TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
片頭痛	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.2) [1.2]	2 (0.7) [0.7]	3 (1.0) [1.0]	-0.8 (-2.7, 1.1)	-0.0 (-2.2, 2.2)
赤血球数減少	0	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.7) [0.7]	3 (1.0) [1.0]	0.4 (-1.0, 1.7)	0.8 (-0.8, 2.3)
体重増加	0	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.7) [0.7]	3 (1.0) [1.0]	0.4 (-1.0, 1.8)	0.8 (-0.8, 2.3)
肺炎	4 (1.6) [1.6]	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.3]	3 (1.0) [1.0]	-1.2 (-3.2, 0.8)	-0.8 (-3.0, 1.4)
歯感染	2 (0.8) [0.8]	0	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.0) [1.0]	-0.8 (-2.4, 0.8)	0.4 (-1.7, 2.4)
腹部圧痛	0	0	2 (0.8) [0.8]	1 (0.4) [0.3]	3 (1.0) [1.0]	0.0	0.8 (-0.8, 2.4)
鼻出血	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	3 (1.0) [1.0]	0.0	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
坐骨神経痛	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	3 (1.0) [1.0]	0.4 (-1.0, 1.7)	0.0
皮脂欠乏性湿疹	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	3 (1.0) [1.0]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
歯周炎	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]	-0.4 (-1.8, 1.0)	0.4 (-1.4, 2.1)
尿中血陽性	0	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]	0.0	0.8 (-0.8, 2.3)
霰粒腫	0	0	3 (1.2) [1.2]	0	3 (1.0) [1.0]	0.0	1.2 (-0.5, 2.9)
深部静脈血栓症	0	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]	0.0	0.8 (-0.8, 2.3)
血小板数増加	0	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]	0.0	0.8 (-0.8, 2.4)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
心室性期外収縮	0	0	1 (0.4) [0.4]	0	3 (1.0) [1.0]	0.0	0.4 (-1.0, 1.7)
膀胱炎	0	3 (1.2) [1.2]	2 (0.8) [0.8]	8 (2.8) [2.8]	2 (0.7) [0.7]	1.2 (-0.5, 3.0)	0.8 (-0.8, 2.4)
下痢	2 (0.8) [0.8]	2 (0.8) [0.8]	2 (0.8) [0.8]	5 (1.8) [1.8]	2 (0.7) [0.7]	0.1 (-1.9, 2.0)	0.0 (-1.9, 1.9)
感覚鈍麻	1 (0.4) [0.4]	4 (1.6) [1.6]	1 (0.4) [0.4]	4 (1.4) [1.4]	2 (0.7) [0.7]	1.2 (-0.9, 3.3)	-0.0 (-1.6, 1.6)
結膜炎	0	2 (0.8) [0.8]	1 (0.4) [0.4]	4 (1.4) [1.4]	2 (0.7) [0.7]	0.8 (-0.8, 2.3)	0.4 (-1.0, 1.7)
脂質異常症	0	4 (1.6) [1.6]	1 (0.4) [0.4]	4 (1.4) [1.4]	2 (0.7) [0.7]	1.6 (-0.3, 3.5)	0.4 (-1.0, 1.7)
そう痒症	6 (2.4) [2.5]	2 (0.8) [0.8]	1 (0.4) [0.4]	3 (1.1) [1.0]	2 (0.7) [0.7]	-1.7 (-4.2, 0.8)	-2.1 (-4.4, 0.3)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
腎結石症	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.8) [0.8]	3 (1.1) [1.0]	2 (0.7) [0.7]	0.4 (-1.6, 2.5)	-0.0 (-1.9, 1.9)
倦怠感	1 (0.4) [0.4]	0	2 (0.8) [0.8]	3 (1.1) [1.1]	2 (0.7) [0.7]	-0.4 (-1.7, 1.0)	0.4 (-1.3, 2.1)
頚部痛	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.8) [0.8]	3 (1.1) [1.1]	2 (0.7) [0.7]	0.4 (-1.3, 2.2)	0.4 (-1.3, 2.1)
回転性めまい	0	2 (0.8) [0.8]	0	3 (1.1) [1.1]	2 (0.7) [0.7]	0.8 (-0.8, 2.4)	0.0
脂漏性皮膚炎	7 (2.9) [2.8]	2 (0.8) [0.8]	2 (0.8) [0.8]	2 (0.7) [0.7]	2 (0.7) [0.7]	-2.0 (-4.6, 0.5)	-2.0 (-4.6, 0.5)
消化不良	3 (1.2) [1.2]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	2 (0.7) [0.7]	-0.7 (-2.6, 1.1)	-0.8 (-2.6, 1.1)
麦粒腫	3 (1.2) [1.2]	0	2 (0.8) [0.8]	2 (0.7) [0.7]	2 (0.7) [0.7]	-1.2 (-2.9, 0.5)	-0.4 (-2.4, 1.6)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
悪寒	2 (0.8) [0.8]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	2 (0.7) [0.7]	-0.4 (-2.2, 1.3)	-0.8 (-2.4, 0.8)
手根管症候群	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.7) [0.7]	2 (0.7) [0.7]	-0.0 (-1.5, 1.5)	0.4 (-1.3, 2.1)
インフルエンザ様疾患	1 (0.4) [0.4]	0	2 (0.8) [0.8]	2 (0.7) [0.7]	2 (0.7) [0.7]	-0.4 (-1.8, 1.0)	0.4 (-1.4, 2.1)
疼痛	1 (0.4) [0.4]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	2 (0.7) [0.7]	-0.0 (-1.5, 1.5)	-0.4 (-1.7, 1.0)
尿中蛋白陽性	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	2 (0.7) [0.7]	-0.0 (-1.6, 1.6)	-0.0 (-1.6, 1.6)
肛門膿瘍	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	2 (0.7) [0.7]	0.4 (-1.0, 1.7)	0.0
肝酵素上昇	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	2 (0.7) [0.7]	0.4 (-1.0, 1.8)	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
椎間板突出	0	0	0	2 (0.7) [0.7]	2 (0.7) [0.7]	0.0	0.0
鼓腸	3 (1.2) [1.2]	0	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]	-1.2 (-2.9, 0.5)	-0.4 (-2.4, 1.6)
鼻炎	3 (1.2) [1.2]	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]	-0.8 (-2.7, 1.1)	-0.4 (-2.5, 1.6)
口内炎	3 (1.2) [1.2]	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]	-0.9 (-2.8, 1.1)	-0.4 (-2.5, 1.6)
口腔カンジダ症	2 (0.8) [0.9]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	2 (0.7) [0.7]	-0.5 (-2.2, 1.3)	-0.5 (-2.2, 1.3)
齲歯	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	2 (0.7) [0.7]	-0.0 (-1.5, 1.5)	-0.4 (-1.7, 1.0)
血尿	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	0.0 (-1.6, 1.6)	0.4 (-1.4, 2.1)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
リンパ球数増加	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]	-0.0 (-1.6, 1.5)	0.4 (-1.4, 2.1)
寝汗	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	0.0 (-1.5, 1.6)	0.0 (-1.5, 1.6)
末梢腫脹	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	2 (0.7) [0.7]	0.0 (-1.5, 1.5)	0.0 (-1.5, 1.6)
前立腺炎	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	0.0 (-1.5, 1.6)	0.0 (-1.5, 1.6)
脂漏性角化症	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	2 (0.7) [0.7]	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 1.0)
外陰部腟カンジダ症	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	2 (0.7) [0.7]	-0.0 (-1.6, 1.5)	-0.0 (-1.6, 1.6)
無症候性COVID-19	0	0	0	1 (0.4) [0.4]	2 (0.7) [0.7]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
結腸異形成	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	2 (0.7) [0.7]	0.4 (-1.0, 1.8)	0.0
ドライアイ	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	2 (0.7) [0.7]	0.4 (-1.0, 1.7)	0.4 (-0.9, 1.8)
小腸炎	0	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	0.4 (-1.0, 1.8)	0.8 (-0.8, 2.4)
骨減少症	0	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]	0.4 (-1.0, 1.7)	0.8 (-0.8, 2.4)
斑状皮疹	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	0.4 (-1.0, 1.8)	0.4 (-1.0, 1.8)
ウイルス感染	0	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]	0.4 (-1.0, 1.7)	0.8 (-0.8, 2.4)
鼻閉	3 (1.2) [1.2]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	-1.2 (-3.0, 0.5)	-0.4 (-2.5, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
异汗性湿疹	2 (0.8) [0.8]	0	0	0	2 (0.7) [0.7]	-0.8 (-2.3, 0.8)	-0.8 (-2.3, 0.8)
急性腎障害	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
眼瞼炎	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	-0.4 (-1.8, 1.0)	0.4 (-1.4, 2.1)
喉頭炎	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
嚥下痛	1 (0.4) [0.4]	0	0	0	2 (0.7) [0.7]	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
蛋白尿	1 (0.4) [0.4]	0	0	0	2 (0.7) [0.7]	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
歯牙破折	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	-0.4 (-1.7, 1.0)	0.4 (-1.3, 2.1)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
光線角化症	0	0	0	0	2 (0.7) [0.7]	0.0	0.0
血中リン減少	0	0	0	0	2 (0.7) [0.7]	0.0	0.0
滑液包炎	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0.0	0.4 (-1.0, 1.8)
子宮頚部上皮異形成	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0.0	0.8 (-0.8, 2.4)
糖尿病	0	0	0	0	2 (0.7) [0.7]	0.0	0.0
腸炎	0	0	0	0	2 (0.7) [0.7]	0.0	0.0
皮膚真菌感染	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0.0	0.8 (-0.8, 2.4)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
内出血発生の増加傾向	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0.0	0.4 (-0.9, 1.8)
関節周囲炎	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0.0	0.8 (-0.8, 2.4)
クリプトコッカス性肺炎	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0.0	0.8 (-0.8, 2.3)
失神寸前の状態	0	0	0	0	2 (0.7) [0.7]	0.0	0.0
そう痒性皮疹	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0.0	0.4 (-0.9, 1.8)
皮膚乳頭腫	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0.0	0.4 (-1.0, 1.7)
傾眠	0	0	0	0	2 (0.7) [0.7]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
白衣性高血圧	0	0	0	0	2 (0.7) [0.7]	0.0	0.0
ウイルス性気道感染	1 (0.4) [0.4]	4 (1.6) [1.6]	0	6 (2.1) [2.1]	1 (0.3) [0.3]	1.2 (-0.8, 3.2)	-0.4 (-1.7, 1.0)
リンパ球減少症	2 (0.8) [0.8]	2 (0.8) [0.8]	1 (0.4) [0.4]	4 (1.4) [1.4]	1 (0.3) [0.3]	0.0 (-1.9, 1.9)	-0.4 (-2.1, 1.3)
高比重リポ蛋白増加	0	3 (1.2) [1.2]	1 (0.4) [0.4]	4 (1.4) [1.4]	1 (0.3) [0.4]	1.2 (-0.5, 2.9)	0.4 (-0.9, 1.8)
筋骨格痛	3 (1.2) [1.2]	2 (0.8) [0.8]	1 (0.4) [0.4]	3 (1.1) [1.0]	1 (0.3) [0.3]	-0.4 (-2.5, 1.7)	-0.8 (-2.7, 1.1)
アトピー性皮膚炎	2 (0.8) [0.8]	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.1) [1.0]	1 (0.3) [0.3]	0.4 (-1.7, 2.4)	-0.4 (-2.1, 1.3)
胃炎	0	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.1) [1.0]	1 (0.3) [0.3]	1.2 (-0.5, 2.9)	0.4 (-1.0, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
皮膚乾燥	5 (2.0) [2.1]	0	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	-2.1 (-4.2, 0.0)	-1.7 (-3.9, 0.6)
末梢性浮腫	3 (1.2) [1.2]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.4]	-0.8 (-2.7, 1.1)	-0.8 (-2.7, 1.1)
接触皮膚炎	2 (0.8) [0.8]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	-0.4 (-2.2, 1.3)	-0.4 (-2.2, 1.3)
肝機能異常	2 (0.8) [0.8]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	1 (0.3) [0.3]	-0.4 (-2.2, 1.3)	-0.8 (-2.4, 0.8)
爪真菌症	2 (0.8) [0.8]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	-0.4 (-2.2, 1.3)	-0.4 (-2.2, 1.3)
肩回旋筋腱板症候群	2 (0.8) [0.8]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	1 (0.3) [0.4]	-0.0 (-1.9, 1.9)	-0.8 (-2.4, 0.8)
食欲減退	1 (0.4) [0.4]	0	0	2 (0.7) [0.7]	1 (0.3) [0.3]	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
排尿困難	1 (0.4) [0.4]	0	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
高血糖	1 (0.4) [0.4]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	1 (0.3) [0.3]	0.4 (-1.4, 2.2)	-0.4 (-1.8, 1.0)
骨粗鬆症	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	-0.0 (-1.6, 1.6)	-0.0 (-1.6, 1.6)
レンサ球菌性咽頭炎	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	0.4 (-1.3, 2.2)	0.0 (-1.5, 1.6)
湿性咳嗽	1 (0.4) [0.4]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	1 (0.3) [0.3]	0.4 (-1.3, 2.2)	-0.4 (-1.8, 0.9)
酒さ	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	0.5 (-1.3, 2.2)	0.0 (-1.5, 1.6)
蜂巣炎	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
ざ瘡様皮膚炎	0	0	0	2 (0.7) [0.7]	1 (0.3) [0.3]	0.0	0.0
単純ヘルペス	0	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	0.8 (-0.8, 2.3)	0.4 (-1.0, 1.7)
過敏性腸症候群	0	0	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
関節腫脹	0	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	0.8 (-0.8, 2.3)	0.4 (-1.0, 1.8)
不正子宮出血	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.0
歯髄炎	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.8)
季節性アレルギー	0	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	0.8 (-0.8, 2.3)	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
歯膿瘍	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.8)
鉄欠乏性貧血	5 (2.0) [2.1]	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]	-2.1 (-4.1, 0.0)	-2.1 (-4.1, 0.0)
口腔内潰瘍形成	2 (0.8) [0.8]	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	-0.8 (-2.4, 0.8)	-0.4 (-2.2, 1.3)
錯感覚	2 (0.8) [0.8]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.4]	-0.4 (-2.2, 1.4)	-0.4 (-2.2, 1.3)
アレルギー性鼻炎	2 (0.8) [0.8]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	-0.4 (-2.2, 1.4)	-0.4 (-2.2, 1.3)
副鼻腔うっ血	2 (0.8) [0.8]	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.4]	-0.8 (-2.4, 0.8)	-0.4 (-2.1, 1.3)
上気道の炎症	2 (0.8) [0.8]	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]	-0.4 (-2.1, 1.4)	-0.8 (-2.3, 0.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
アレルギー性結膜炎	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	-0.0 (-1.6, 1.5)	-0.0 (-1.6, 1.6)
嚥下障害	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0 (-1.5, 1.5)	0.0 (-1.5, 1.6)
斑状出血	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
鉄欠乏	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.4]	-0.4 (-1.7, 1.0)	0.0 (-1.5, 1.6)
靭帯捻挫	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0 (-1.5, 1.6)	0.0 (-1.5, 1.6)
四肢損傷	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 1.0)
膿疱	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
斑状丘疹状皮疹	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	-0.0 (-1.5, 1.5)	0.0 (-1.5, 1.6)
直腸出血	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.4]	-0.4 (-1.8, 1.0)	0.0
