16.09	-71.9	(-114.5, -29 3)	20.94	0.002**
	PLACEBO	18	5.7	6.1	2.2	16.62				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.3	-42.8	9.26	-40.0	(-65.7, -14.3)	12.59	0.003**
	PLACEBO	18	6.4	6.1	-2.8	8.75				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.2	-49.5	14.15	-51.4	(-89.9, -12.8)	18.74	0.011*
	PLACEBO	15	6.9	5.9	1.9	13.44				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.0	-97.5	10.94	-81.4	(-110.6, -52 1)	13.80	<0.001***
	PLACEBO	10	6.2	6.0	-16.1	12.02				
LOCF WEEK 64										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-69.7	16.07	-73.0	(-115.6, -30 5)	20.92	0.001**
	PLACEBO	18	5.7	6.1	3.4	16.60				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.1	-43.9	9.15	-41.1	(-66.5, -15.7)	12.44	0.002**

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	18	6.4	6.1	-2.8	8.64				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.2	-50.4	10.34	-37.6	(-65.7, -9.4)	13.69	0.011*
	PLACEBO	15	6.9	5.6	-12.8	9.82				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.4	-94.0	11.04	-76.7	(-106.2, -47 1)	13.93	<0.001***
	PLACEBO	10	6.2	6.0	-17.3	12.14				
LOCF WEEK 76										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-68.8	16.17	-70.7	(-113.6, -27 9)	21.04	0.002**
	PLACEBO	18	5.7	6.1	1.9	16.70				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.2	-43.4	9.19	-40.5	(-66.1, -15.0)	12.50	0.003**
	PLACEBO	18	6.4	6.1	-2.8	8.68				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.2	-49.8	15.68	-53.9	(-96.6, -11.2)	20.77	0.015*
	PLACEBO	15	6.9	5.9	4.1	14.89				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.2	-95.8	11.08	-79.1	(-108.7, -49.4)	13.98	<0.001***
	PLACEBO	10	6.2	6.0	-16.7	12.18				
LOCF WEEK 88										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.7	-68.8	16.17	-70.7	(-113.6, -27 9)	21.04	0.002**
	PLACEBO	18	5.7	6.1	1.9	16.70				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	3.2	-43.4	9.19	-40.5	(-66.1, -15.0)	12.50	0.003**
	PLACEBO	18	6.4	6.1	-2.8	8.68				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.2	-49.8	15.68	-53.9	(-96.6, -11.2)	20.77	0.015*
	PLACEBO	15	6.9	5.9	4.1	14.89				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	10	7.4	1.5	-93.2	11.01	-75.6	(-105.1, -46 2)	13.89	<0.001***
	PLACEBO	10	6.2	6.0	-17.6	12.11				
OBSERVED CASE WEEK 1										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	4.0	-38.6	6.48	-0.8	(-17.7, 16.2)	8.35	0.928
	PLACEBO	19	5.9	3.6	-37.9	6.33				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	4.5	-32.6	5.37	-2.9	(-17.8, 12.0)	7.30	0.698
	PLACEBO	18	6.4	4.4	-29.7	5.07				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	5.3	-18.0	6.12	1.8	(-15.2, 18.8)	8.27	0.831
	PLACEBO	14	6.7	5.8	-19.8	5.99				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	7.1	-0.4	5.44	1.3	(-13.3, 15.9)	6.87	0.852
	PLACEBO	10	6.2	6.2	-1.7	5.98				
OBSERVED CASE WEEK 2										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.5	2.6	-61.5	7.32	2.0	(-17.1, 21.2)	9.41	0.830
	PLACEBO	19	5.9	2.3	-63.6	7.05				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.9	-54.3	5.97	-7.2	(-24.1, 9.7)	8.26	0.390
	PLACEBO	17	6.3	3.1	-47.1	5.88				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.7	-30.2	6.92	2.8	(-16.5, 22.0)	9.35	0.768
	PLACEBO	14	6.7	4.7	-33.0	6.78				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	6.5	-4.9	9.82	-18.3	(-44.5, 8.0)	12.39	0.160
	PLACEBO	10	6.2	6.9	13.4	10.79				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE										
WEEK 3										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.5	2.0	-67.4	7.73	3.7	(-16.5, 23.9)	9.93	0.709
	PLACEBO	19	5.9	1.9	-71.2	7.43				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.4	-60.0	6.00	-4.3	(-20.9, 12.4)	8.16	0.606
	PLACEBO	18	6.4	2.7	-55.7	5.67				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.4	-39.3	8.99	10.5	(-14.0, 35.0)	11.91	0.387
	PLACEBO	15	6.9	3.6	-49.7	8.54				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	6.0	-16.3	9.45	-14.9	(-40.7, 11.0)	12.13	0.239
	PLACEBO	9	6.4	6.3	-1.4	10.67				
OBSERVED CASE										
WEEK 4										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.2	-65.9	7.32	8.3	(-10.9, 27.5)	9.44	0.387
	PLACEBO	19	5.9	1.7	-74.1	7.16				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.6	-57.5	6.61	4.0	(-14.3, 22.4)	8.99	0.659
	PLACEBO	18	6.4	2.3	-61.5	6.24				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.3	-42.1	8.99	12.3	(-12.2, 36.8)	11.91	0.312
	PLACEBO	15	6.9	3.3	-54.4	8.54				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.8	-15.5	9.28	-22.5	(-47.9, 2.8)	11.91	0.078
	PLACEBO	9	6.4	6.6	7.0	10.48				
OBSERVED CASE										
WEEK 5										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	18	6.4	1.8	-70.8	7.26	0.3	(-17.8, 18.5)	8.92	0.971
	PLACEBO	19	5.9	1.8	-71.2	6.73				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.5	-59.0	6.29	4.7	(-13.0, 22.4)	8.66	0.590
	PLACEBO	17	6.5	2.2	-63.8	6.08				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.2	-45.0	9.36	10.7	(-14.8, 36.2)	12.40	0.395
	PLACEBO	15	6.9	3.2	-55.7	8.89				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.7	-20.2	11.29	-21.1	(-52.2, 10.0)	14.59	0.169
	PLACEBO	9	6.2	6.1	0.9	12.73				
OBSERVED CASE WEEK 6										
	UPA 30 MG QD/									
	UPA 30 MG QD	17	6.4	1.6	-74.7	7.80	-1.6	(-21.1, 17.9)	9.57	0.870
	PLACEBO	19	5.9	1.7	-73.2	7.11				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.9	3.2	-46.5	7.64	17.0	(-3.8, 37.7)	10.16	0.106
	PLACEBO	18	6.4	2.2	-63.5	6.91				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-46.5	8.74	10.2	(-13.6, 33.9)	11.57	0.388
	PLACEBO	15	6.9	3.2	-56.6	8.30				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.4	-24.6	11.48	-15.3	(-46.9, 16.3)	14.82	0.317
	PLACEBO	9	6.2	5.6	-9.2	12.94				
OBSERVED CASE WEEK 7										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	1.5	-75.5	6.83	-1.3	(-18.4, 15.8)	8.40	0.878
	PLACEBO	19	5.9	1.6	-74.2	6.33				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.8	-51.2	9.42	7.9	(-18.3, 34.0)	12.81	0.543

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	18	6.4	2.5	-59.1	8.90				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.7	-49.3	9.97	12.9	(-14.3, 40.0)	13.21	0.338
	PLACEBO	15	6.9	2.8	-62.2	9.47				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.1	-32.7	10.00	-21.9	(-48.6, 4.9)	12.61	0.102
	PLACEBO	10	6.2	5.7	-10.8	10.99				
OBSERVED CASE WEEK 8										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.5	1.4	-75.6	6.71	-0.6	(-18.2, 16.9)	8.62	0.944
	PLACEBO	19	5.9	1.5	-75.0	6.45				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.8	-52.0	8.81	3.3	(-21.1, 27.8)	11.98	0.784
	PLACEBO	18	6.4	2.7	-55.3	8.32				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-49.5	9.52	11.3	(-14.6, 37.2)	12.60	0.378
	PLACEBO	15	6.9	2.9	-60.8	9.04				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.2	-33.7	11.79	-21.5	(-53.0, 10.0)	14.87	0.168
	PLACEBO	10	6.2	5.8	-12.3	12.96				
OBSERVED CASE WEEK 9										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	1.5	-75.1	6.64	3.7	(-12.9, 20.3)	8.16	0.655
	PLACEBO	19	5.9	1.3	-78.8	6.15				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.7	-54.2	7.47	2.8	(-17.9, 23.6)	10.16	0.784
	PLACEBO	18	6.4	2.6	-57.0	7.06				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.8	-50.6	9.75	6.6	(-19.9, 33.2)	12.91	0.612
	PLACEBO	15	6.9	3.0	-57.3	9.26				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.1	-41.0	12.20	-30.1	(-62.8, 2.5)	15.39	0.068
	PLACEBO	10	6.2	6.1	-10.9	13.41				
OBSERVED CASE WEEK 10										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.1	-67.1	7.31	9.7	(-8.6, 27.9)	8.98	0.290
	PLACEBO	19	5.9	1.4	-76.8	6.77				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.7	-52.1	6.26	6.4	(-11.0, 23.8)	8.51	0.458
	PLACEBO	18	6.4	2.5	-58.5	5.91				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.7	-52.9	8.82	3.5	(-21.0, 28.0)	11.91	0.771
	PLACEBO	14	6.6	3.2	-56.4	8.66				
	PLACEBO/									
	UPA 30 MG QD	9	7.3	5.3	-42.9	12.68	-29.5	(-63.6, 4.6)	15.99	0.085
	PLACEBO	10	6.2	6.1	-13.4	13.60				
OBSERVED CASE WEEK 11										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.4	-63.5	7.51	15.0	(-3.7, 33.8)	9.22	0.113
	PLACEBO	19	5.9	1.3	-78.5	6.95				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.9	2.4	-58.1	7.39	4.0	(-16.1, 24.1)	9.82	0.685
	PLACEBO	18	6.4	2.3	-62.1	6.68				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.5	-56.0	7.92	1.1	(-21.0, 23.1)	10.70	0.921
	PLACEBO	14	6.6	3.2	-57.1	7.77				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.0	-44.9	13.87	-35.0	(-72.1, 2.1)	17.50	0.063
	PLACEBO	10	6.2	6.1	-9.9	15.24				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE										
WEEK 12										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.4	-61.7	8.11	14.9	(-6.4, 36.1)	10.45	0.164
	PLACEBO	19	5.9	1.4	-76.6	7.92				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.5	-53.6	7.26	9.0	(-11.2, 29.1)	9.87	0.372
	PLACEBO	18	6.4	2.2	-62.5	6.86				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.6	-54.2	8.96	-0.8	(-25.2, 23.6)	11.87	0.947
	PLACEBO	15	6.9	2.9	-53.5	8.51				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	4.7	-51.2	11.91	-33.6	(-65.5, -1.8)	15.03	0.040*
	PLACEBO	10	6.2	5.9	-17.5	13.09				
OBSERVED CASE										
WEEK 13										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.4	-62.0	7.77	13.3	(-7.0, 33.6)	9.97	0.191
	PLACEBO	18	6.1	1.5	-75.3	7.88				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.9	2.3	-57.3	7.02	7.3	(-11.8, 26.4)	9.34	0.443
	PLACEBO	18	6.4	2.1	-64.6	6.35				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.6	-52.7	8.60	3.5	(-19.9, 26.9)	11.39	0.760
	PLACEBO	15	6.9	2.9	-56.2	8.17				
	PLACEBO/									
	UPA 30 MG QD	9	7.5	4.9	-48.4	11.87	-34.8	(-67.0, -2.5)	15.12	0.036*
	PLACEBO	10	6.2	6.2	-13.7	12.78				
OBSERVED CASE										
WEEK 14										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	18	6.4	2.3	-60.6	7.07	21.1	(3.3, 39.0)	8.76	0.022*
	PLACEBO	17	6.0	1.0	-81.7	6.89				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.6	-49.8	7.58	12.5	(-8.6, 33.5)	10.31	0.236
	PLACEBO	18	6.4	2.2	-62.3	7.16				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-48.6	9.08	14.4	(-10.3, 39.1)	12.03	0.242
	PLACEBO	15	6.9	2.7	-63.0	8.63				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.1	-46.8	11.42	-36.1	(-66.6, -5.5)	14.41	0.023*
	PLACEBO	10	6.2	6.3	-10.7	12.56				
OBSERVED CASE WEEK 15										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.4	-59.6	6.93	21.1	(2.7, 39.5)	9.04	0.026*
	PLACEBO	17	6.0	1.0	-80.7	7.14				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.5	-50.6	7.96	9.1	(-13.0, 31.2)	10.82	0.407
	PLACEBO	18	6.4	2.3	-59.7	7.52				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	14	6.4	3.6	-54.6	9.15	6.8	(-18.0, 31.6)	12.04	0.575
	PLACEBO	15	6.9	2.9	-61.5	8.52				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.0	-50.0	11.52	-40.2	(-71.0, -9.4)	14.53	0.014*
	PLACEBO	10	6.2	6.5	-9.9	12.66				
OBSERVED CASE WEEK 16										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.6	-57.0	8.49	14.8	(-8.0, 37.7)	11.19	0.195
	PLACEBO	16	6.3	1.7	-71.9	8.78				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.5	2.3	-53.9	6.94	5.1	(-13.9, 24.2)	9.32	0.588

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	18	6.4	2.3	-59.0	6.37				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.6	-54.5	9.51	1.1	(-25.4, 27.5)	12.85	0.933
	PLACEBO	14	6.6	3.2	-55.6	9.34				
	PLACEBO/									
	UPA 30 MG QD	9	7.3	5.7	-41.7	8.62	-30.5	(-53.6, -7.3)	10.87	0.013*
	PLACEBO	10	6.2	6.6	-11.2	9.25				
OBSERVED CASE ENTRY OF PERIOD 2										
	UPA 30 MG QD/									
	UPA 30 MG QD	19	6.5	2.4	-59.1	7.80	15.6	(-4.8, 36.0)	10.06	0.130
	PLACEBO	19	5.9	1.4	-74.7	7.62				
	UPA 15 MG QD/									
	UPA 15 MG QD	16	6.7	2.5	-51.1	7.30	8.9	(-11.4, 29.2)	9.93	0.378
	PLACEBO	18	6.4	2.3	-60.0	6.90				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.7	-54.2	9.85	5.1	(-21.8, 31.9)	13.05	0.701
	PLACEBO	15	6.9	2.9	-59.3	9.36				
	PLACEBO/									
	UPA 30 MG QD	10	7.4	5.1	-47.1	11.02	-38.8	(-68.3, -9.3)	13.90	0.013*
	PLACEBO	10	6.2	6.6	-8.3	12.11				
OBSERVED CASE WEEK 17										
	UPA 30 MG QD/									
	UPA 30 MG QD	18	6.4	2.4	-52.8	10.20	-17.7	(-43.2, 7.9)	12.54	0.168
	PLACEBO	18	5.7	3.1	-35.1	9.99				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.9	2.4	-54.1	8.50	-17.9	(-41.4, 5.5)	11.44	0.128
	PLACEBO	17	6.3	3.8	-36.2	8.00				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.1	-51.3	10.48	-12.2	(-40.8, 16.3)	13.87	0.386
	PLACEBO	15	6.9	4.3	-39.1	9.95				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	8	7.1	3.0	-60.2	10.20	-50.6	(-79.1, -22.1)	13.21	0.002**
	PLACEBO	9	5.8	6.0	-9.6	10.74				
OBSERVED CASE WEEK 18										
	UPA 30 MG QD/									
	UPA 30 MG QD	17	6.3	2.5	-58.3	10.60	-43.5	(-70.0, -17.0)	12.98	0.002**
	PLACEBO	18	5.7	4.7	-14.8	10.20				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.9	2.5	-52.3	10.33	-42.6	(-70.7, -14.5)	13.74	0.004**
	PLACEBO	18	6.4	5.6	-9.7	9.34				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	4.0	-52.2	10.59	-23.7	(-53.2, 5.8)	14.31	0.111
	PLACEBO	14	6.6	4.9	-28.5	10.40				
	PLACEBO/									
	UPA 30 MG QD	8	7.1	1.8	-76.2	10.06	-84.4	(-111.5, -57 2)	12.65	<0.001***
	PLACEBO	10	6.2	6.9	8.2	10.49				
OBSERVED CASE WEEK 19										
	UPA 30 MG QD/									
	UPA 30 MG QD	16	6.3	2.6	-68.6	13.40	-59.6	(-91.0, -28.1)	15.40	<0.001***
	PLACEBO	18	5.7	5.5	-9.0	12.06				
	UPA 15 MG QD/									
	UPA 15 MG QD	15	6.7	3.1	-40.2	10.38	-35.2	(-63.9, -6.6)	13.98	0.018*
	PLACEBO	17	6.3	5.7	-4.9	9.61				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	15	6.3	3.9	-52.7	9.54	-39.3	(-65.8, -12.7)	12.89	0.005**
	PLACEBO	14	6.6	5.4	-13.4	9.37				
	PLACEBO/									
	UPA 30 MG QD	8	7.1	1.5	-79.8	13.36	-86.1	(-122.1, -50.0)	16.79	<0.001***
	PLACEBO	10	6.2	6.6	6.2	13.92				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE WEEK 20										
	UPA 30 MG QD/									
	UPA 30 MG QD	16	6.3	2.8	-63.8	18.31	-67.9	(-117.4, -18.4)	24.08	0.009**
	PLACEBO	14	5.4	5.4	4.1	18.58				
	UPA 15 MG QD/									
	UPA 15 MG QD	14	6.8	3.2	-41.1	9.84	-33.1	(-61.2, -5.0)	13.60	0.023*
	PLACEBO	13	6.2	5.5	-8.0	10.17				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	13	6.4	3.5	-60.8	11.58	-37.8	(-70.4, -5.2)	15.74	0.025*
	PLACEBO	13	6.5	5.1	-23.0	11.24				
	PLACEBO/									
	UPA 30 MG QD	8	7.3	1.8	-77.1	13.32	-88.6	(-124.7, -52 5)	16.85	<0.001***
	PLACEBO	10	6.2	6.9	11.5	13.90				
OBSERVED CASE WEEK 21										
	UPA 30 MG QD/									
	UPA 30 MG QD	15	6.1	1.7	-77.0	10.20	-67.1	(-99.1, -35.2)	15.22	<0.001***
	PLACEBO	7	5.7	5.7	-9.9	12.00				
	UPA 15 MG QD/									
	UPA 15 MG QD	8	7.9	3.0	-49.0	20.62	-3.1	(-80.3, 74.0)	34.10	0.929
	PLACEBO	5	5.3	4.3	-45.9	26.84				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	6	6.0	2.9	-62.8	11.94	-18.3	(-72.2, 35.5)	20.94	0.421
	PLACEBO	3	5.9	2.9	-44.5	16.53				
	PLACEBO/									
	UPA 30 MG QD	7	7.7	1.7	-93.7	15.74	-112.3	(-171.6, -52 9)	24.26	0.004**
	PLACEBO	3	5.8	6.6	18.5	18.26				
OBSERVED CASE WEEK 22										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	14	6.0	2.0	-68.6	11.37	-57.3	(-95.5, -19.2)	17.99	0.006**
	PLACEBO	6	5.6	5.2	-11.2	13.98				
	UPA 15 MG QD/									
	UPA 15 MG QD	8	7.7	2.4	-53.8	13.95	-21.4	(-80.6, 37.8)	26.16	0.435
	PLACEBO	5	5.3	4.2	-32.4	21.76				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	5	6.1	2.9	-59.3	33.52	-76.6	(-232.0, 78.8)	55.97	0.243
	PLACEBO	3	5.9	4.5	17.3	43.67				
	PLACEBO/									
	UPA 30 MG QD	8	7.5	1.3	-87.8	8.64	-70.8	(-114.3, -27 3)	17.78	0.007**
	PLACEBO	2	6.9	5.6	-17.0	15.54				
OBSERVED CASE WEEK 23										
	UPA 30 MG QD/									
	UPA 30 MG QD	14	6.0	2.1	-64.3	12.61	-43.5	(-90.0, 3.1)	21.82	0.065
	PLACEBO	5	5.4	4.6	-20.9	16.85				
	UPA 15 MG QD/									
	UPA 15 MG QD	8	7.7	2.3	-55.1	11.71	-24.9	(-74.6, 24.8)	21.96	0.286
	PLACEBO	5	5.3	4.5	-30.2	18.27				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	5	6.1	2.8	-49.0	51.04	-120.0	(-480.1, 240.2)	113.16	0.367
	PLACEBO	2	4.9	4.6	71.0	94.55				
	PLACEBO/									
	UPA 30 MG QD	9	7.4	1.0	-90.1	7.69	-62.9	(-101.0, -24.8)	16.11	0.006**
	PLACEBO	2	6.9	4.9	-27.2	14.16				
OBSERVED CASE WEEK 24										
	UPA 30 MG QD/									
	UPA 30 MG QD	14	6.1	2.2	-68.4	10.50	-44.0	(-87.5, -0.5)	20.28	0.048*
	PLACEBO	4	5.2	3.8	-24.4	17.18				
	UPA 15 MG QD/									
	UPA 15 MG QD	8	7.7	2.4	-61.0	11.40	-35.0	(-96.7, 26.8)	25.23	0.215