皮膚剥脱	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
外陰腟真菌感染	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	-0.0 (-1.6, 1.5)	-0.0 (-1.6, 1.6)
無月経	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.8)
痔瘻	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
足関節部骨折	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
大動脈硬化症	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
虫垂炎	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.0
不整脈	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.0
節足動物咬傷	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.0
喘息	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.8)
血中アルブミン増加	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.4]	0.4 (-1.0, 1.8)	0.4 (-0.9, 1.8)
血中ブドウ糖増加	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
血中鉄減少	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.0
血圧上昇	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.0
体温上昇	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.8)
カンピロバクター胃腸炎	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.0
皮膚嚢腫	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	0.4 (-1.0, 1.8)	0.4 (-1.0, 1.8)
薬物性肝障害	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.8)
月経困難症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
異形成	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.0
勃起不全	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.0
足骨折	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.0
せつ	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.4]	0.4 (-1.0, 1.8)	0.0
歯肉炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.4 (-1.0, 1.8)	0.0
単径ヘルニア	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.0
大腸感染	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.4 (-1.0, 1.8)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
リンパ節症	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
リンパ球百分率減少	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.7)
平均赤血球容積増加	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.0
小球性貧血	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
筋断裂	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
筋痙縮	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.0
眼充血	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.4]	0.4 (-1.0, 1.8)	0.4 (-0.9, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
爪囲炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.4 (-1.0, 1.8)	0.0
足底筋膜炎	0	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
洞性徐脈	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	0.4 (-1.0, 1.8)	0.4 (-1.0, 1.7)
腫脹	0	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
癜風	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.4 (-1.0, 1.7)
抜歯	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.0	0.0
埋伏歯	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
トランスアミナーゼ上昇	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.0	0.0
腟分泌物	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]	0.4 (-1.0, 1.8)	0.0
ビタミンD減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]	0.4 (-1.0, 1.7)	0.0
白血球数増加	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]	0.4 (-1.0, 1.8)	0.4 (-1.0, 1.7)
尿中白血球陽性	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.4]	0.4 (-1.0, 1.7)	0.0
低ナトリウム血症	2 (0.8) [0.9]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.9 (-2.5, 0.8)	-0.5 (-2.2, 1.3)
白癬感染	2 (0.8) [0.8]	0	0	0	1 (0.3) [0.4]	-0.8 (-2.4, 0.8)	-0.8 (-2.4, 0.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
急性呼吸不全	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
心房細動	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
骨挫傷	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.7, 1.0)	0.0 (-1.5, 1.6)
肋軟骨炎	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
結節性紅斑	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.7, 1.0)	0.0 (-1.5, 1.6)
側腹部痛	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.7, 1.0)	0.0 (-1.5, 1.6)
しゃっくり	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
低血圧	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
角膜炎	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.7, 1.0)	0.0 (-1.5, 1.6)
爪破損	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
歯周病	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.0 (-1.6, 1.6)
光線過敏性反応	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	-0.4 (-1.7, 1.0)	0.0 (-1.5, 1.6)
失神	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
腱炎	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
臍ヘルニア	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
結腸腺癌	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
肛門の炎症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
肛門ポリープ	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
アナフィラキシー反応	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
大動脈雑音	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
無水晶体眼	0	0	0	0	1 (0.3) [0.3]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
失声症	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
皮脂欠乏症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
第一度房室ブロック	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
細菌感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
良性脾腫瘍	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
二束ブロック	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
血中アルカリホスファターゼ増加	0	0	0	0	1 (0.3) [0.3]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
血中ブドウ糖減少	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
血中トリグリセリド増加	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
骨痛	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
ボーエン病	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
感染性滑液包炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
膀胱結石	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
炭水化物耐性低下	0	0	0	0	1 (0.3) [0.3]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
心不全	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
頚動脈硬化症	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
脳血管発作	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
頚髄圧迫	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
頚部脊柱管狭窄症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
軟骨軟化症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
慢性左室不全	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
角膜浮腫	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
サイトメガロウイルス性大腸炎	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
片耳難聴	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
便意切迫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
歯嚢胞	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
歯科インプラント埋込み	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
抑うつ気分	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
アレルギー性皮膚炎	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
爪の皮膚糸状菌症	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
皮様嚢腫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
憩室炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
口内乾燥	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
労作性呼吸困難	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
肺気腫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
感染性腸炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
エンテロウイルス感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
眼外傷	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
変色便	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
転倒	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
線維腫	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
線維性組織球腫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
葉酸欠乏	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
真菌感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
胃腸管動静脈奇形	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
陰部単純ヘルペス	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
歯肉膿瘍	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
緑内障	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
顆粒球数減少	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
血腫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
尿中ヘモグロビン陽性	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
手足口病	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
B型肝炎DNA測定陽性	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
ヘルペス眼感染	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
帯状疱疹性髄膜炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
高カルシウム血症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
高ナトリウム血症	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
緊張性膀胱	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
高尿酸血症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
過換気	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
聴力低下	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
咬傷感染	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
炎症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
故意の自傷行為	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
瘢痕そう痒感	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
黒子	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
四肢外傷性切断	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
口唇腫脹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
肝障害	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
肝機能検査値上昇	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
腰部脊柱管狭窄症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
腰椎骨折	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
肺過膨脹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
肺浸潤	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
腫瘤	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
平均赤血球容積異常	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
機械性蕁麻疹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
メニエール病	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
髄膜腫	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
代謝症候群	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
排尿異常	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
僧帽弁閉鎖不全症	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
脊髄症	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
神経圧迫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
好中球百分率増加	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
小結節	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
非感染性気管支炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
非感染性歯肉炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
肥満	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
爪甲剥離症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
口腔障害	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
起立性低血圧	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
骨炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
耳漏	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
乳頭腫ウイルス感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
丘疹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
心膜炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
末梢動脈閉塞性疾患	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
静脈炎	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
胸膜感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
ウイルス性肺炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
頻尿	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
睡眠の質低下	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
ヘルペス後神経痛	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
処置後出血	0	0	0	0	1 (0.3) [0.3]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
閉経後出血	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
閉経後	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
前立腺腫瘤	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
総蛋白増加	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
膿皮症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
直腸分泌物	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
直腸ポリープ	0	0	0	0	1 (0.3) [0.3]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
鼻漏	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
続発性副腎皮質機能不全	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
精液変色	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
皮膚潰瘍	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
小細胞癌	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
脊椎炎性脊髄症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
皮膚有棘細胞癌	0	0	0	0	1 (0.3) [0.3]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
子宮頚部扁平上皮癌	0	0	0	0	1 (0.3) [0.4]	0.0	0.0
くも膜下出血	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
皮下組織膿瘍	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
上室性頻脈	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
顔面腫脹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
緊張性頭痛	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
咽喉刺激感	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
血小板増加症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
甲状腺腫瘤	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
股部白癬	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
耳鳴	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
細菌性扁桃炎	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
歯の脱落	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
上気道咳症候群	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
尿管結石症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.7)
尿中ケトン体陽性	0	0	0	0	1 (0.3) [0.4]	0.0	0.0
ワクチン接種部位疼痛	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
ガードネレラ菌性膣炎	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
視野欠損	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
ウォルフ・パーキンソン・ホワイト症候群	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]	0.0	0.4 (-0.9, 1.8)
創傷感染	0	0	0	0	1 (0.3) [0.3]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
手首関節骨折	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]	0.0	0.4 (-1.0, 1.8)
乾皮症	0	0	0	0	1 (0.3) [0.3]	0.0	0.0
脂肪肝	0	2 (0.8) [0.8]	0	4 (1.4) [1.4]	0	0.8 (-0.8, 2.4)	0.0
変形性関節症	2 (0.8) [0.8]	0	0	3 (1.1) [1.1]	0	-0.8 (-2.3, 0.8)	-0.8 (-2.3, 0.8)
紅斑性皮疹	1 (0.4) [0.4]	1 (0.4) [0.4]	0	3 (1.1) [1.0]	0	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 1.0)
皮膚裂傷	1 (0.4) [0.4]	3 (1.2) [1.2]	0	3 (1.1) [1.1]	0	0.8 (-1.1, 2.7)	-0.4 (-1.7, 1.0)
カンピロバクター感染	0	1 (0.4) [0.4]	0	3 (1.1) [1.0]	0	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
硬化性胆管炎	0	0	0	3 (1.1) [1.1]	0	0.0	0.0
耳痛	0	1 (0.4) [0.4]	0	3 (1.1) [1.1]	0	0.4 (-1.0, 1.8)	0.0
関節損傷	0	2 (0.8) [0.8]	0	3 (1.1) [1.0]	0	0.8 (-0.8, 2.4)	0.0
大腸炎	3 (1.2) [1.2]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0	-0.4 (-2.5, 1.6)	-1.2 (-2.9, 0.5)
筋骨格系胸痛	2 (0.8) [0.8]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	-0.4 (-2.2, 1.4)	-0.8 (-2.4, 0.8)
膿痂疹	1 (0.4) [0.4]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 1.0)
脊椎関節障害	1 (0.4) [0.4]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
人工流産	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0	0.8 (-0.8, 2.4)	0.0
ダニ皮膚炎	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0	0.8 (-0.8, 2.3)	0.0
血中カルシウム増加	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	0.4 (-1.0, 1.8)	0.0
血中カリウム減少	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0	0.8 (-0.8, 2.3)	0.0
呼吸困難	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	0.4 (-1.0, 1.8)	0.0
月経過多	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	0.4 (-1.0, 1.7)	0.0
単球数増加	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	0.4 (-1.0, 1.8)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
骨壊死	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	0.4 (-1.0, 1.7)	0.0
過量投与	0	0	0	2 (0.7) [0.7]	0	0.0	0.0
外傷後疼痛	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0	0.8 (-0.8, 2.3)	0.0
毛孔性皮疹	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	0.4 (-1.0, 1.8)	0.0
睡眠障害	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0	0.4 (-1.0, 1.7)	0.0
下腹部痛	3 (1.2) [1.2]	0	0	1 (0.4) [0.3]	0	-1.2 (-3.0, 0.5)	-1.2 (-2.9, 0.5)
低カリウム血症	3 (1.2) [1.2]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.8 (-2.7, 1.1)	-1.2 (-2.9, 0.5)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
痔出血	2 (0.8) [0.8]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.4 (-2.1, 1.3)	-0.8 (-2.3, 0.8)
動悸	2 (0.8) [0.8]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.4 (-2.2, 1.3)	-0.8 (-2.4, 0.8)
アミラーゼ増加	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 1.0)
裂肛	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
乳房嚢胞	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.0 (-1.5, 1.5)	-0.4 (-1.7, 1.0)
カンジダ感染	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
うっ血性心不全	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
サイトメガロウイルス感染	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 1.0)
糸球体濾過率減少	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.0 (-1.5, 1.6)	-0.4 (-1.7, 1.0)
浸潤性乳癌	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	-0.0 (-1.6, 1.6)	-0.4 (-1.8, 1.0)
肝損傷	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.0 (-1.6, 1.5)	-0.4 (-1.8, 0.9)
下気道感染	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.0 (-1.5, 1.5)	-0.4 (-1.7, 1.0)
不規則月経	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
肉離れ	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.0 (-1.5, 1.5)	-0.4 (-1.7, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
筋骨格硬直	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
筋炎	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.0 (-1.5, 1.5)	-0.4 (-1.7, 1.0)
神経皮膚炎	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
外耳炎	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
腎盂腎炎	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.0 (-1.5, 1.5)	-0.4 (-1.7, 1.0)
皮膚亀裂	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
頻脈	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
２型糖尿病	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
膣出血	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	-0.0 (-1.5, 1.5)	-0.4 (-1.7, 1.0)
静脈血栓症	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
腹壁膿瘍	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
嚢胞性ざ瘡	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
不安障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
大動脈瘤	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
関節炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
細菌性関節炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
無力症	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
完全房室ブロック	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
細菌検査陽性	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
肺の良性新生物	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
胆道ジスキネジア	0	0	0	1 (0.4) [0.3]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
ブラストシスティス感染	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
出血性静脈瘤	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
血中アルブミン減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
血中重炭酸塩減少	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
血中コレステロール減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
血中葉酸減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
血中カリウム増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
血中ナトリウム増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
血中トリグリセリド異常	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
骨密度減少	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
脳損傷	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
乳房膿瘍	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
乳房痛	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
気管支の良性新生物	0	0	0	1 (0.4) [0.3]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
灼熱感	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
軟骨萎縮	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
胸部不快感	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
慢性閉塞性肺疾患	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
クロストリジウム・ディフィシレ大腸炎	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
ばち状指	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
性交出血	0	0	0	1 (0.4) [0.4]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
虚血性大腸炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
コロナウイルス感染	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
感音性難聴	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
びまん性脱毛症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
注意力障害	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
性交困難	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
大腸菌性尿路感染	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
外骨腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
毒性物質曝露	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
四肢拘縮	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
眼感染	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
眼刺激	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
眼そう痒症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
眼部腫脹	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
線維筋痛	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
仙骨骨折	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
胃潰瘍	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
消化器痛	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
全身性浮腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
ジルベール症候群	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
尿中ブドウ糖陽性	0	0	0	1 (0.4) [0.4]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
甲状腺腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
痛風	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
握力低下	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
肛径部膿瘍	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
血管腫	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
皮膚血管腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
ヘマトクリット減少	0	0	0	1 (0.4) [0.3]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
熱射病	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
ヘリコバクター感染	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
ヘルペス性皮膚炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
耳帯状疱疹	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
陰嚢水瘤	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
多汗症	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
高トランスアミナーゼ血症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
感染性皮膚嚢腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
間擦疹	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
腸閉塞	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
腸管ポリープ	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
関節滲出液	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
関節硬直	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
流涙増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
靭帯断裂	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
口唇障害	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
リパーゼ増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
低比重リポ蛋白減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
腰仙部神経根障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
リンパ球百分率増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
黄斑浮腫	0	0	0	1 (0.4) [0.4]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
乳腺炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
メラノサイト性母斑	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
前兆を伴う片頭痛	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
汗疹	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
筋拘縮	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
近視	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
鼻潰瘍	0	0	0	1 (0.4) [0.4]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
後頭神経痛	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
浮腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
食道カンジダ症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
食道炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
卵巣胚細胞良性奇形腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
掌蹠膿疱症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
汎血球減少症	0	0	0	1 (0.4) [0.4]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
パニック発作	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
脂肪織炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
口囲皮膚炎	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
扁桃周囲炎	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
毛巣嚢胞	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
多嚢胞性卵巣	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
プレアルブミン減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