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	2	5.9	4.7	-26.0	23.35				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	5	6.1	2.9	-51.4	44.06	-111.0	(-421.9, 199.8)	97.67	0.338
	PLACEBO	2	4.9	4.2	59.7	81.61				
	PLACEBO/									
	UPA 30 MG QD	8	7.5	1.1	-90.0	7.95	-79.0	(-119.0, -39.0)	16.35	0.003**
	PLACEBO	2	6.9	5.9	-11.0	14.29				
OBSERVED CASE WEEK 25										
	UPA 30 MG QD/									
	UPA 30 MG QD	12	5.8	1.6	-74.0	12.89	-51.1	(-94.7, -7.4)	20.04	0.026*
	PLACEBO	4	5.2	4.0	-23.0	15.52				
	UPA 15 MG QD/									
	UPA 15 MG QD	7	8.1	2.2	-67.0	18.71	-36.4	(-131.3, 58.5)	38.78	0.384
	PLACEBO	3	5.0	5.1	-30.6	30.61				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	4	6.3	3.0	-41.4	56.01	-108.0	(-590.4, 374.4)	112.12	0.437
	PLACEBO	2	4.9	4.4	66.6	95.56				
	PLACEBO/									
	UPA 30 MG QD	9	7.4	0.7	-94.2	5.69	-89.9	(-118.0, -61.7)	11.91	<0.001***
	PLACEBO	2	6.9	6.4	-4.3	10.47				
OBSERVED CASE WEEK 26										
	UPA 30 MG QD/									
	UPA 30 MG QD	13	6.0	1.5	-79.7	9.23	-57.2	(-92.6, -21.9)	16.36	0.004**
	PLACEBO	4	5.2	4.3	-22.5	13.40				
	UPA 15 MG QD/									
	UPA 15 MG QD	7	8.1	2.4	-59.9	19.67	-26.2	(-126.0, 73.6)	40.77	0.544
	PLACEBO	3	5.0	5.0	-33.7	32.18				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	4	6.3	2.8	-43.5	53.43	-117.6	(-577.7, 342.6)	106.95	0.386
	PLACEBO	2	4.9	4.9	74.0	91.15				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	8	7.3	0.8	-93.8	5.15	-92.2	(-118.0, -66 3)	10.56	<0.001***
	PLACEBO	2	6.9	6.6	-1.6	9.23				
OBSERVED CASE WEEK 27										
	UPA 30 MG QD/									
	UPA 30 MG QD	13	6.0	1.4	-87.7	9.70	-51.7	(-88.9, -14.6)	17.19	0.010**
	PLACEBO	4	5.2	4.1	-36.0	14.07				
	UPA 15 MG QD/									
	UPA 15 MG QD	7	8.1	2.4	-61.3	19.05	-28.4	(-125.0, 68.2)	39.49	0.499
	PLACEBO	3	5.0	4.7	-32.9	31.16				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	4	6.3	2.7	-45.0	51.30	-120.5	(-562.4, 321.4)	102.70	0.361
	PLACEBO	2	4.9	5.1	75.5	87.53				
	PLACEBO/									
	UPA 30 MG QD	8	7.3	0.5	-97.9	5.31	-100.4	(-127.1, -73.7)	10.89	<0.001***
	PLACEBO	2	6.9	6.8	2.5	9.52				
OBSERVED CASE WEEK 28										
	UPA 30 MG QD/									
	UPA 30 MG QD	12	6.0	1.5	-84.8	9.01	-59.1	(-93.5, -24.7)	15.79	0.003**
	PLACEBO	4	5.2	4.5	-25.7	12.86				
	UPA 15 MG QD/									
	UPA 15 MG QD	8	7.7	2.7	-56.1	15.45	-38.0	(-138.6, 62.5)	41.09	0.391
	PLACEBO	2	5.1	5.1	-18.1	41.32				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	4	6.3	2.6	-45.1	47.41	-130.6	(-538.9, 277.7)	94.90	0.303
	PLACEBO	2	4.9	5.6	85.5	80.88				
	PLACEBO/									
	UPA 30 MG QD	8	7.3	0.6	-98.3	6.91	-112.9	(-147.6, -78 2)	14.17	<0.001***
	PLACEBO	2	6.9	7.4	14.6	12.38				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE										
WEEK 29										
	UPA 30 MG QD/									
	UPA 30 MG QD	12	6.0	1.4	-86.8	9.50	-53.1	(-89.4, -16.8)	16.64	0.008**
	PLACEBO	4	5.2	4.2	-33.7	13.56				
	UPA 15 MG QD/									
	UPA 15 MG QD	8	7.7	3.0	-52.0	10.99	-10.0	(-69.5, 49.6)	24.33	0.696
	PLACEBO	2	5.9	3.9	-42.1	22.51				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	4	6.3	2.6	-40.9	48.22	-148.4	(-563.7, 267.0)	96.53	0.264
	PLACEBO	2	4.9	6.5	107.4	82.28				
	PLACEBO/									
	UPA 30 MG QD	7	7.8	0.9	-93.7	8.14	-105.3	(-147.7, -62.8)	16.51	0.001**
	PLACEBO	2	6.9	7.5	11.6	14.35				
OBSERVED CASE										
WEEK 30										
	UPA 30 MG QD/									
	UPA 30 MG QD	13	6.0	1.7	-80.9	8.95	-51.8	(-86.0, -17.5)	15.87	0.006**
	PLACEBO	4	5.2	4.1	-29.1	12.99				
	UPA 15 MG QD/									
	UPA 15 MG QD	8	7.7	3.0	-50.9	16.05	-19.6	(-103.2, 64.0)	35.35	0.596
	PLACEBO	3	5.0	4.9	-31.3	30.71				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	4	6.3	3.0	-40.2	53.11	-165.8	(-623.2, 291.6)	106.31	0.259
	PLACEBO	2	4.9	7.3	125.6	90.61				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	0.5	-97.4	8.04	-111.5	(-155.1, -67 9)	15.70	0.002**
	PLACEBO	2	6.9	7.5	14.0	13.46				
OBSERVED CASE										
WEEK 31										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	12	6.2	1.7	-82.9	8.42	-51.3	(-83.8, -18.9)	14.89	0.005**
	PLACEBO	4	5.2	3.9	-31.5	12.14				
	UPA 15 MG QD/									
	UPA 15 MG QD	6	7.9	2.7	-52.7	26.15	-11.6	(-144.8, 121.7)	51.84	0.832
	PLACEBO	3	5.0	5.1	-41.1	39.28				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	4	6.3	3.1	-37.3	50.54	-161.0	(-596.4, 274.3)	101.18	0.252
	PLACEBO	2	4.9	7.1	123.8	86.23				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	0.5	-96.4	6.84	-100.3	(-137.4, -63 3)	13.35	0.002**
	PLACEBO	2	6.9	7.0	4.0	11.44				
OBSERVED CASE WEEK 32										
	UPA 30 MG QD/									
	UPA 30 MG QD	13	6.0	1.6	-80.3	9.02	-53.3	(-87.8, -18.7)	15.98	0.005**
	PLACEBO	4	5.2	4.0	-27.0	13.09				
	UPA 15 MG QD/									
	UPA 15 MG QD	7	7.4	2.7	-55.7	17.54	-25.2	(-115.7, 65.4)	37.00	0.522
	PLACEBO	3	5.0	4.9	-30.5	31.11				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	3	6.7	3.1	-9.5	84.15	-131.9	(-1741.3, 1477.6)	126.66	0.487
	PLACEBO	2	4.9	6.4	122.3	114.69				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	0.5	-96.6	7.10	-104.8	(-143.3, -66 3)	13.87	0.002**
	PLACEBO	2	6.9	7.2	8.2	11.89				
OBSERVED CASE WEEK 33										
	UPA 30 MG QD/									
	UPA 30 MG QD	10	6.0	1.5	-87.0	12.45	-47.4	(-90.3, -4.5)	19.25	0.034*
	PLACEBO	4	5.2	3.7	-39.6	14.69				
	UPA 15 MG QD/									
	UPA 15 MG QD	5	7.3	2.9	-49.2	17.59	-18.7	(-107.9, 70.5)	28.03	0.552

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	2	5.9	3.7	-30.5	25.70				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	2	5.9	1.1	-65.1	80.48	-138.9	(-1609.4, 1331.6)	115.73	0.442
	PLACEBO	2	4.9	6.4	73.8	80.48				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	0.6	-97.4	9.83	-95.5	(-148.8, -42 2)	19.20	0.008**
	PLACEBO	2	6.9	6.3	-1.9	16.45				
OBSERVED CASE WEEK 34										
	UPA 30 MG QD/									
	UPA 30 MG QD	14	6.2	1.4	-87.7	9.60	-46.6	(-83.5, -9.7)	17.22	0.017*
	PLACEBO	4	5.2	3.8	-41.1	14.17				
	UPA 15 MG QD/									
	UPA 15 MG QD	5	7.3	3.0	-47.1	16.94	-18.7	(-104.6, 67.2)	27.00	0.539
	PLACEBO	2	5.9	3.9	-28.4	24.75				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	2	5.9	1.3	-60.4	91.83	-112.4	(-1790.2, 1565.5)	132.05	0.551
	PLACEBO	2	4.9	5.1	51.9	91.83				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	0.6	-97.0	8.38	-94.8	(-140.2, -49.4)	16.36	0.004**
	PLACEBO	2	6.9	6.4	-2.2	14.02				
OBSERVED CASE WEEK 35										
	UPA 30 MG QD/									
	UPA 30 MG QD	13	6.0	1.3	-83.5	9.68	-57.2	(-95.3, -19.0)	17.52	0.007**
	PLACEBO	3	6.5	5.2	-26.3	15.96				
	UPA 15 MG QD/									
	UPA 15 MG QD	4	8.0	2.9						NA
	PLACEBO	1	4.9	3.3						
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	2	5.9	1.5	-58.9	89.82	-116.9	(-1757.9, 1524.1)	129.15	0.532
	PLACEBO	2	4.9	5.5	58.0	89.82				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	6	7.5	0.8	-94.3	9.27	-84.7	(-135.0, -34 5)	18.10	0.009**
	PLACEBO	2	6.9	5.9	-9.6	15.51				
OBSERVED CASE WEEK 36										
	UPA 30 MG QD/									
	UPA 30 MG QD	11	6.0	1.3	-85.6	10.25	-49.7	(-90.5, -8.8)	18.34	0.022*
	PLACEBO	3	6.5	4.8	-35.9	16.54				
	UPA 15 MG QD/									
	UPA 15 MG QD	5	7.3	3.0	-48.8	24.83	-6.6	(-246.7, 233.4)	55.80	0.916
	PLACEBO	1	4.9	3.1	-42.2	45.18				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	2	5.9	1.5	-60.2	85.68	-127.5	(-1692.9, 1437.9)	123.20	0.489
	PLACEBO	2	4.9	6.1	67.3	85.68				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	1.2	-88.6	8.26	-72.4	(-117.2, -27.6)	16.13	0.011*
	PLACEBO	2	6.9	5.6	-16.2	13.83				
OBSERVED CASE WEEK 37										
	UPA 30 MG QD/									
	UPA 30 MG QD	12	6.0	1.3	-84.3	10.44	-51.4	(-92.7, -10.0)	18.80	0.020*
	PLACEBO	3	6.5	4.8	-33.0	17.07				
	UPA 15 MG QD/									
	UPA 15 MG QD	5	7.3	2.9	-50.2	18.77	-21.3	(-116.4, 73.9)	29.90	0.528
	PLACEBO	2	5.9	3.6	-28.9	27.42				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	1	4.5	0.0	-117.1	0.00	-233.8		0.00	NA
	PLACEBO	2	4.9	6.4	116.7	0.00				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	1.1	-91.0	8.08	-81.0	(-124.8, -37 2)	15.78	0.007**
	PLACEBO	2	6.9	5.8	-10.0	13.52				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
OBSERVED CASE										
WEEK 38										
	UPA 30 MG QD/									
	UPA 30 MG QD	12	6.0	1.3	-80.8	10.75	-52.5	(-95.1, -9.9)	19.36	0.020*
	PLACEBO	3	6.5	5.0	-28.3	17.57				
	UPA 15 MG QD/									
	UPA 15 MG QD	4	8.0	3.2	-50.8	38.94	-29.4	(-257.6, 198.8)	53.04	0.635
	PLACEBO	2	5.9	3.7	-21.3	41.84				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	2	5.9	1.4	-56.8	100.02	-121.7	(-1949.2, 1705.8)	143.83	0.553
	PLACEBO	2	4.9	5.5	64.9	100.02				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	0.9	-93.3	7.47	-75.7	(-116.2, -35 2)	14.58	0.007**
	PLACEBO	2	6.9	5.3	-17.6	12.50				
OBSERVED CASE										
WEEK 39										
	UPA 30 MG QD/									
	UPA 30 MG QD	11	6.0	1.5	-76.1	11.27	-49.2	(-94.2, -4.3)	20.16	0.035*
	PLACEBO	3	6.5	5.1	-26.9	18.19				
	UPA 15 MG QD/									
	UPA 15 MG QD	4	8.0	2.8	-54.3	26.91	-28.9	(-186.6, 128.8)	36.65	0.513
	PLACEBO	2	5.9	3.8	-25.5	28.92				
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	2	5.9	2.6	-41.3	114.54	-92.7	(-2185.4, 2000.0)	164.70	0.674
	PLACEBO	2	4.9	4.8	51.4	114.54				
	PLACEBO/									
	UPA 30 MG QD	6	7.5	1.2	-90.5	8.76	-71.0	(-118.4, -23 5)	17.10	0.014*
	PLACEBO	2	6.9	5.1	-19.6	14.66				
OBSERVED CASE										
WEEK 40										
	UPA 30 MG QD/									

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	UPA 30 MG QD	12	6.0	1.4	-80.2	10.61	-54.1	(-96.1, -12.1)	19.10	0.016*
	PLACEBO	3	6.5	5.1	-26.1	17.34				
UPA 15 MG QD/										
	UPA 15 MG QD	5	7.3	2.7	-60.6	14.31	-29.9	(-102.5, 42.6)	22.80	0.280
	PLACEBO	2	5.9	3.8	-30.6	20.90				
UPA 7.5 MG QD/										
	UPA 7.5 MG QD	1	4.5	0.0	-116.6	0.00	-198.6		0.00	NA
	PLACEBO	2	4.9	4.8	82.0	0.00				
PLACEBO/										
	UPA 30 MG QD	6	7.5	1.0	-92.2	8.35	-67.1	(-112.4, -21 9)	16.30	0.015*
	PLACEBO	2	6.9	4.8	-25.0	13.97				
OBSERVED CASE WEEK 52										
UPA 30 MG QD/										
	UPA 30 MG QD	11	5.9	1.0	-78.1	13.74	-113.2	(-194.8, -31.7)	35.36	0.013*
	PLACEBO	1	6.2	8.0	35.1	36.78				
UPA 15 MG QD/										
	UPA 15 MG QD	4	7.1	3.3	-38.4	33.06	-16.5	(-754.9, 721.9)	58.11	0.824
	PLACEBO	1	7.0	4.0	-21.9	66.93				
UPA 7.5 MG QD/										
	UPA 7.5 MG QD	0								NA
	PLACEBO	2	4.9	5.0	69.6	0.00				
PLACEBO/										
	UPA 30 MG QD	8	7.8	1.1	-92.0	7.56	-16.2	(-76.5, 44.1)	23.47	0.520
	PLACEBO	1	8.5	1.0	-75.8	20.05				
OBSERVED CASE WEEK 64										
UPA 30 MG QD/										
	UPA 30 MG QD	9	5.3	0.9	-74.6	18.50				NA
	PLACEBO	0								
UPA 15 MG QD/										
	UPA 15 MG QD	2	8.6	1.5	-84.1	0.00				NA