肛門周囲痛	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
前立腺特異性抗原増加	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
総蛋白減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
肺挫傷	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
丘疹性皮疹	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
レイノー現象	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
直腸異形成	0	0	0	1 (0.4) [0.4]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
血沈亢進	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
腎機能障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
網状赤血球数減少	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
網膜静脈閉塞	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
皮膚腫瘤	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
睡眠時無呼吸症候群	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
会話障害	0	0	0	1 (0.4) [0.4]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
脾腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
スポーツ損傷	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
ブドウ球菌検査陽性	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
ストレス骨折	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
軟骨下機能不全骨折	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
硬膜下滲出液	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
胸椎骨折	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
甲状腺腺腫	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
脛骨骨折	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
弾発指	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
過少体重	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
尿閉	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
尿検査異常	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
尿中白血球エステラーゼ陽性	0	0	0	1 (0.4) [0.3]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
子宮平滑筋腫	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
水痘帯状疱疹ウイルス感染	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0	0.4 (-1.0, 1.7)	0.0
ウイルス性咽頭炎	0	0	0	1 (0.4) [0.4]	0	0.0	0.0
硝子体浮遊物	0	0	0	1 (0.4) [0.3]	0	0.0	0.0
創傷	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	0.4 (-1.0, 1.8)	0.0
肛門そう痒症	2 (0.8) [0.8]	0	0	0	0	-0.8 (-2.4, 0.8)	-0.8 (-2.4, 0.8)
腹部膿瘍	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
腹部腫瘤	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
異常便	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
急性心内膜炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
急性心筋梗塞	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
動物による引っかき傷	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
強直性脊椎炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
肛門直腸感染	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
抗核抗体増加	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
腸炎性関節炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
細菌性腟症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
バルトリン嚢腫	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
気管支拡張症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
頚髄神経根障害	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
尾骨痛	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
大腸腺腫	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
結膜充血	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
角膜混濁	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
クッシング症候群	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
皮膚糸状菌症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
医療機器に対する不耐性	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
薬物過敏症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
薬効欠如	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
機能不全性子宮出血	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
味覚不全	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
耳部腫脹	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
好酸球増加症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
てんかん	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
上強膜炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
本態性振戦	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
外耳道の外骨腫	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
眼瞼障害	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
眼瞼発疹	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
大腿ヘルニア	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
歯肉腫脹	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
舌痛	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
耐糖能障害	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
糖尿	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
出血性関節症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
血便排泄	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
ヘモフィルス感染	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
喀血	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
血栓性痔核	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
熱中症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
水腎症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
知覚過敏	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
高リパーゼ血症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
高体温症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
低リン酸血症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
損傷	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
間質性肺疾患	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
椎間板変性症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
易刺激性	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
大腸穿孔	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
白血球増加症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
白血球尿	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
リンパ球増加症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
閉経期症状	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
精神障害	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
中耳滲出液	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
伝染性軟属腫	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
口腔嚢胞	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
粘膜乾燥	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
粘液便	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
筋力低下	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
腎石灰沈着症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
末梢性ニューロパチー	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
非心臓性胸痛	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
卵巣静脈血栓症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
膵炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
眼窩周囲腫脹	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
光線性皮膚症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
血小板数減少	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
ニューモシスチス・イロベチイ肺炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
直腸炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
肺出血	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
壊疽性膿皮症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
直腸攣縮	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
直腸しぶり	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
肋骨骨折	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
交通事故	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
異物感	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
セラチア感染	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
皮膚灼熱感	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
皮膚びらん	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
皮膚色素過剰	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
脊椎圧迫骨折	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
変形性脊椎症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
ブドウ球菌感染	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
皮下血腫	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
自殺念慮	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
腱痛	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) n (%) [SSA%]	UPA 30 mg QD (N=291) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
腱鞘炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
血小板減少症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)
トリコモナス症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
潰瘍性角膜炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
ぶどう膜炎	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 0.9)
ウイルス血症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.7, 1.0)	-0.4 (-1.7, 1.0)
外陰腟そう痒症	1 (0.4) [0.4]	0	0	0	0	-0.4 (-1.8, 1.0)	-0.4 (-1.8, 1.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

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表 2.7.4.7-96.

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UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
Any adverse event	674 (499.4) [494.1]	629 (315.4) [315.5]	695 (318.1) [317.5]	1133 (273.8) [273.3]	1212 (285.1) [293.2]
血液およびリンパ系障害	31 (23.0) [22.2]	30 (15.0) [15.0]	21 (9.6) [9.6]	46 (11.1) [11.4]	37 (8.7) [8.6]
貧血	13 (9.6) [9.2]	10 (5.0) [5.1]	9 (4.1) [4.1]	16 (3.9) [4.0]	12 (2.8) [2.7]
好酸球増加症	1 (0.7) [0.7]	0	0	0	0
内出血発生の増加傾向	0	0	1 (0.5) [0.4]	0	2 (0.5) [0.7]
鉄欠乏性貧血	5 (3.7) [3.8]	0	0	1 (0.2) [0.3]	1 (0.2) [0.2]
白血球増加症	1 (0.7) [0.8]	0	0	0	0
白血球減少症	3 (2.2) [2.0]	9 (4.5) [4.5]	1 (0.5) [0.5]	13 (3.1) [3.1]	5 (1.2) [1.1]
リンパ節症	0	0	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
血液およびリンパ系障害 (Cont.)					
リンパ球増加症	1 (0.7) [0.8]	0	0	0	0
リンパ球減少症	3 (2.2) [2.0]	3 (1.5) [1.5]	1 (0.5) [0.5]	5 (1.2) [1.3]	3 (0.7) [0.6]
小球性貧血	0	0	1 (0.5) [0.4]	1 (0.2) [0.3]	1 (0.2) [0.4]
好中球減少症	3 (2.2) [2.1]	7 (3.5) [3.4]	6 (2.7) [2.8]	7 (1.7) [1.8]	11 (2.6) [2.4]
汎血球減少症	0	0	0	1 (0.2) [0.3]	0
脾腫	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
血小板減少症	1 (0.7) [0.8]	0	0	0	0
血小板増加症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
心臓障害	6 (4.4) [4.4]	4 (2.0) [2.0]	8 (3.7) [3.7]	6 (1.4) [1.5]	14 (3.3) [3.4]
急性心筋梗塞	1 (0.7) [0.7]	0	0	0	0
不整脈	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	1 (0.2) [0.2]
心房細動	1 (0.7) [0.8]	0	0	0	1 (0.2) [0.2]
完全房室ブロック	0	0	0	1 (0.2) [0.3]	0
第一度房室ブロック	0	0	0	0	1 (0.2) [0.2]
二束ブロック	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
心不全	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
うっ血性心不全	1 (0.7) [0.8]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
慢性左室不全	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
心臓障害 (Cont.)					
僧帽弁閉鎖不全症	0	0	0	0	1 (0.2) [0.2]
動悸	2 (1.5) [1.5]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
心膜炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
洞性徐脈	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]
上室性頻脈	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
頻脈	1 (0.7) [0.7]	0	0	1 (0.2) [0.3]	0
心室性期外収縮	0	0	1 (0.5) [0.5]	0	3 (0.7) [0.6]
ウォルフ・パーキンソン・ホワイト症候群	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
先天性、家族性および遺伝性障害	0	1 (0.5) [0.5]	2 (0.9) [0.9]	2 (0.5) [0.4]	2 (0.5) [0.5]
皮様嚢腫	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
胃腸管動静脈奇形	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
ジルベール症候群	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
陰嚢水瘤	0	0	0	1 (0.2) [0.2]	0
耳および迷路障害	3 (2.2) [2.3]	4 (2.0) [2.0]	1 (0.5) [0.5]	8 (1.9) [2.1]	7 (1.6) [1.6]
感音性難聴	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
片耳難聴	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
耳痛	0	1 (0.5) [0.5]	0	3 (0.7) [0.8]	0
耳部腫脹	1 (0.7) [0.7]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
耳および迷路障害 (Cont.)					
外耳道の外骨腫	1 (0.7) [0.8]	0	0	0	0
聴力低下	0	0	0	0	1 (0.2) [0.2]
メニエール病	0	0	0	0	1 (0.2) [0.2]
中耳滲出液	1 (0.7) [0.8]	0	0	0	0
耳漏	0	0	0	0	1 (0.2) [0.2]
耳鳴	0	0	0	0	1 (0.2) [0.2]
回転性めまい	0	2 (1.0) [1.0]	0	4 (1.0) [1.0]	2 (0.5) [0.4]
内分泌障害	1 (0.7) [0.7]	1 (0.5) [0.5]	0	1 (0.2) [0.3]	2 (0.5) [0.5]
クッシング症候群	1 (0.7) [0.7]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
内分泌障害 (Cont.)					
甲状腺腫	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
続発性副腎皮質機能不全	0	0	0	0	1 (0.2) [0.2]
甲状腺腫瘤	0	0	0	0	1 (0.2) [0.2]
眼障害	12 (8.9) [9.0]	10 (5.0) [4.9]	11 (5.0) [5.0]	16 (3.9) [3.7]	17 (4.0) [4.2]
無水晶体眼	0	0	0	0	1 (0.2) [0.2]
眼瞼炎	1 (0.7) [0.8]	0	2 (0.9) [0.9]	0	2 (0.5) [0.6]
白内障	1 (0.7) [0.8]	3 (1.5) [1.4]	2 (0.9) [0.9]	5 (1.2) [1.2]	3 (0.7) [0.7]
霰粒腫	0	0	3 (1.4) [1.4]	0	3 (0.7) [0.7]
結膜充血	1 (0.7) [0.7]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
眼障害 (Cont.)					