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO	0								
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	0								NA
	PLACEBO	2	4.9	2.5	-15.2	0.00				
	PLACEBO/									
	UPA 30 MG QD	7	7.8	1.9	-97.3	14.82	-40.6	(-150.5, 69.4)	39.60	0.364
	PLACEBO	1	8.5	1.0	-56.8	27.76				
OBSERVED CASE WEEK 76										
	UPA 30 MG QD/									
	UPA 30 MG QD	6	5.7	0.2	-93.1	0.00				NA
	PLACEBO	0								
	UPA 15 MG QD/									
	UPA 15 MG QD	2	8.6	2.0	-78.8	0.00				NA
	PLACEBO	0								
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	0								NA
	PLACEBO	2	4.9	5.0	82.0	0.00				
	PLACEBO/									
	UPA 30 MG QD	4	7.6	0.5	-107.0	17.29	-48.4	(-719.2, 622.4)	52.79	0.528
	PLACEBO	1	8.5	1.0	-58.6	37.94				
OBSERVED CASE WEEK 88										
	UPA 30 MG QD/									
	UPA 30 MG QD	3	5.4	0.0	-100.0	0.00				NA
	PLACEBO	0								
	UPA 15 MG QD/									
	UPA 15 MG QD	2	8.6	2.0	-78.8	0.00				NA
	PLACEBO	0								
	UPA 7.5 MG QD/									
	UPA 7.5 MG QD	0								NA
	PLACEBO	1	7.1	1.0	-86.0	0.00				

IMPUTATION VISIT	TREATMENT SEQUENCE	N	BASELINE MEAN	VISIT MEAN	WITHIN GROUP -PERCENT CHANGE FROM BASELINE- LSMEAN	SE	BETWEEN GROUP COMPARISON ---------- COMPARED TO PLACEBO ---------- LSMEAN DIFF	95% CI	SE	P-VALUE [A]
	PLACEBO/									
	UPA 30 MG QD	1	4.0	0.0	-100.0	0.00				NA
	PLACEBO	0								

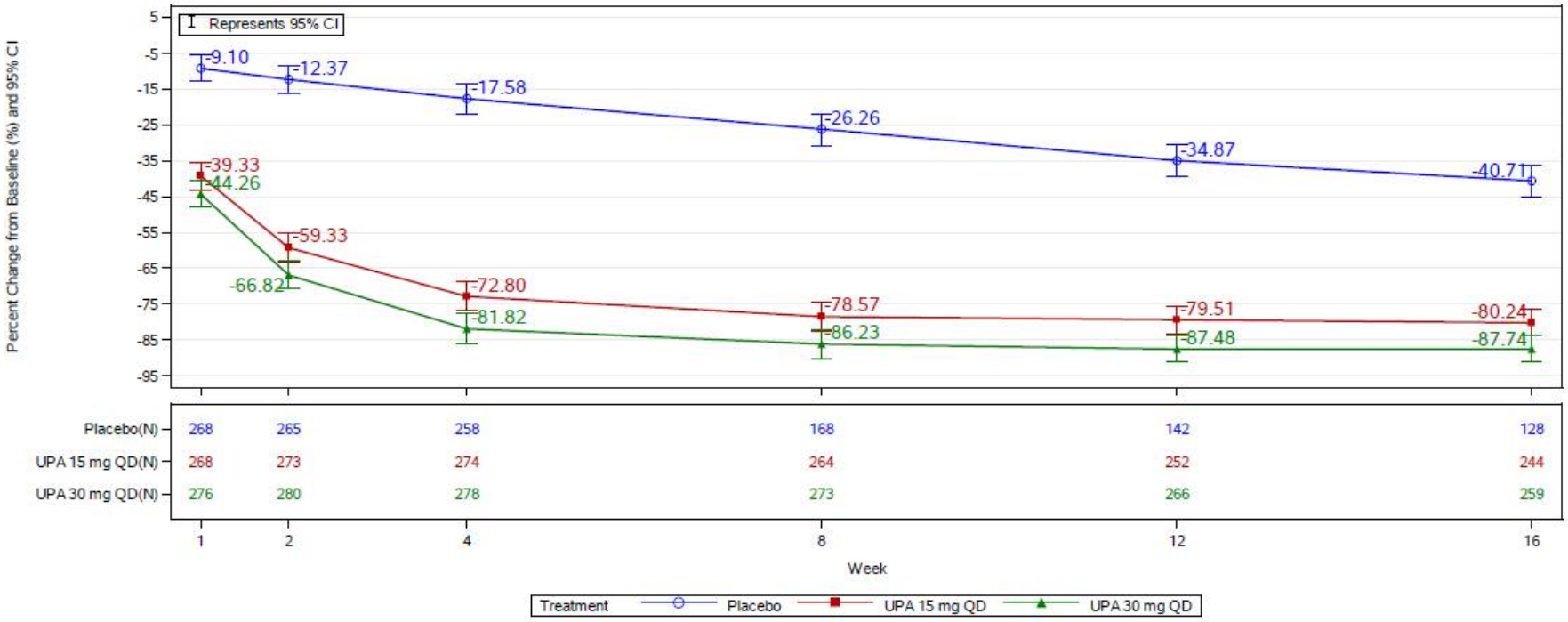
NA = NOT APPLICABLE.
STRATA IS DEFINED AS EASI 75 RESPONDER AT THE ENTRY OF PERIOD 2 (YES, NO).
[A] P-VALUES WERE CALCULATED FROM ANCOVA WITH STRATA, BASELINE VALUE AND THE TREATMENT IN THE MODEL.
***, **, * STATISTICALLY SIGNIFICANT AT 0.001, 0.01, AND 0.05 LEVEL, RESPECTIVELY.

Program Source Code: [redacted]

相互参照：M16-048 試験 CSR Table 14.2　2.4.1

2.7.3.6 付録

図 2.7.3.6-1. 二重盲検投与期の来院時別での EASI スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-045 試験

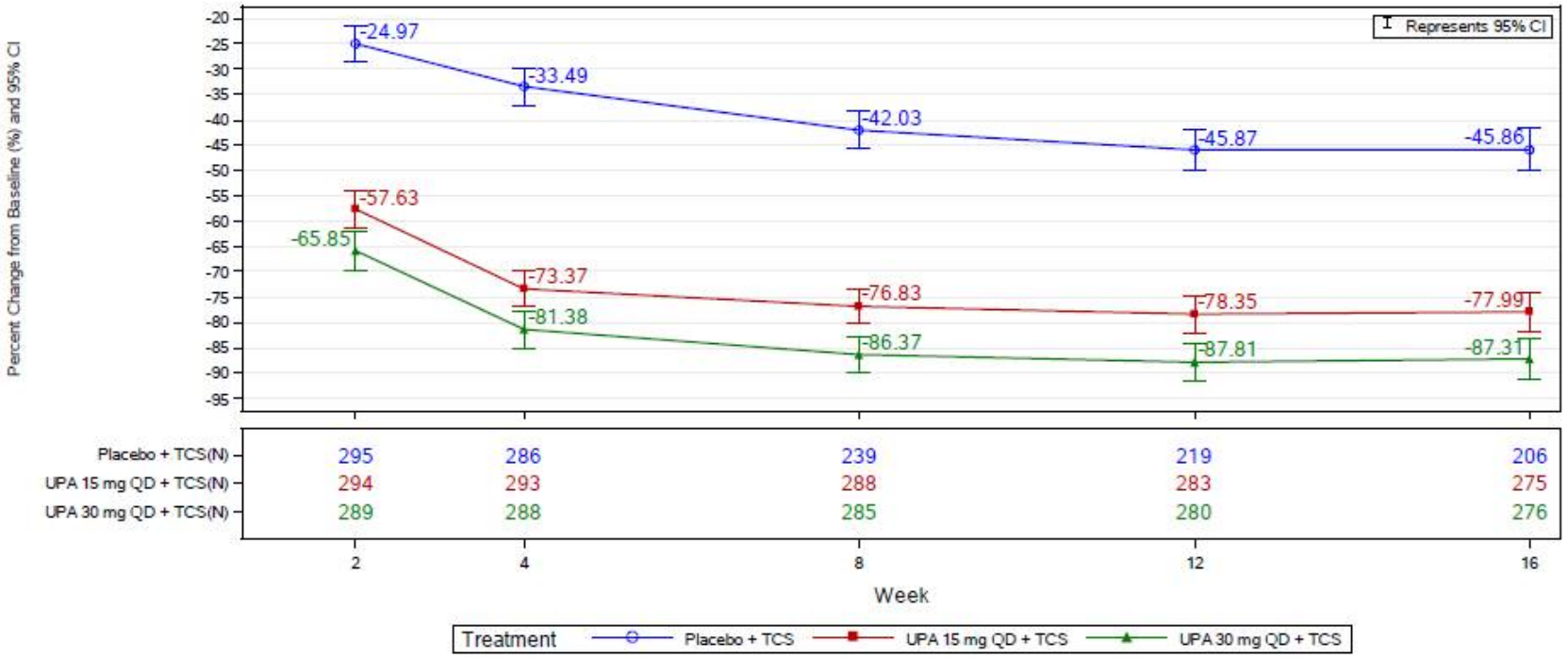


CI = confidence interval; EASI = Eczema Area and Severity Index; QD = once daily; UPA = upadacitinib

Note：Measurements after receiving rescue treatment are considered as missing. Within group LS mean and 95% CI are displayed in this figure, based on MMRM. MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

相互参照：M16-045 試験 CSR W16 Figure 14.2　20.4.1

図 2.7.3.6-2.　　二重盲検投与期の来院時別での EASI スコアのベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-047 試験

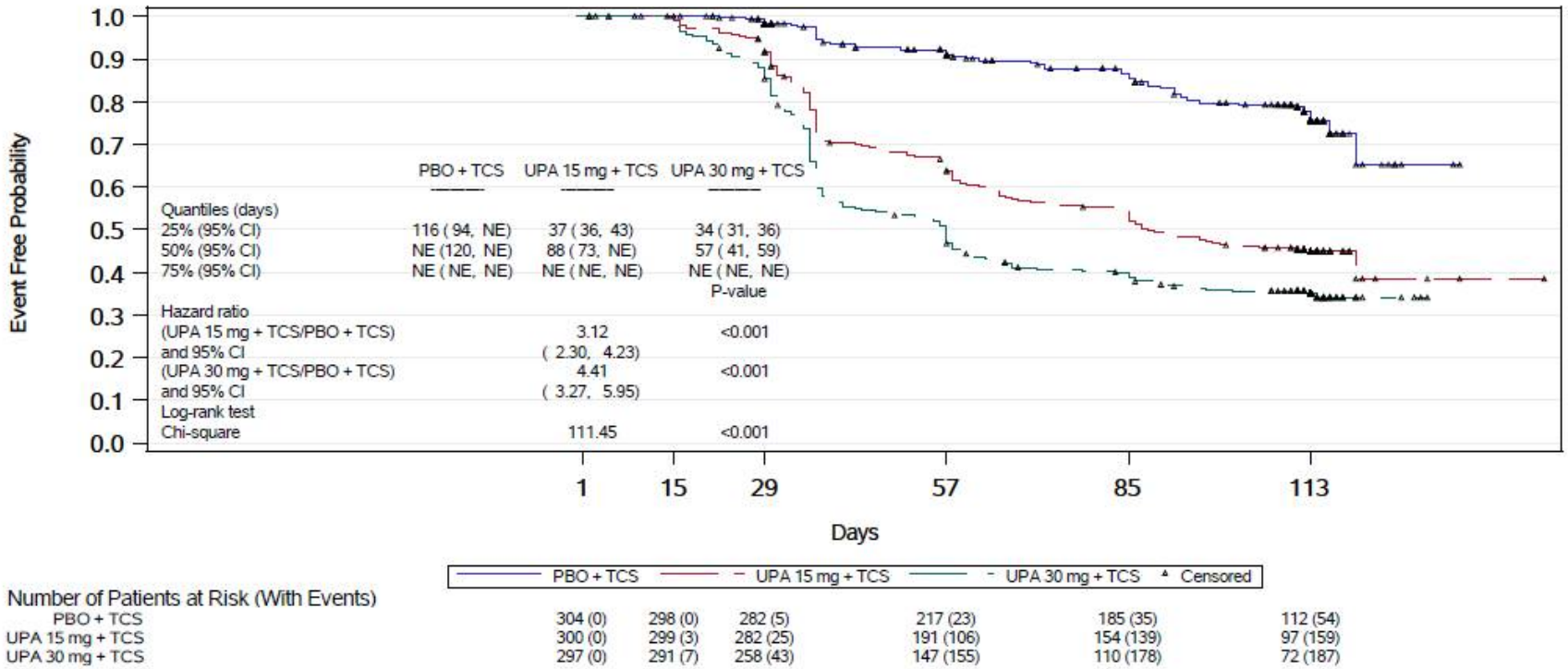


CI = confidence interval; EASI = Eczema Area and Severity Index; QD = once daily; UPA = upadacitinib

Note：Measurements after receiving rescue treatment are considered as missing. Within group LS mean and 95% CI are displayed in this figure, based on MMRM. MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Baseline is defined as the last non-missing value prior to the first dose of study drug or randomization if no study drug is given. Subjects with only non-missing percent change from Baseline values are included in analysis.

相互参照：M16-047 試験 CSR W16 Figure 14.2　20.4.1

図 2.7.3.6-3. EASI 75 を達成した被験者が，投与 16 週時までに初めてすべての副腎皮質ステロイド外用薬の投与を中断するまでの期間： M16-047 試験

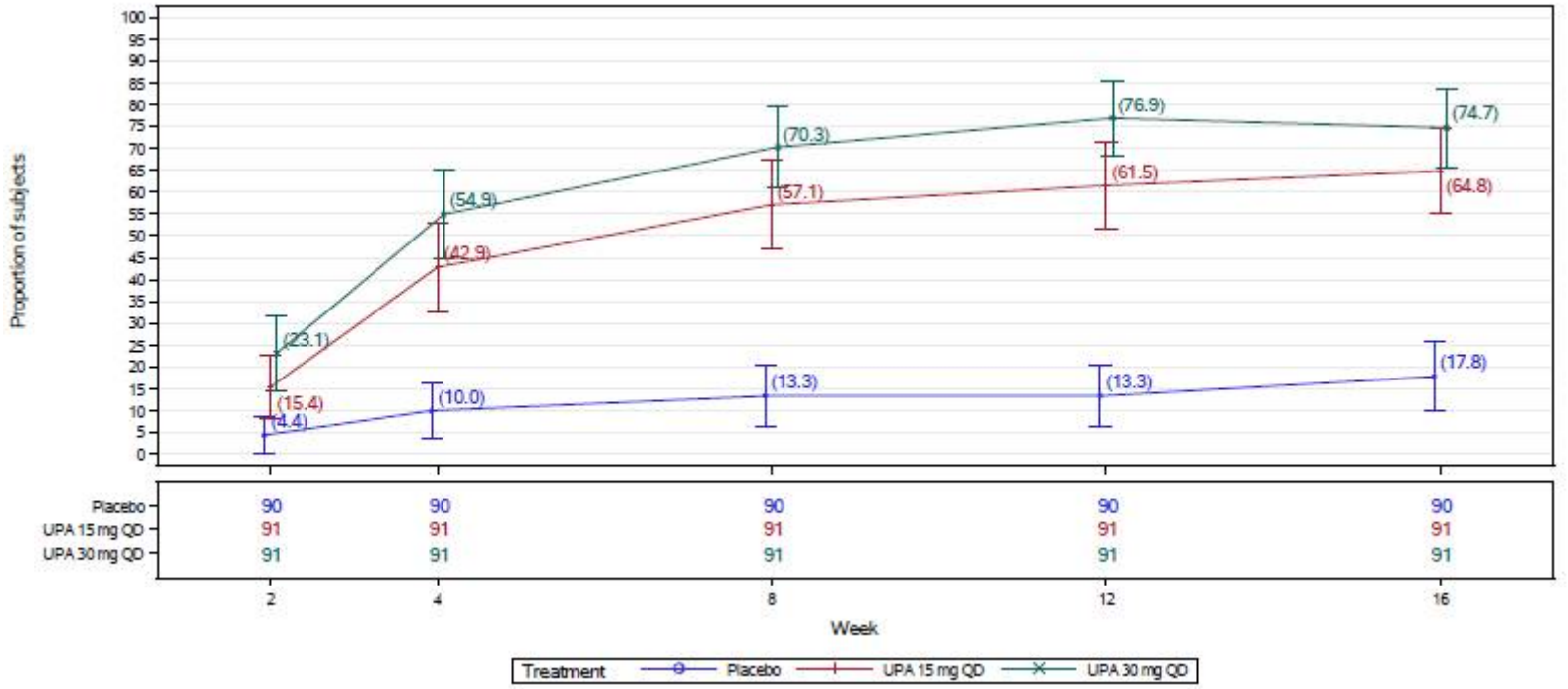


CI = confidence interval; EASI = Eczema Area and Severity Index; PBO = placebo; TCS = topical corticosteroids; UPA = upadacitinib

Note：Discontinuation of all TCS was defined as when the subject stops all TCS treatment for > 7 consecutive days. Days after the start of systemic rescue were not considered as TCS-free days.

相互参照：M16-047 試験 CSR W16 Figure 14.2　23.1.1

図 2.7.3.6-4.　　二重盲検投与期の来院時別の EASI 75 を達成した被験者の割合（NRI，ITT 集団）：M17-377 試験

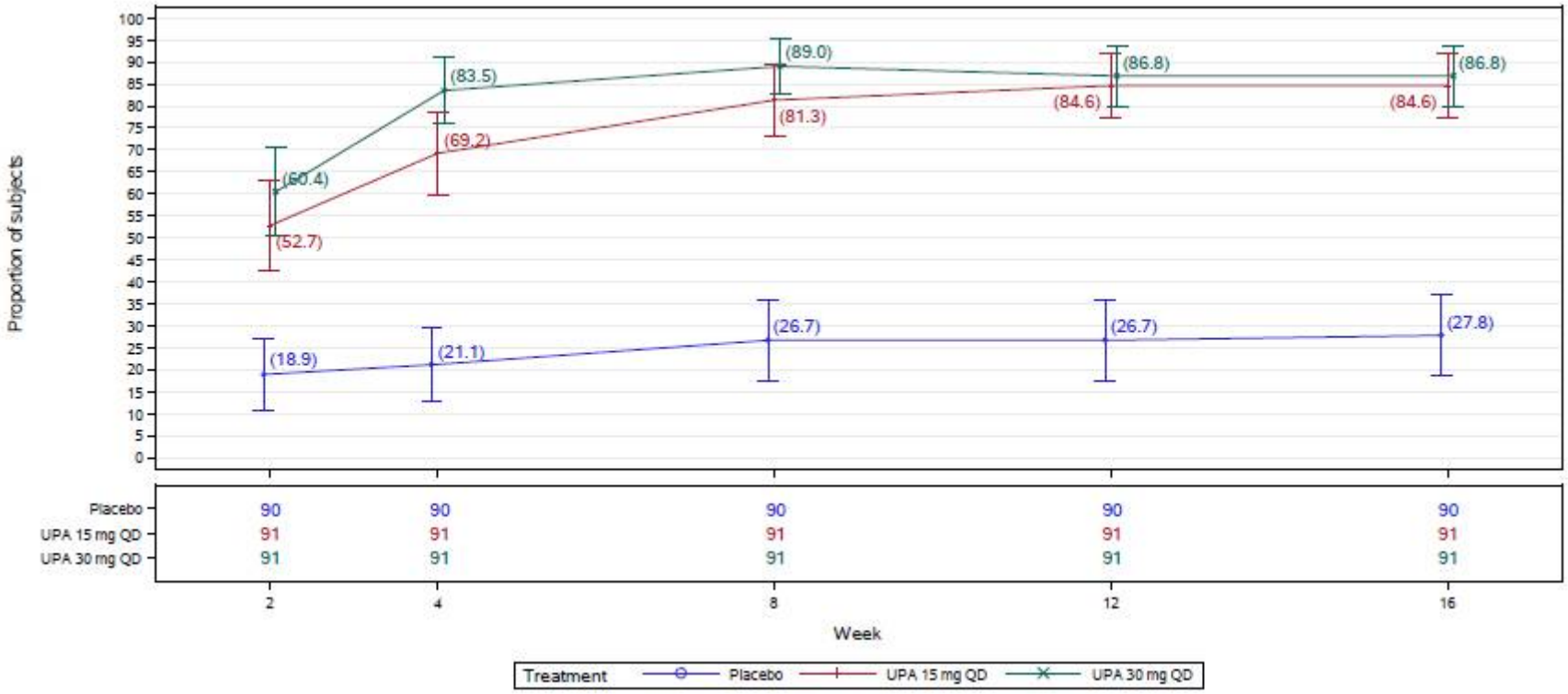


CI = confidence interval; DB = double blind; NRI = non-responder imputation; QD = once daily, UPA = upadacitinib.

Note:　Within each stratum, 95% CI for difference was calculated based on normal approximation to the binomial distribution.

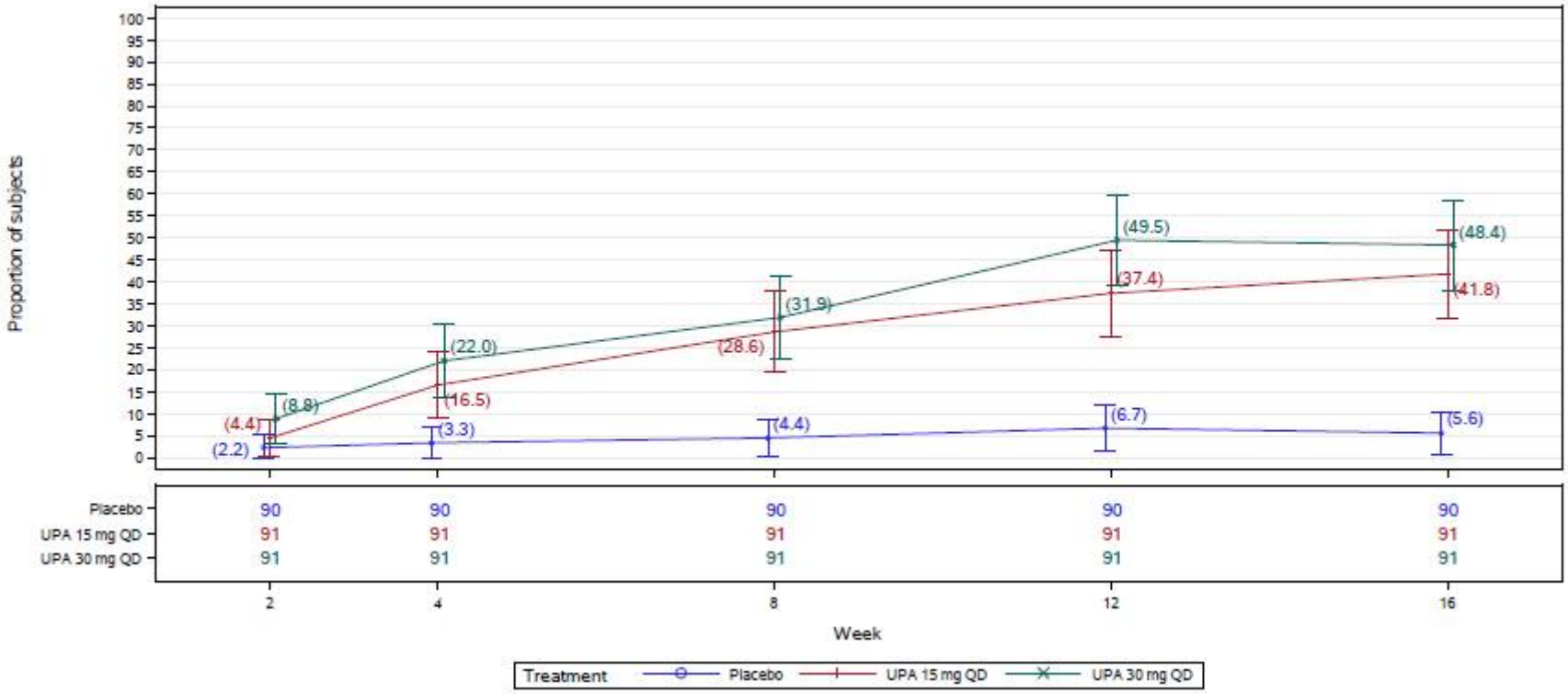
相互参照：M17-377 試験 CSR W52 Figure 14.2　1.1.1