アレルギー性結膜炎	1 (0.7) [0.8]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	2 (0.5) [0.4]
角膜浮腫	0	0	0	0	1 (0.2) [0.2]
角膜混濁	1 (0.7) [0.8]	0	0	0	0
ドライアイ	0	1 (0.5) [0.5]	1 (0.5) [0.4]	1 (0.2) [0.2]	2 (0.5) [0.6]
上強膜炎	1 (0.7) [0.8]	0	0	0	0
眼刺激	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
眼そう痒症	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
眼部腫脹	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
眼瞼障害	1 (0.7) [0.7]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
眼障害 (Cont.)					
眼瞼発疹	1 (0.7) [0.7]	0	0	0	0
緑内障	0	0	0	0	1 (0.2) [0.2]
角膜炎	1 (0.7) [0.7]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
流涙増加	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
黄斑浮腫	0	0	0	1 (0.2) [0.3]	0
近視	0	0	0	1 (0.2) [0.2]	0
眼充血	0	1 (0.5) [0.5]	1 (0.5) [0.4]	1 (0.2) [0.3]	1 (0.2) [0.4]
眼窩周囲腫脹	1 (0.7) [0.8]	0	0	0	0
網膜静脈閉塞	0	0	0	1 (0.2) [0.3]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
眼障害 (Cont.)					
潰瘍性角膜炎	1 (0.7) [0.7]	0	0	0	0
ぶどう膜炎	1 (0.7) [0.8]	0	0	0	0
硝子体浮遊物	0	0	0	1 (0.2) [0.2]	0
胃腸障害	152 (112.6) [111.3]	90 (45.1) [45.0]	89 (40.7) [40.5]	164 (39.6) [40.0]	146 (34.3) [36.3]
腹部膨満	1 (0.7) [0.7]	2 (1.0) [1.0]	5 (2.3) [2.3]	2 (0.5) [0.5]	6 (1.4) [1.5]
腹部腫瘤	1 (0.7) [0.8]	0	0	0	0
腹痛	6 (4.4) [4.7]	7 (3.5) [3.5]	4 (1.8) [1.8]	11 (2.7) [2.6]	7 (1.6) [1.9]
下腹部痛	4 (3.0) [2.8]	0	0	1 (0.2) [0.2]	0
上腹部痛	2 (1.5) [1.5]	4 (2.0) [2.1]	2 (0.9) [0.9]	6 (1.4) [1.6]	4 (0.9) [1.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
腹部圧痛	0	0	2 (0.9) [0.9]	1 (0.2) [0.2]	3 (0.7) [0.8]
異常便	1 (0.7) [0.7]	0	0	0	0
裂肛	1 (0.7) [0.7]	0	0	1 (0.2) [0.3]	0
痔瘻	0	0	3 (1.4) [1.4]	1 (0.2) [0.3]	4 (0.9) [0.9]
肛門の炎症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
肛門ポリープ	0	0	0	0	1 (0.2) [0.2]
肛門そう痒症	2 (1.5) [1.5]	0	0	0	0
アフタ性潰瘍	2 (1.5) [1.6]	1 (0.5) [0.5]	3 (1.4) [1.4]	1 (0.2) [0.2]	4 (0.9) [0.9]
大腸炎	3 (2.2) [2.1]	2 (1.0) [0.9]	0	2 (0.5) [0.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
虚血性大腸炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
潰瘍性大腸炎	81 (60.0) [58.7]	37 (18.6) [18.6]	21 (9.6) [9.6]	65 (15.7) [16.2]	36 (8.5) [9.1]
結腸異形成	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	2 (0.5) [0.4]
便秘	2 (1.5) [1.3]	4 (2.0) [2.1]	6 (2.7) [2.7]	7 (1.7) [1.8]	10 (2.4) [2.3]
便意切迫	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
齲歯	1 (0.7) [0.7]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	2 (0.5) [0.5]
歯嚢胞	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
下痢	2 (1.5) [1.3]	2 (1.0) [1.1]	2 (0.9) [0.9]	5 (1.2) [1.2]	2 (0.5) [0.6]
口内乾燥	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
消化不良	3 (2.2) [2.0]	1 (0.5) [0.5]	1 (0.5) [0.5]	2 (0.5) [0.4]	2 (0.5) [0.5]
嚥下障害	1 (0.7) [0.7]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
小腸炎	0	1 (0.5) [0.5]	2 (0.9) [0.9]	1 (0.2) [0.3]	2 (0.5) [0.6]
腸炎	0	0	0	0	2 (0.5) [0.4]
変色便	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
大腿ヘルニア	1 (0.7) [0.7]	0	0	0	0
鼓腸	3 (2.2) [2.2]	0	2 (0.9) [0.9]	1 (0.2) [0.2]	2 (0.5) [0.6]
胃潰瘍	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
胃炎	0	3 (1.5) [1.5]	1 (0.5) [0.5]	3 (0.7) [0.7]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
消化器痛	0	0	0	1 (0.2) [0.3]	0
胃食道逆流性疾患	3 (2.2) [2.1]	1 (0.5) [0.5]	3 (1.4) [1.4]	3 (0.7) [0.8]	3 (0.7) [0.8]
歯肉腫脹	1 (0.7) [0.8]	0	0	0	0
舌痛	1 (0.7) [0.8]	0	0	0	0
血便排泄	1 (0.7) [0.8]	0	0	0	0
痔出血	2 (1.5) [1.3]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
痔核	1 (0.7) [0.7]	4 (2.0) [1.9]	2 (0.9) [0.9]	8 (1.9) [2.0]	4 (0.9) [1.0]
血栓性痔核	1 (0.7) [0.8]	0	0	0	0
鼠径ヘルニア	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
腸閉塞	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
腸管ポリープ	0	0	0	1 (0.2) [0.2]	0
過敏性腸症候群	0	0	1 (0.5) [0.4]	2 (0.5) [0.4]	1 (0.2) [0.4]
大腸穿孔	1 (0.7) [0.8]	0	0	0	0
大腸ポリープ	2 (1.5) [1.5]	0	1 (0.5) [0.5]	2 (0.5) [0.4]	5 (1.2) [1.1]
口唇障害	0	0	0	1 (0.2) [0.3]	0
口唇腫脹	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
口腔嚢胞	1 (0.7) [0.8]	0	0	0	0
口腔内潰瘍形成	2 (1.5) [1.6]	0	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
粘液便	1 (0.7) [0.8]	0	0	0	0
悪心	6 (4.4) [4.7]	4 (2.0) [1.9]	5 (2.3) [2.3]	12 (2.9) [2.7]	7 (1.6) [1.7]
非感染性歯肉炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
嚥下痛	1 (0.7) [0.7]	0	0	0	2 (0.5) [0.4]
食道炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
口腔障害	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
膵炎	1 (0.7) [0.8]	0	0	0	0
歯周病	1 (0.7) [0.8]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
肛門周囲痛	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
直腸炎	1 (0.7) [0.7]	0	0	0	0
直腸分泌物	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
直腸異形成	0	0	0	2 (0.5) [0.5]	0
直腸出血	1 (0.7) [0.8]	0	2 (0.9) [0.9]	1 (0.2) [0.2]	2 (0.5) [0.7]
直腸ポリープ	0	0	0	0	1 (0.2) [0.2]
直腸攣縮	1 (0.7) [0.8]	0	0	0	0
直腸しぶり	1 (0.7) [0.8]	0	0	0	0
口内炎	3 (2.2) [2.3]	1 (0.5) [0.5]	4 (1.8) [1.8]	1 (0.2) [0.2]	4 (0.9) [0.9]
埋伏歯	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
歯の脱落	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
歯痛	0	4 (2.0) [2.0]	3 (1.4) [1.4]	7 (1.7) [1.8]	7 (1.6) [1.6]
臍ヘルニア	1 (0.7) [0.8]	0	0	0	1 (0.2) [0.2]
嘔吐	1 (0.7) [0.8]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	4 (0.9) [0.9]
一般・全身障害および投与部位の状態	29 (21.5) [21.8]	22 (11.0) [11.0]	38 (17.4) [17.3]	71 (17.2) [16.8]	73 (17.2) [18.0]
無力症	0	0	0	1 (0.2) [0.3]	0
胸部不快感	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
胸痛	1 (0.7) [0.7]	3 (1.5) [1.5]	2 (0.9) [0.9]	3 (0.7) [0.8]	4 (0.9) [1.0]
悪寒	2 (1.5) [1.5]	2 (1.0) [1.0]	0	4 (1.0) [0.8]	2 (0.5) [0.6]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)					
医療機器に対する不耐性	1 (0.7) [0.8]	0	0	0	0
薬効欠如	1 (0.7) [0.8]	0	0	0	0
異形成	0	0	0	1 (0.2) [0.3]	1 (0.2) [0.2]
疲労	5 (3.7) [3.9]	2 (1.0) [1.0]	4 (1.8) [1.8]	14 (3.4) [3.1]	10 (2.4) [2.2]
全身性浮腫	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
高体温症	1 (0.7) [0.8]	0	0	0	0
炎症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
インフルエンザ様疾患	1 (0.7) [0.8]	0	2 (0.9) [0.9]	2 (0.5) [0.4]	2 (0.5) [0.4]
注射部位疼痛	0	1 (0.5) [0.5]	4 (1.8) [1.8]	14 (3.4) [3.4]	13 (3.1) [2.9]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)					
倦怠感	1 (0.7) [0.7]	0	2 (0.9) [0.9]	5 (1.2) [1.3]	2 (0.5) [0.5]
腫瘤	0	0	2 (0.9) [0.9]	0	2 (0.5) [0.7]
粘膜乾燥	1 (0.7) [0.8]	0	0	0	0
小結節	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
非心臓性胸痛	1 (0.7) [0.8]	0	0	0	0
浮腫	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
末梢性浮腫	3 (2.2) [2.1]	1 (0.5) [0.5]	1 (0.5) [0.4]	2 (0.5) [0.4]	1 (0.2) [0.4]
疼痛	1 (0.7) [0.7]	1 (0.5) [0.5]	0	3 (0.7) [0.6]	2 (0.5) [0.4]
末梢腫脹	1 (0.7) [0.7]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	2 (0.5) [0.6]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)					
発熱	8 (5.9) [6.0]	8 (4.0) [4.0]	16 (7.3) [7.3]	17 (4.1) [4.3]	27 (6.4) [6.9]
異物感	1 (0.7) [0.8]	0	0	0	0
腫脹	0	0	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
顔面腫脹	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
ワクチン接種部位疼痛	0	0	0	0	1 (0.2) [0.2]
肝胆道系障害	4 (3.0) [2.9]	7 (3.5) [3.4]	2 (0.9) [0.9]	14 (3.4) [3.4]	3 (0.7) [0.8]
胆道ジスキネジア	0	0	0	1 (0.2) [0.2]	0
硬化性胆管炎	0	0	0	3 (0.7) [0.7]	0
薬物性肝障害	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
肝胆道系障害 (Cont.)					