図 2.7.3.6-5.　　二重盲検投与期の来院時別の EASI 50 を達成した被験者の割合（NRI，ITT 集団）：M17-377 試験



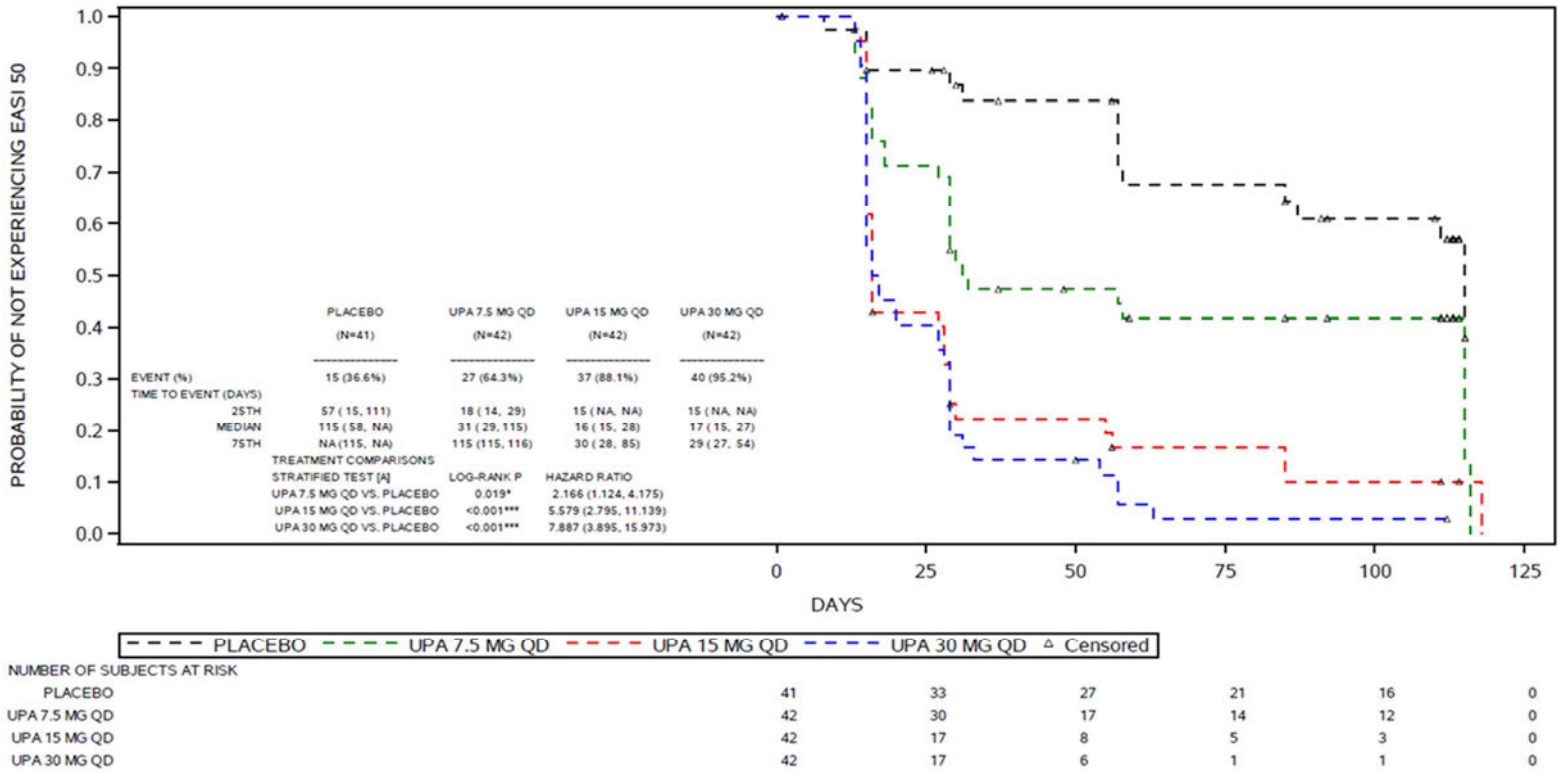
Note: Within each stratum, 95% CI for difference was calculated based on normal approximation to the binomial distribution.
相互参照：M17-377 試験 CSR W52 Figure 14.2　1.2

図 2.7.3.6-6.　　二重盲検投与期の来院時別の EASI 90 を達成した被験者の割合（NRI，ITT 集団）：M17-377 試験



Note: Within each stratum, 95% CI for difference was calculated based on normal approximation to the binomial distribution.
相互参照：M17-377 試験 CSR W52 Figure 14.2　1.3

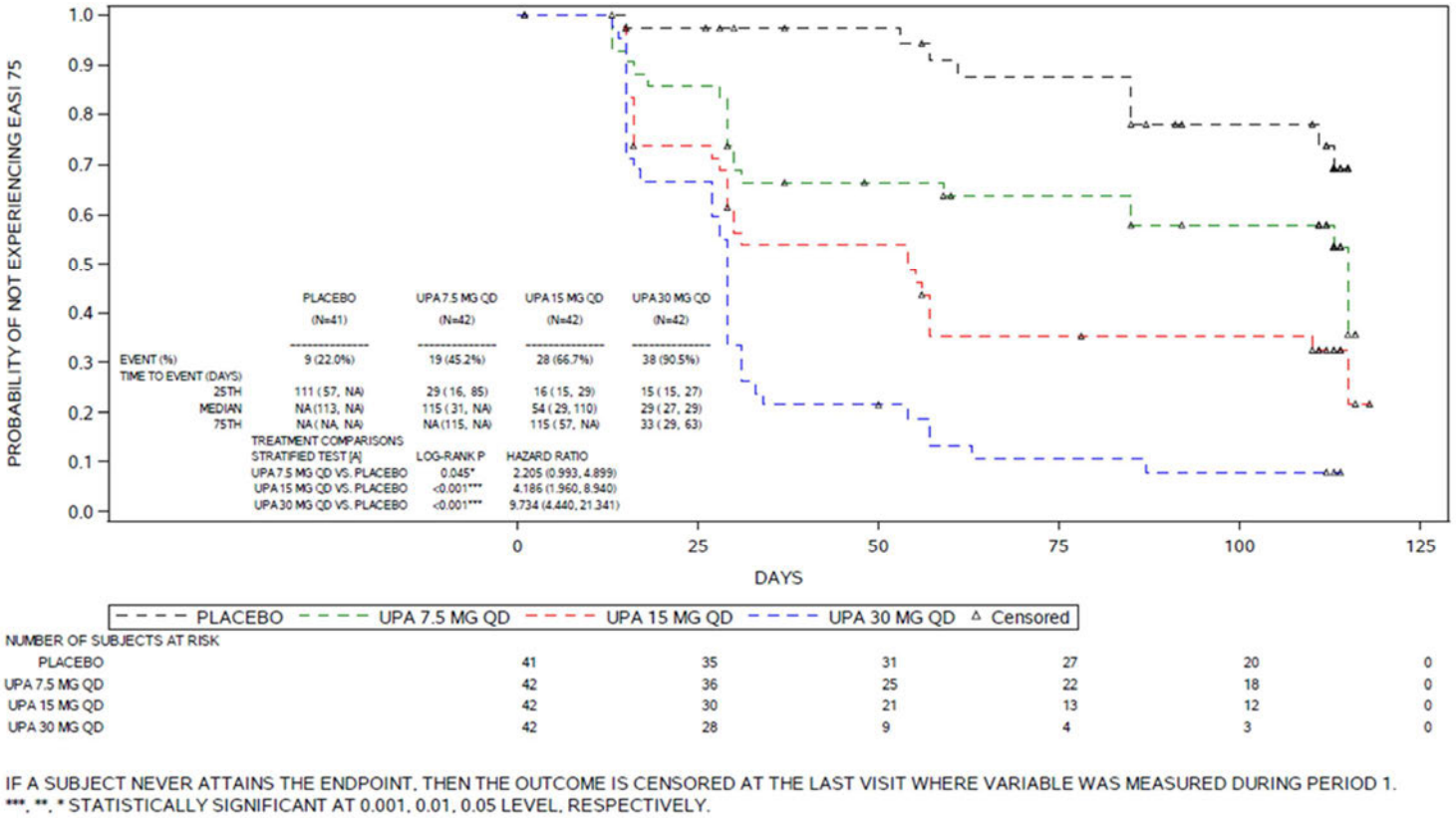
図 2.7.3.6-7. 第 1 ピリオドで EASI 50 を達成するまでの期間（OC，第 1 ピリオドの ITT 集団）：M16-048 試験



EASI = Eczema Area and Severity Index; QD = once daily; UPA = upadacitinib

相互参照：M16-048 試験 CSR Figure 3

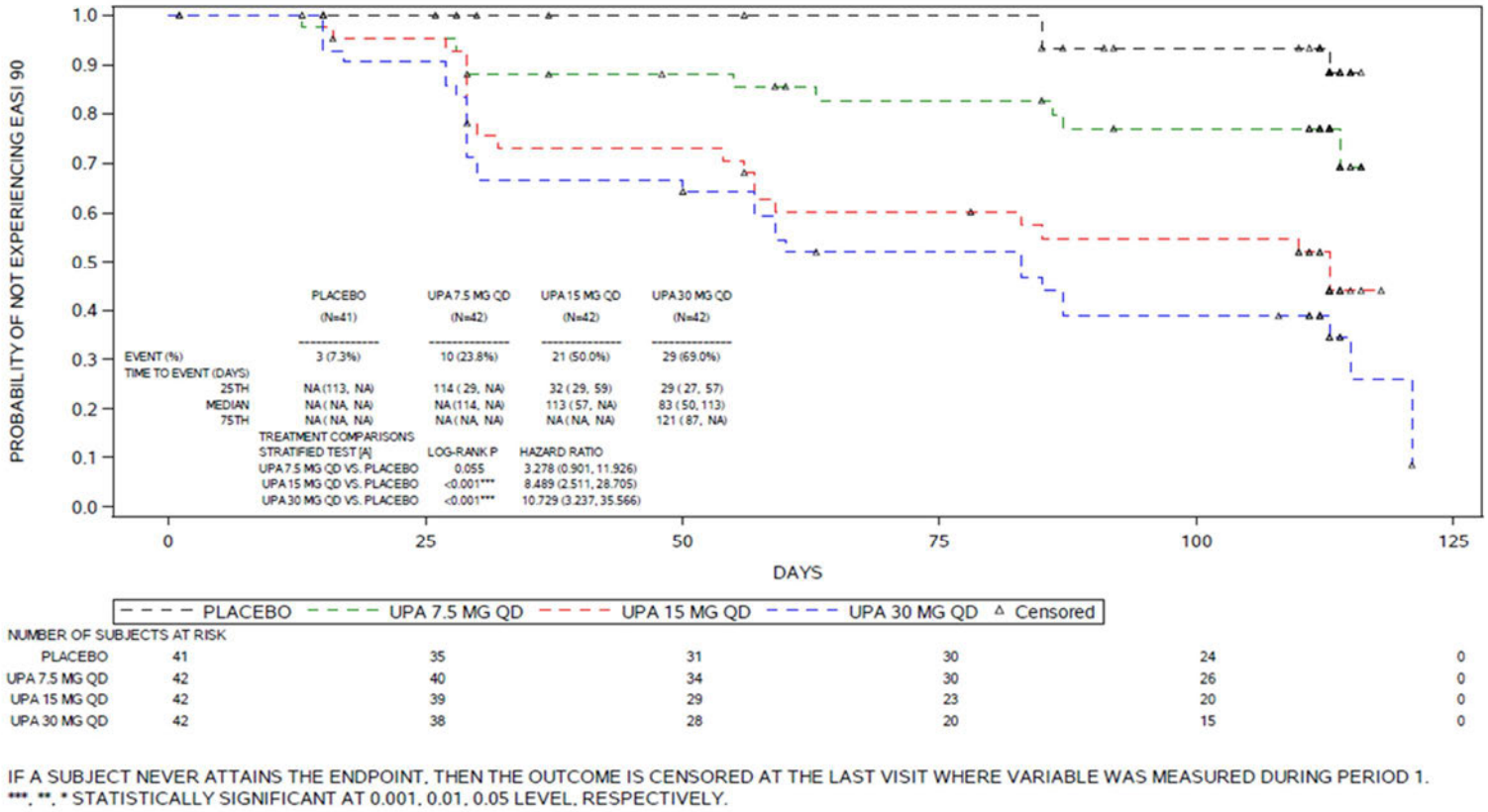
図 2.7.3.6-8.　　第 1 ピリオドで EASI 75 を達成するまでの期間（OC，第 1 ピリオドの ITT 集団）：M16-048 試験