肝機能異常	3 (2.2) [2.1]	2 (1.0) [0.9]	0	3 (0.7) [0.7]	1 (0.2) [0.2]
脂肪肝	0	2 (1.0) [1.0]	0	4 (1.0) [1.0]	0
高トランスアミナーゼ血症	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
肝障害	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
肝損傷	1 (0.7) [0.8]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
免疫系障害	1 (0.7) [0.8]	2 (1.0) [0.9]	1 (0.5) [0.5]	2 (0.5) [0.5]	2 (0.5) [0.4]
アナフィラキシー反応	0	0	0	0	1 (0.2) [0.2]
薬物過敏症	1 (0.7) [0.8]	0	0	0	0
季節性アレルギー	0	2 (1.0) [0.9]	1 (0.5) [0.5]	2 (0.5) [0.5]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症	126 (93.4) [92.6]	162 (81.2) [81.1]	183 (83.8) [83.7]	267 (64.5) [64.7]	310 (72.9) [74.2]
腹部膿瘍	1 (0.7) [0.8]	0	0	0	0
腹壁膿瘍	0	0	0	1 (0.2) [0.2]	0
ダニ皮膚炎	0	2 (1.0) [0.9]	0	2 (0.5) [0.5]	0
急性心内膜炎	1 (0.7) [0.7]	0	0	0	0
肛門膿瘍	0	2 (1.0) [0.9]	0	3 (0.7) [0.7]	2 (0.5) [0.4]
肛門直腸感染	2 (1.5) [1.3]	0	0	0	0
虫垂炎	0	0	0	1 (0.2) [0.3]	1 (0.2) [0.2]
細菌性関節炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
無症候性COVID-19	0	0	0	1 (0.2) [0.3]	2 (0.5) [0.5]
細菌感染	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
細菌性膣症	1 (0.7) [0.8]	0	0	0	0
ブラストシスティス感染	0	0	0	1 (0.2) [0.3]	0
乳房膿瘍	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
気管支炎	3 (2.2) [2.1]	6 (3.0) [2.9]	1 (0.5) [0.5]	7 (1.7) [1.7]	3 (0.7) [0.7]
感染性滑液包炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
COVID-19	8 (5.9) [6.4]	5 (2.5) [2.5]	11 (5.0) [5.0]	16 (3.9) [4.0]	30 (7.1) [6.8]
COVID-19肺炎	1 (0.7) [0.8]	1 (0.5) [0.5]	2 (0.9) [0.9]	5 (1.2) [1.3]	6 (1.4) [1.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
カンピロバクター胃腸炎	0	0	0	1 (0.2) [0.3]	1 (0.2) [0.2]
カンピロバクター感染	0	1 (0.5) [0.5]	0	3 (0.7) [0.7]	0
カンジダ感染	1 (0.7) [0.8]	0	0	1 (0.2) [0.2]	0
蜂巣炎	0	1 (0.5) [0.5]	0	4 (1.0) [1.0]	2 (0.5) [0.5]
クロストリジウム・ディフィシレ大腸炎	0	0	0	1 (0.2) [0.3]	0
クロストリジウム・ディフィシレ感染	2 (1.5) [1.5]	1 (0.5) [0.5]	2 (0.9) [0.9]	3 (0.7) [0.8]	4 (0.9) [1.2]
結膜炎	0	2 (1.0) [0.9]	1 (0.5) [0.5]	4 (1.0) [0.9]	2 (0.5) [0.4]
コロナウイルス感染	0	0	0	1 (0.2) [0.3]	0
膀胱炎	0	3 (1.5) [1.6]	3 (1.4) [1.4]	10 (2.4) [2.4]	4 (0.9) [0.9]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
サイトメガロウイルス性大腸炎	0	0	0	0	1 (0.2) [0.2]
サイトメガロウイルス感染	1 (0.7) [0.8]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
毛嚢虫症	0	3 (1.5) [1.4]	2 (0.9) [0.9]	3 (0.7) [0.7]	4 (0.9) [0.9]
皮膚糸状菌症	1 (0.7) [0.8]	0	0	0	0
爪の皮膚糸状菌症	0	0	0	0	1 (0.2) [0.2]
憩室炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
耳感染	0	1 (0.5) [0.5]	2 (0.9) [0.9]	3 (0.7) [0.7]	3 (0.7) [0.6]
感染性腸炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
エンテロウイルス感染	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
大腸菌性尿路感染	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
眼感染	0	0	0	1 (0.2) [0.3]	0
毛包炎	4 (3.0) [3.0]	4 (2.0) [2.1]	10 (4.6) [4.6]	4 (1.0) [1.0]	13 (3.1) [3.1]
真菌感染	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
皮膚真菌感染	0	0	2 (0.9) [0.9]	0	2 (0.5) [0.4]
せつ	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	1 (0.2) [0.4]
胃腸炎	4 (3.0) [3.0]	5 (2.5) [2.6]	3 (1.4) [1.4]	5 (1.2) [1.3]	9 (2.1) [2.0]
ウイルス性胃腸炎	0	0	2 (0.9) [0.9]	2 (0.5) [0.4]	4 (0.9) [1.0]
陰部単純ヘルペス	0	0	0	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
歯肉膿瘍	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
歯肉炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	1 (0.2) [0.2]
単径部膿瘍	0	0	0	1 (0.2) [0.2]	0
ヘモフィルス感染	1 (0.7) [0.7]	0	0	0	0
手足口病	0	0	0	0	1 (0.2) [0.2]
ヘリコバクター感染	0	0	0	1 (0.2) [0.2]	0
ヘルペス性皮膚炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
ヘルペス眼感染	0	0	0	0	1 (0.2) [0.2]
単純ヘルペス	0	2 (1.0) [0.9]	1 (0.5) [0.5]	2 (0.5) [0.5]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
帯状疱疹	0	11 (5.5) [5.4]	15 (6.9) [6.9]	20 (4.8) [4.8]	26 (6.1) [6.0]
帯状疱疹性髄膜炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
耳帯状疱疹	0	0	0	1 (0.2) [0.3]	0
麦粒腫	3 (2.2) [2.2]	0	2 (0.9) [0.9]	2 (0.5) [0.4]	2 (0.5) [0.4]
膿痂疹	1 (0.7) [0.8]	1 (0.5) [0.5]	0	2 (0.5) [0.4]	0
咬傷感染	0	0	0	0	1 (0.2) [0.2]
感染性皮膚嚢腫	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
インフルエンザ	3 (2.2) [2.2]	7 (3.5) [3.6]	10 (4.6) [4.6]	10 (2.4) [2.3]	12 (2.8) [2.9]
大腸感染	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
喉頭炎	1 (0.7) [0.8]	0	1 (0.5) [0.5]	0	2 (0.5) [0.4]
潜伏結核	0	0	2 (0.9) [0.9]	1 (0.2) [0.2]	4 (0.9) [0.9]
下気道感染	1 (0.7) [0.7]	1 (0.5) [0.5]	0	2 (0.5) [0.4]	0
乳腺炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
伝染性軟属腫	1 (0.7) [0.7]	0	0	0	0
上咽頭炎	21 (15.6) [14.8]	32 (16.0) [16.6]	38 (17.4) [17.4]	44 (10.6) [10.8]	48 (11.3) [11.5]
食道カンジダ症	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
爪真菌症	2 (1.5) [1.5]	1 (0.5) [0.5]	1 (0.5) [0.5]	2 (0.5) [0.5]	1 (0.2) [0.2]
口腔カンジダ症	2 (1.5) [1.6]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	2 (0.5) [0.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	4 (3.0) [3.1]	7 (3.5) [3.4]	8 (3.7) [3.6]	7 (1.7) [1.7]	18 (4.2) [4.8]
外耳炎	1 (0.7) [0.8]	0	0	1 (0.2) [0.2]	0
乳頭腫ウイルス感染	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
爪囲炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	1 (0.2) [0.2]
歯周炎	1 (0.7) [0.8]	0	2 (0.9) [0.9]	0	4 (0.9) [0.9]
扁桃周囲炎	0	0	0	1 (0.2) [0.2]	0
咽頭炎	4 (3.0) [2.9]	2 (1.0) [1.0]	1 (0.5) [0.5]	2 (0.5) [0.5]	3 (0.7) [0.8]
レンサ球菌性咽頭炎	1 (0.7) [0.7]	2 (1.0) [1.0]	1 (0.5) [0.5]	2 (0.5) [0.4]	1 (0.2) [0.2]
毛巣嚢胞	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
胸膜感染	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
ニューモシスチス・イロベチイ肺炎	1 (0.7) [0.8]	0	0	0	0
肺炎	4 (3.0) [2.8]	1 (0.5) [0.5]	2 (0.9) [0.9]	1 (0.2) [0.2]	3 (0.7) [0.7]
クリプトコッカス性肺炎	0	0	2 (0.9) [0.9]	0	2 (0.5) [0.5]
ウイルス性肺炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
歯髄炎	0	1 (0.5) [0.5]	1 (0.5) [0.5]	2 (0.5) [0.4]	1 (0.2) [0.2]
膿疱	1 (0.7) [0.8]	0	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]
腎盂腎炎	1 (0.7) [0.7]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
膿皮症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
ウイルス性気道感染	1 (0.7) [0.7]	4 (2.0) [2.0]	0	6 (1.4) [1.5]	1 (0.2) [0.2]
鼻炎	3 (2.2) [2.1]	1 (0.5) [0.5]	2 (0.9) [0.9]	1 (0.2) [0.2]	2 (0.5) [0.4]
セラチア感染	1 (0.7) [0.7]	0	0	0	0