EASI = Eczema Area and Severity Index; QD = once daily; UPA = upadacitinib

相互参照：M16-048 試験 CSR Figure 4

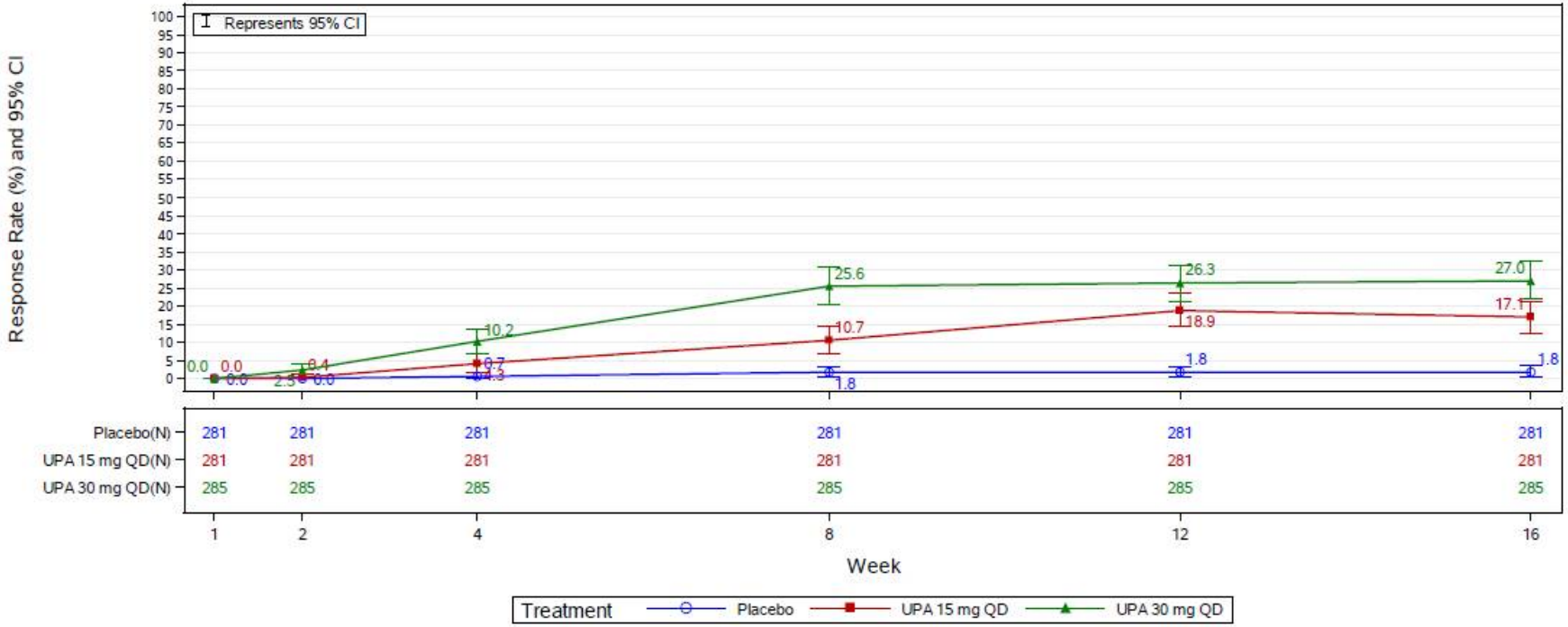
図 2.7.3.6-9.　　第 1 ピリオドで EASI 90 を達成するまでの期間（OC，第 1 ピリオドの ITT 集団）：M16-048 試験



EASI = Eczema Area and Severity Index; QD = once daily; UPA = upadacitinib

相互参照：M16-048 試験 CSR Figure 5

図 2.7.3.6-10. 二重盲検投与期の来院時別の vIGA-AD スコアが 0 であり，かつベースラインと比較して 2 グレード以上改善した被験者の割合（NRI-C, ITT_M 集団）：M16-045 試験



CI = confidence interval; NRI = non-responder imputation; QD = once daily, UPA = upadacitinib; vIGA-AD validated Investigator Global Assessment for atopic dermatitis

Note：NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19. 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.

相互参照：M16-045 試験 CSR W16 Figure 14.2　21.2.1

図 2.7.3.6-11. 二重盲検投与期の来院時別の vIGA-AD スコアが 0 であり，かつベースラインと比較して 2 グレード以上改善した被験者の割合（NRI-C, ITT_M 集団）：M16-047 試験

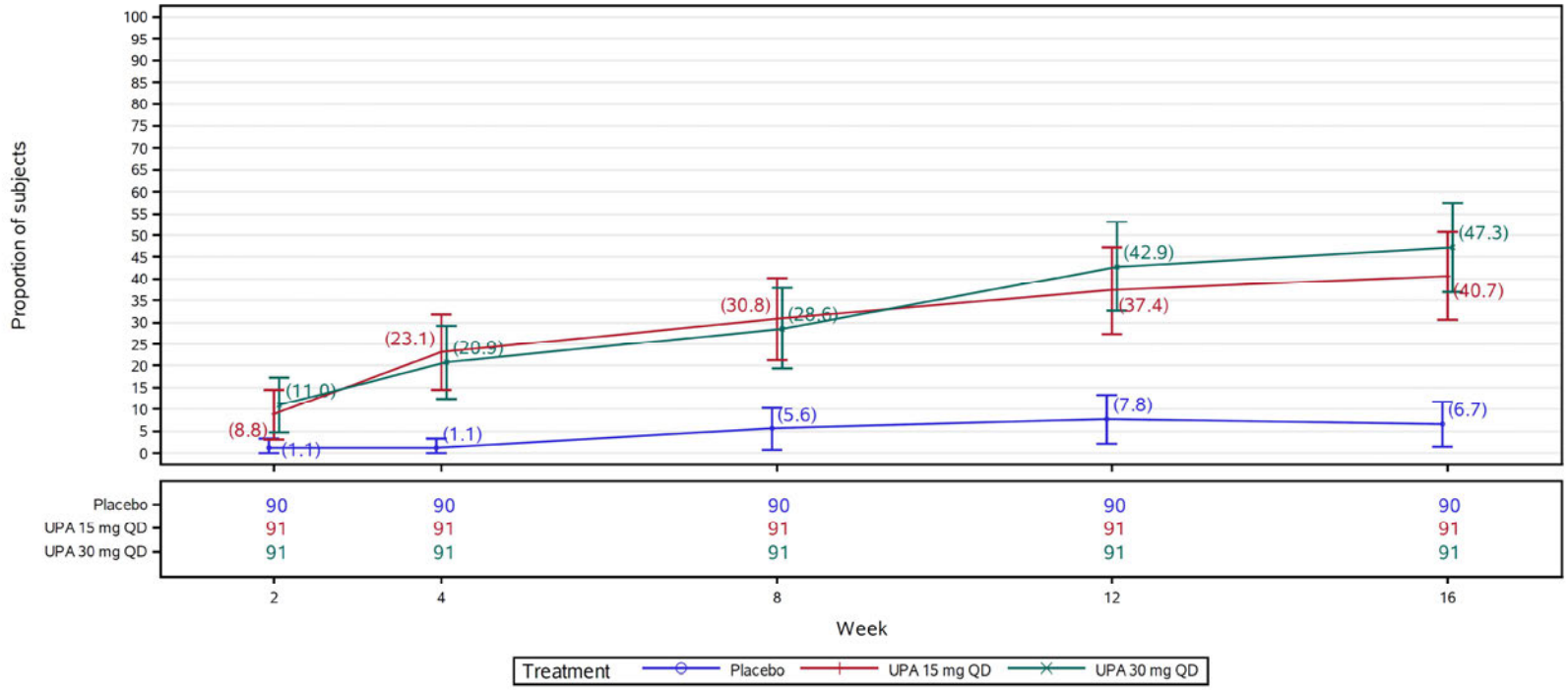


CI = confidence interval; NRI = non-responder imputation; QD = once daily, UPA = upadacitinib; vIGA-AD validated Investigator Global Assessment for atopic dermatitis

Note：NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19. 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.

相互参照：M16-047 試験 CSR W16 Figure 14.2__21.2.1

図 2.7.3.6-12. 二重盲検投与期の来院時別の vIGA-AD スコアが 0 又は 1 であり，かつベースラインと比較して 2 グレード以上改善した被験者の割合（NRI，ITT 集団）：M17-377 試験

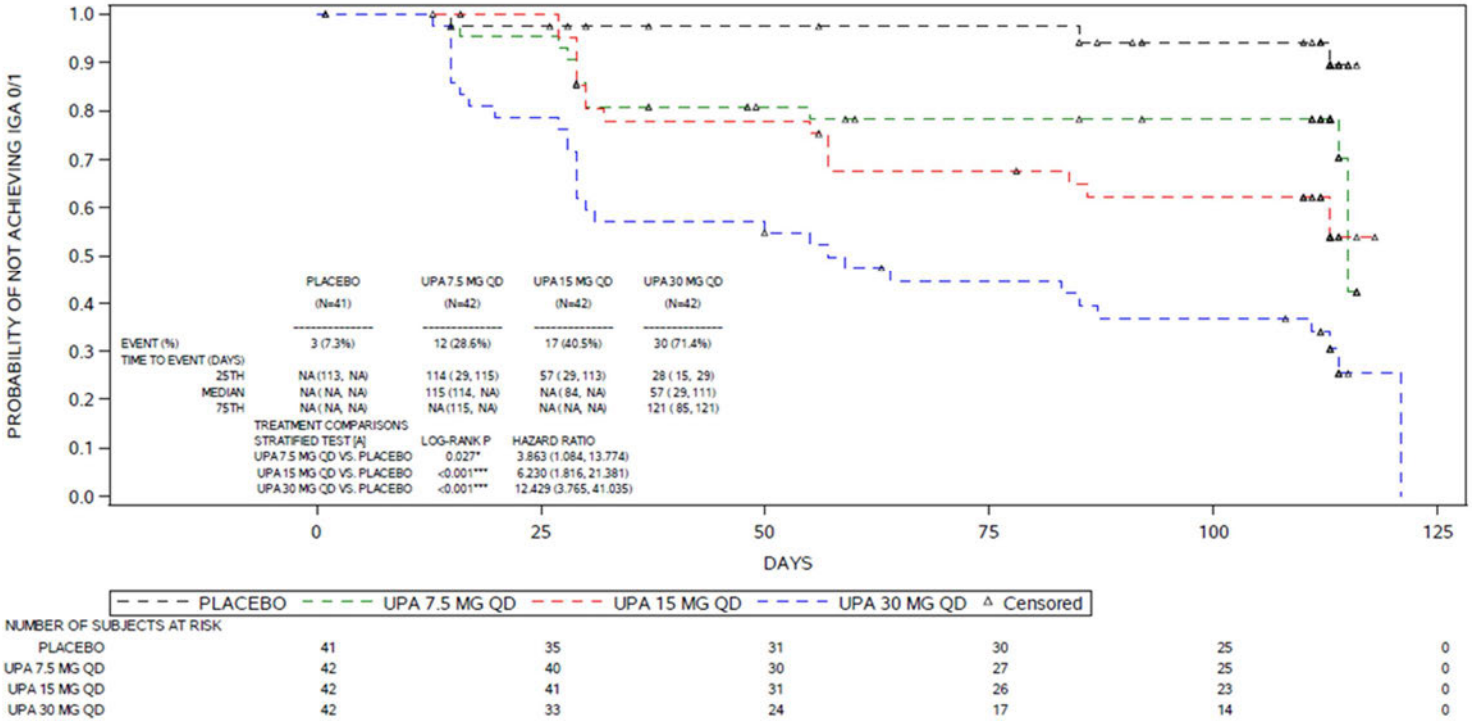


CI = confidence interval; DB = double blind; NRI = non-responder imputation; QD = once daily, UPA = upadacitinib; vIGA-AD validated Investigator Global Assessment for atopic dermatitis.

Note: Within each stratum, 95% CI for difference was calculated based on normal approximation to the binomial distribution.

相互参照：M17-377 試験 CSR W24 Figure 2

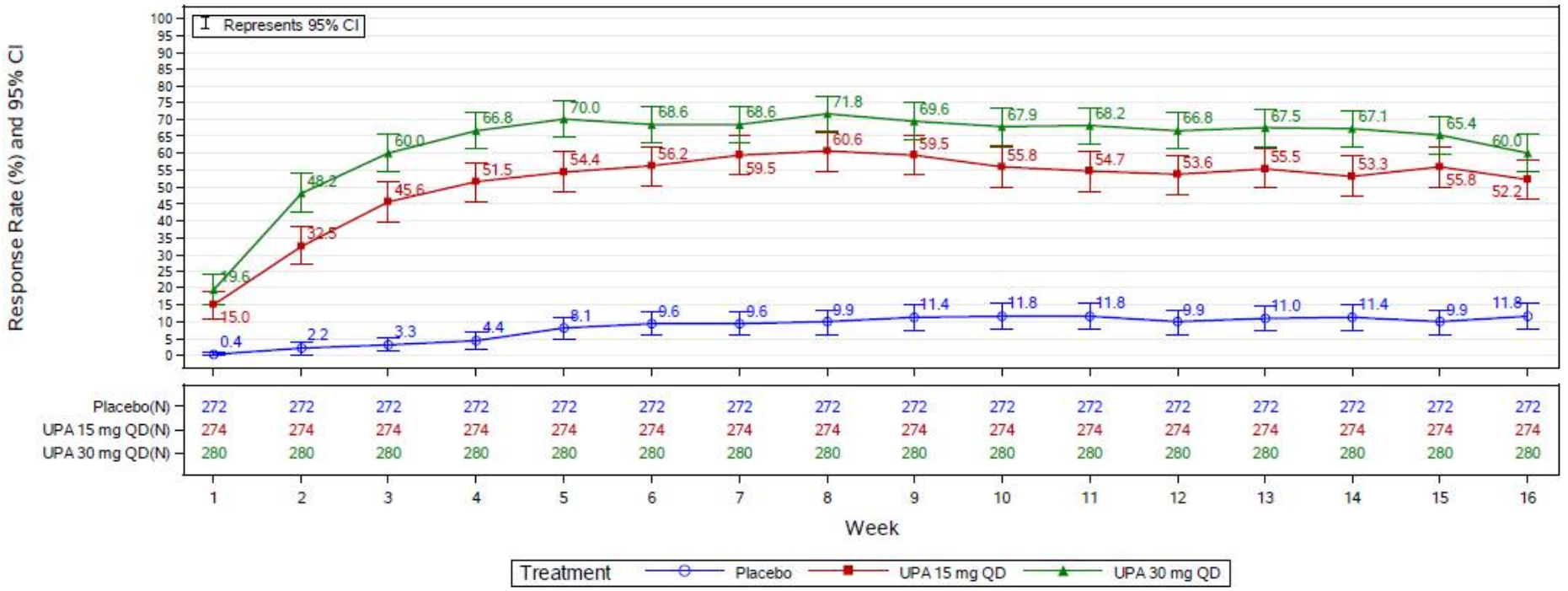
図 2.7.3.6-13.　第 1 ピリオドで IGA スコアが 0 又は 1 を達成するまでの期間（OC，第 1 ピリオドの ITT 集団）：M16-048 試験



IGA = Investigator Global Assessment; QD = once daily; UPA = upadacitinib

相互参照：M16-048 試験 CSR Figure 6

図 2.7.3.6-14. 最悪のかゆみの NRS がベースラインで 4 以上であった被験者のうち，二重盲検投与期の来院時別での最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合（NRI-C，ITT_M 集団）：M16-045 試験

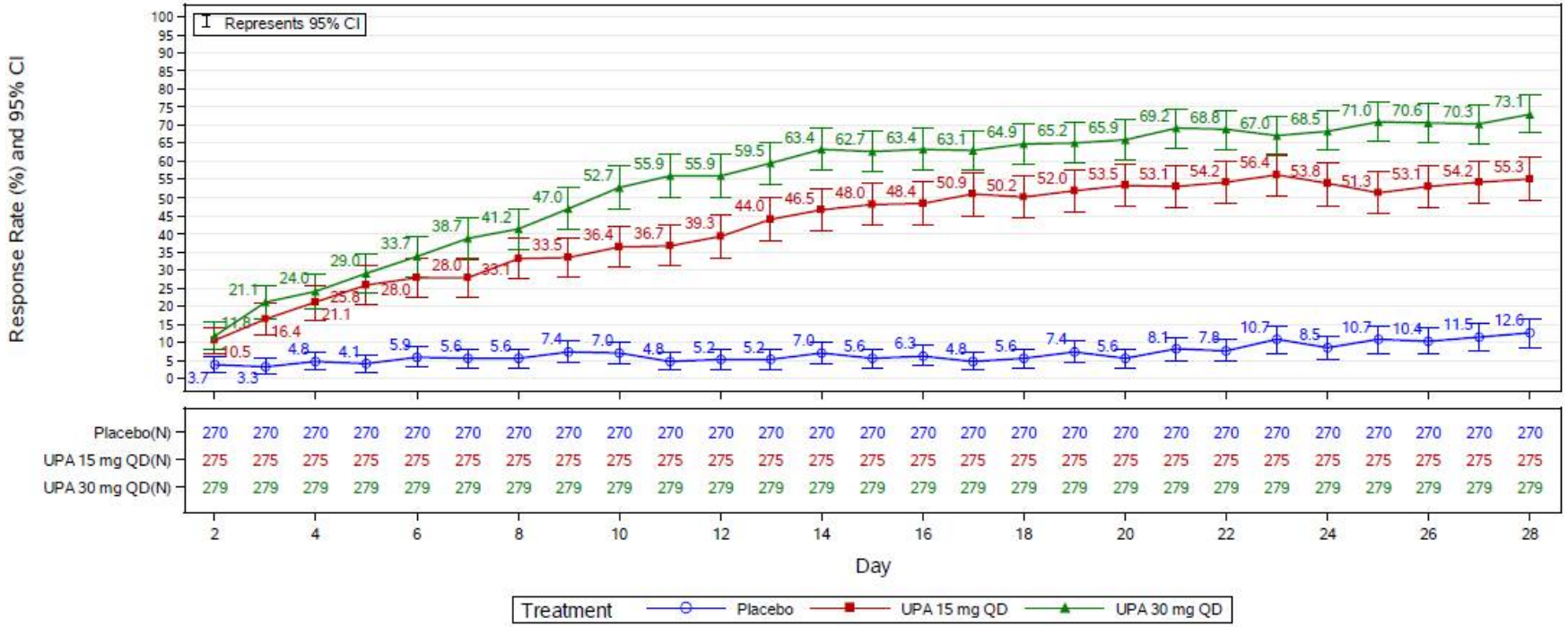


CI = confidence interval; NRI = non-responder imputation; NRS = Numerical Rating Scale; QD = once daily, UPA = upadacitinib

Note：NRI-C is non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19. Baseline refers to the last available rolling average before the date of first administration of study drug. The weekly rolling average will be calculated up to Week 16. 95% CI for response rate is the synthetic result based on Student's t-distribution from PROC MIANALYZE procedure if there are missing data due to COVID-19 or is based on the normal approximation to the binomial distribution if there are no missing data due to COVID-19.

相互参照：M16-045 試験 CSRW16 Figure 14.2 22.1.1

図 2.7.3.6-15.　最悪のかゆみの NRS がベースラインで 4 以上であった被験者のうち，投与 28 日後までの 1 日ごとの最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合（NRI-NC，ITT_M 集団）：M16-045 試験

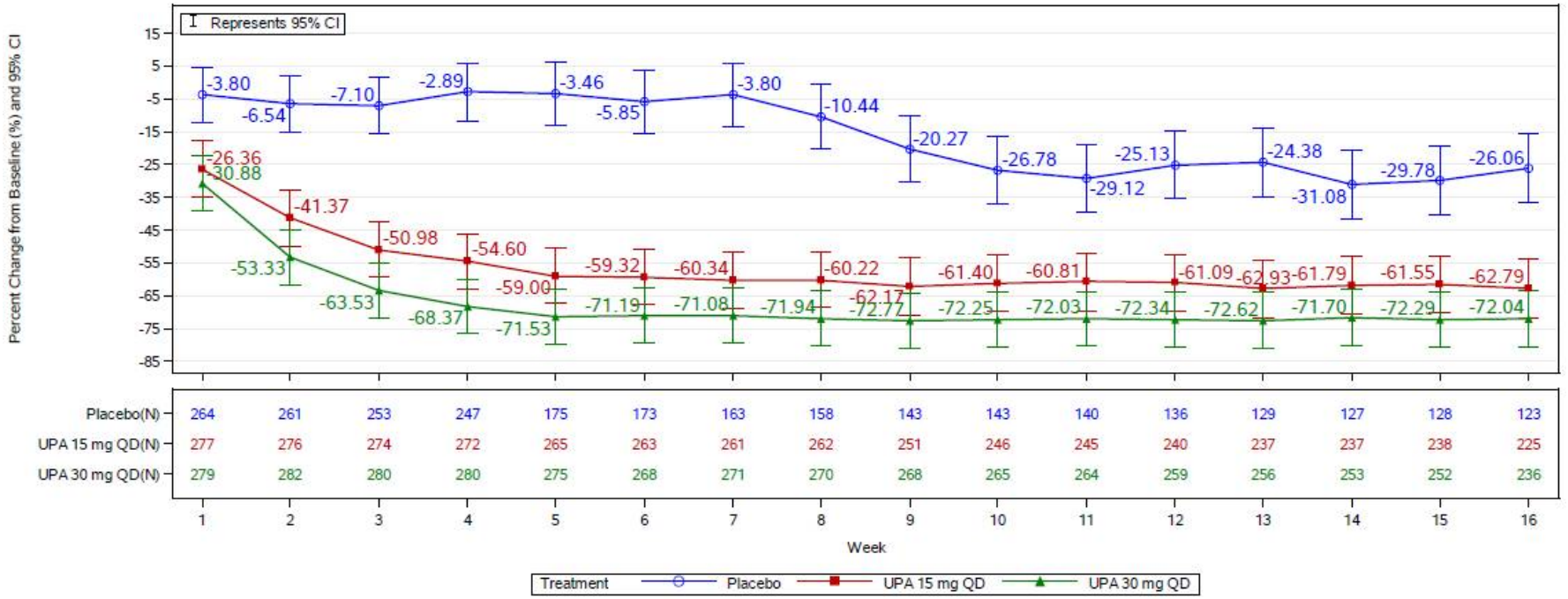


CI = confidence interval; NRI = non-responder imputation; NRS = Numerical Rating Scale; QD = once daily, UPA = upadacitinib

Note：NRI-NC is non-responder imputation with no special data handling for missing due to COVID-19. Baseline refers to the last available daily assessment before the date of first administration of study drug. 95% CI for response rate is based on the normal approximation to the binomial distribution.

相互参照：M16-045 試験 CSR W16 Figure 14.2　22.2.1

図 2.7.3.6-16.　二重盲検投与期の来院時別での最悪のかゆみの NRS のベースラインからの変化率（%）（MMRM，ITT_M 集団）：M16-045 試験



CI = confidence interval; NRS = Numerical Rating Scale; QD = once daily, UPA = upadacitinib

Note：Measurements after receiving rescue treatment are considered as missing. The weekly rolling average will be calculated up to Week 16. Within group LS mean and 95% CI are displayed in this figure, based on MMRM. MMRM is the Mixed-Effect Model Repeat Measurement with Baseline, treatment, visit, treatment by visit interaction, and strata (Baseline vIGA-AD categories and age [adolescent vs. adult]) in the model. An unstructured covariance matrix is used. If the model cannot converge, AR(1) or CS covariance matrix will be used. Baseline refers to the last available rolling average before the date of first administration of study drug. Subjects with only non-missing percent change from Baseline values are included in analysis.

相互参照：M16-045 試験 CSRW16 Figure 14.2　22.3.1