副鼻腔炎	4 (3.0) [3.1]	2 (1.0) [1.0]	3 (1.4) [1.3]	6 (1.4) [1.6]	6 (1.4) [1.6]
ブドウ球菌感染	1 (0.7) [0.7]	0	0	0	0
皮下組織膿瘍	0	0	0	0	1 (0.2) [0.2]
股部白癬	0	0	0	0	1 (0.2) [0.2]
白癬感染	2 (1.5) [1.5]	0	0	0	1 (0.2) [0.4]
足部白癬	2 (1.5) [1.3]	3 (1.5) [1.6]	1 (0.5) [0.5]	4 (1.0) [1.0]	3 (0.7) [0.6]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
癜風	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
扁桃炎	1 (0.7) [0.7]	2 (1.0) [0.9]	3 (1.4) [1.4]	4 (1.0) [1.0]	3 (0.7) [0.7]
細菌性扁桃炎	0	0	0	0	1 (0.2) [0.2]
歯膿瘍	0	1 (0.5) [0.5]	1 (0.5) [0.5]	2 (0.5) [0.5]	1 (0.2) [0.2]
歯感染	3 (2.2) [2.3]	0	3 (1.4) [1.4]	1 (0.2) [0.3]	3 (0.7) [0.8]
トリコモナス症	1 (0.7) [0.8]	0	0	0	0
上気道感染	9 (6.7) [6.1]	13 (6.5) [6.5]	14 (6.4) [6.4]	17 (4.1) [4.0]	15 (3.5) [3.6]
尿路感染	7 (5.2) [5.5]	10 (5.0) [5.1]	4 (1.8) [1.8]	16 (3.9) [3.7]	9 (2.1) [2.4]
ガードネレラ菌性腟炎	0	0	0	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
水痘帯状疱疹ウイルス感染	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
ウイルス血症	1 (0.7) [0.7]	0	0	0	0
ウイルス感染	0	1 (0.5) [0.5]	2 (0.9) [0.9]	1 (0.2) [0.2]	2 (0.5) [0.6]
ウイルス性咽頭炎	0	0	0	1 (0.2) [0.3]	0
ウイルス性上気道感染	4 (3.0) [2.8]	1 (0.5) [0.5]	4 (1.8) [1.8]	1 (0.2) [0.3]	5 (1.2) [1.2]
外陰部腟カンジダ症	1 (0.7) [0.8]	1 (0.5) [0.5]	2 (0.9) [0.9]	1 (0.2) [0.2]	7 (1.6) [1.9]
外陰腟真菌感染	1 (0.7) [0.8]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
創傷感染	0	0	0	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症	13 (9.6) [9.3]	14 (7.0) [6.9]	12 (5.5) [5.5]	30 (7.2) [7.0]	19 (4.5) [4.3]
動物による引っかき傷	1 (0.7) [0.8]	0	0	0	0
足関節部骨折	0	0	0	1 (0.2) [0.2]	1 (0.2) [0.2]
節足動物咬傷	0	0	0	1 (0.2) [0.2]	1 (0.2) [0.2]
骨挫傷	1 (0.7) [0.7]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
挫傷	0	0	3 (1.4) [1.4]	2 (0.5) [0.4]	4 (0.9) [0.9]
毒性物質曝露	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
眼外傷	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
転倒	0	0	0	0	1 (0.2) [0.2]
足骨折	0	0	0	2 (0.5) [0.4]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)					
仙骨骨折	0	0	0	1 (0.2) [0.2]	0
熱中症	1 (0.7) [0.7]	0	0	0	0
熱射病	0	0	0	1 (0.2) [0.3]	0
損傷	1 (0.7) [0.8]	0	0	0	0
関節損傷	0	2 (1.0) [1.0]	0	3 (0.7) [0.6]	0
靭帯断裂	0	0	0	1 (0.2) [0.2]	0
靭帯捻挫	1 (0.7) [0.7]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]
四肢損傷	1 (0.7) [0.8]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	1 (0.2) [0.2]
四肢外傷性切断	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)					
腰椎骨折	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
筋断裂	0	0	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]
肉離れ	1 (0.7) [0.7]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
過量投与	0	0	0	2 (0.5) [0.4]	0
処置後出血	0	0	0	0	1 (0.2) [0.2]
外傷後疼痛	0	2 (1.0) [1.0]	0	2 (0.5) [0.4]	0
肺挫傷	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
肋骨骨折	1 (0.7) [0.7]	0	0	0	0
交通事故	1 (0.7) [0.8]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)					
皮膚裂傷	1 (0.7) [0.7]	3 (1.5) [1.5]	0	3 (0.7) [0.8]	0
脊椎圧迫骨折	1 (0.7) [0.8]	0	0	0	0
スポーツ損傷	0	0	0	1 (0.2) [0.3]	0
ストレス骨折	0	0	0	1 (0.2) [0.2]	0
皮下血腫	1 (0.7) [0.7]	0	0	0	0
胸椎骨折	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
脛骨骨折	0	0	0	1 (0.2) [0.3]	0
歯牙破折	1 (0.7) [0.7]	0	2 (0.9) [0.9]	0	2 (0.5) [0.5]
創傷	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)					
手首関節骨折	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
臨床検査	29 (21.5) [21.3]	102 (51.1) [51.5]	104 (47.6) [47.6]	154 (37.2) [37.1]	184 (43.3) [44.3]
アラニンアミノトランスフェラーゼ増加	1 (0.7) [0.7]	9 (4.5) [4.7]	7 (3.2) [3.2]	12 (2.9) [3.0]	12 (2.8) [2.7]
アミラーゼ増加	1 (0.7) [0.8]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
抗核抗体増加	1 (0.7) [0.7]	0	0	0	0
大動脈雑音	0	0	0	0	1 (0.2) [0.2]
アスパラギン酸アミノトランスフェラーゼ増加	2 (1.5) [1.5]	9 (4.5) [4.8]	5 (2.3) [2.3]	10 (2.4) [2.6]	10 (2.4) [2.2]
細菌検査陽性	0	0	0	1 (0.2) [0.2]	0
血中アルブミン減少	0	2 (1.0) [0.9]	0	2 (0.5) [0.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
血中アルブミン増加	0	1 (0.5) [0.5]	1 (0.5) [0.4]	1 (0.2) [0.3]	1 (0.2) [0.4]
血中アルカリホスファターゼ増加	0	0	0	0	1 (0.2) [0.2]
血中重炭酸塩減少	0	0	0	1 (0.2) [0.2]	0
血中ビリルビン増加	0	3 (1.5) [1.5]	3 (1.4) [1.4]	3 (0.7) [0.8]	5 (1.2) [1.2]
血中カルシウム増加	0	1 (0.5) [0.5]	0	2 (0.5) [0.4]	0
血中コレステロール減少	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
血中コレステロール増加	0	2 (1.0) [1.0]	6 (2.7) [2.7]	2 (0.5) [0.4]	8 (1.9) [1.9]
血中クレアチンホスホキナーゼ増加	5 (3.7) [3.9]	16 (8.0) [8.1]	22 (10.1) [10.1]	24 (5.8) [5.8]	41 (9.6) [9.2]
血中クレアチニン増加	2 (1.5) [1.3]	0	4 (1.8) [1.8]	0	4 (0.9) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
血中葉酸減少	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
血中ブドウ糖減少	0	0	0	0	1 (0.2) [0.2]
血中ブドウ糖増加	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
血中鉄減少	0	0	0	1 (0.2) [0.2]	1 (0.2) [0.2]
血中リン減少	0	0	0	0	2 (0.5) [0.6]
血中カリウム減少	0	2 (1.0) [1.0]	0	2 (0.5) [0.4]	0
血中カリウム増加	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
血圧上昇	0	0	0	1 (0.2) [0.2]	1 (0.2) [0.2]
血中ナトリウム増加	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
血中トリグリセリド異常	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
血中トリグリセリド増加	0	0	0	0	1 (0.2) [0.2]
尿中血陽性	0	0	2 (0.9) [0.9]	0	4 (0.9) [0.9]
体温上昇	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
骨密度減少	0	0	0	1 (0.2) [0.2]	0
炭水化物耐性低下	0	0	0	0	1 (0.2) [0.2]
γ-グルタミルトランスフェラーゼ増加	1 (0.7) [0.8]	5 (2.5) [2.6]	1 (0.5) [0.5]	10 (2.4) [2.6]	4 (0.9) [0.9]
糸球体濾過率減少	1 (0.7) [0.7]	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
尿中ブドウ糖陽性	0	0	0	1 (0.2) [0.3]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
顆粒球数減少	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
握力低下	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
ヘマトクリット減少	0	0	0	1 (0.2) [0.2]	0
ヘモグロビン減少	1 (0.7) [0.8]	2 (1.0) [0.9]	1 (0.5) [0.5]	4 (1.0) [0.9]	5 (1.2) [1.2]
尿中ヘモグロビン陽性	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
肝酵素上昇	0	1 (0.5) [0.5]	1 (0.5) [0.5]	2 (0.5) [0.4]	2 (0.5) [0.4]
B型肝炎DNA測定陽性	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
高比重リポ蛋白増加	0	3 (1.5) [1.5]	1 (0.5) [0.4]	4 (1.0) [0.9]	1 (0.2) [0.4]
リパーゼ増加	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
肝機能検査値上昇	0	0	1 (0.5) [0.5]	0	2 (0.5) [0.4]
低比重リポ蛋白減少	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
低比重リポ蛋白増加	0	1 (0.5) [0.5]	6 (2.7) [2.7]	1 (0.2) [0.2]	6 (1.4) [1.6]
リンパ球数減少	2 (1.5) [1.4]	5 (2.5) [2.5]	5 (2.3) [2.3]	8 (1.9) [1.8]	8 (1.9) [2.3]
リンパ球数増加	1 (0.7) [0.8]	1 (0.5) [0.5]	2 (0.9) [0.9]	1 (0.2) [0.2]	2 (0.5) [0.6]
リンパ球百分率減少	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
リンパ球百分率増加	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
平均赤血球容積異常	0	0	0	0	1 (0.2) [0.2]
平均赤血球容積増加	0	0	0	1 (0.2) [0.3]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
単球数増加	0	1 (0.5) [0.5]	0	2 (0.5) [0.5]	0
好中球数減少	4 (3.0) [3.0]	5 (2.5) [2.5]	12 (5.5) [5.5]	10 (2.4) [2.4]	19 (4.5) [4.4]
好中球数増加	2 (1.5) [1.4]	2 (1.0) [1.0]	2 (0.9) [0.9]	4 (1.0) [0.9]	3 (0.7) [0.8]
好中球百分率増加	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
血小板数減少	1 (0.7) [0.7]	0	0	0	0
血小板数増加	0	0	2 (0.9) [0.9]	0	3 (0.7) [0.9]
プレアルブミン減少	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
前立腺特異性抗原増加	0	0	0	1 (0.2) [0.3]	0
総蛋白減少	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
総蛋白増加	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
尿中蛋白陽性	1 (0.7) [0.8]	2 (1.0) [1.1]	1 (0.5) [0.4]	3 (0.7) [0.8]	2 (0.5) [0.6]
赤血球数減少	0	1 (0.5) [0.5]	2 (0.9) [0.9]	2 (0.5) [0.4]	4 (0.9) [1.0]
血沈亢進	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
網状赤血球数減少	0	0	0	1 (0.2) [0.3]	0
ブドウ球菌検査陽性	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
トランスアミナーゼ上昇	0	0	0	1 (0.2) [0.3]	1 (0.2) [0.2]
尿検査異常	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
尿中ケトン体陽性	0	0	0	0	1 (0.2) [0.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
尿中白血球エステラーゼ陽性	0	0	0	2 (0.5) [0.4]	0
ビタミンD減少	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	1 (0.2) [0.2]
体重増加	0	1 (0.5) [0.5]	2 (0.9) [0.9]	2 (0.5) [0.5]	3 (0.7) [0.7]
白血球数減少	3 (2.2) [2.1]	5 (2.5) [2.5]	6 (2.7) [2.7]	8 (1.9) [1.9]	11 (2.6) [2.7]
白血球数増加	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]
尿中白血球陽性	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	1 (0.2) [0.4]
代謝および栄養障害	16 (11.9) [11.5]	18 (9.0) [9.3]	15 (6.9) [6.9]	32 (7.7) [8.0]	30 (7.1) [7.2]
食欲減退	1 (0.7) [0.7]	0	0	2 (0.5) [0.5]	1 (0.2) [0.2]
糖尿病	0	0	0	0	2 (0.5) [0.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
代謝および栄養障害 (Cont.)					
脂質異常症	0	4 (2.0) [2.0]	1 (0.5) [0.5]	4 (1.0) [0.9]	2 (0.5) [0.4]
葉酸欠乏	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
耐糖能障害	1 (0.7) [0.7]	0	0	0	0
痛風	0	2 (1.0) [1.1]	0	2 (0.5) [0.5]	0
高カルシウム血症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
高コレステロール血症	2 (1.5) [1.3]	4 (2.0) [2.2]	4 (1.8) [1.9]	6 (1.4) [1.6]	9 (2.1) [2.1]
高血糖	1 (0.7) [0.8]	3 (1.5) [1.6]	0	5 (1.2) [1.3]	1 (0.2) [0.2]
高リパーゼ血症	1 (0.7) [0.8]	0	0	0	0
高脂血症	0	1 (0.5) [0.5]	2 (0.9) [0.9]	5 (1.2) [1.2]	3 (0.7) [0.9]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
代謝および栄養障害 (Cont.)					
高ナトリウム血症	0	0	0	0	1 (0.2) [0.2]
高尿酸血症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
低カリウム血症	3 (2.2) [2.1]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
低ナトリウム血症	2 (1.5) [1.6]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
低リン酸血症	1 (0.7) [0.8]	0	0	0	0
鉄欠乏	1 (0.7) [0.7]	0	1 (0.5) [0.4]	1 (0.2) [0.2]	1 (0.2) [0.4]
代謝症候群	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
肥満	0	0	0	0	1 (0.2) [0.2]
2型糖尿病	1 (0.7) [0.7]	0	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
代謝および栄養障害 (Cont.)					
過少体重	0	0	0	1 (0.2) [0.2]	0
ビタミンD欠乏	2 (1.5) [1.3]	3 (1.5) [1.5]	2 (0.9) [0.9]	4 (1.0) [1.0]	4 (0.9) [0.9]
筋骨格系および結合組織障害	78 (57.8) [56.7]	42 (21.1) [21.3]	35 (16.0) [16.0]	97 (23.4) [23.3]	67 (15.8) [17.2]
強直性脊椎炎	1 (0.7) [0.7]	0	0	0	0
関節痛	25 (18.5) [18.7]	13 (6.5) [6.6]	8 (3.7) [3.6]	27 (6.5) [6.6]	19 (4.5) [5.1]
関節炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
腸炎性関節炎	3 (2.2) [2.0]	0	0	0	0
関節障害	7 (5.2) [5.1]	1 (0.5) [0.5]	3 (1.4) [1.4]	4 (1.0) [1.1]	3 (0.7) [0.7]
背部痛	10 (7.4) [7.4]	7 (3.5) [3.7]	1 (0.5) [0.5]	13 (3.1) [3.3]	5 (1.2) [1.3]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
骨痛	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
滑液包炎	0	0	1 (0.5) [0.5]	0	2 (0.5) [0.6]
軟骨萎縮	0	0	0	1 (0.2) [0.2]	0
頚部脊柱管狭窄症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
軟骨軟化症	0	0	2 (0.9) [0.9]	0	2 (0.5) [0.5]
ばち状指	0	0	0	1 (0.2) [0.2]	0
尾骨痛	1 (0.7) [0.7]	0	0	0	0
肋軟骨炎	2 (1.5) [1.5]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
外骨腫	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
四肢拘縮	0	0	0	1 (0.2) [0.3]	0
線維筋痛	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
側腹部痛	1 (0.7) [0.7]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
出血性関節症	1 (0.7) [0.8]	0	0	0	0
椎間板変性症	1 (0.7) [0.8]	0	0	0	0
椎間板突出	0	0	0	2 (0.5) [0.5]	2 (0.5) [0.6]
関節滲出液	0	0	0	1 (0.2) [0.2]	0
関節硬直	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
関節腫脹	0	2 (1.0) [1.0]	1 (0.5) [0.5]	2 (0.5) [0.4]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
腰部脊柱管狭窄症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
筋拘縮	0	0	0	1 (0.2) [0.3]	0
筋痙縮	0	0	0	1 (0.2) [0.2]	1 (0.2) [0.2]
筋力低下	1 (0.7) [0.7]	0	0	0	0
筋骨格系胸痛	3 (2.2) [2.1]	1 (0.5) [0.5]	0	2 (0.5) [0.5]	0
筋骨格痛	3 (2.2) [2.1]	2 (1.0) [1.0]	1 (0.5) [0.5]	3 (0.7) [0.7]	1 (0.2) [0.2]
筋骨格硬直	1 (0.7) [0.7]	0	0	1 (0.2) [0.2]	0
筋肉痛	2 (1.5) [1.3]	2 (1.0) [1.0]	1 (0.5) [0.5]	10 (2.4) [2.4]	6 (1.4) [1.5]
筋炎	1 (0.7) [0.7]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
頚部痛	1 (0.7) [0.8]	2 (1.0) [1.1]	2 (0.9) [0.9]	3 (0.7) [0.8]	2 (0.5) [0.5]
骨炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
変形性関節症	2 (1.5) [1.3]	0	0	3 (0.7) [0.7]	0
骨壊死	0	1 (0.5) [0.5]	0	2 (0.5) [0.5]	0
骨減少症	0	1 (0.5) [0.5]	2 (0.9) [0.9]	1 (0.2) [0.2]	2 (0.5) [0.6]
骨粗鬆症	1 (0.7) [0.8]	1 (0.5) [0.5]	1 (0.5) [0.5]	2 (0.5) [0.4]	1 (0.2) [0.2]
四肢痛	4 (3.0) [2.6]	1 (0.5) [0.5]	3 (1.4) [1.4]	3 (0.7) [0.8]	9 (2.1) [2.5]
関節周囲炎	0	0	2 (0.9) [0.9]	0	2 (0.5) [0.4]
足底筋膜炎	0	0	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
肩回旋筋腱板症候群	2 (1.5) [1.5]	2 (1.0) [0.9]	0	2 (0.5) [0.5]	1 (0.2) [0.4]
変形性脊椎症	1 (0.7) [0.7]	0	0	0	0
脊椎関節障害	1 (0.7) [0.8]	1 (0.5) [0.5]	0	3 (0.7) [0.6]	0
軟骨下機能不全骨折	0	0	0	1 (0.2) [0.2]	0
腱痛	1 (0.7) [0.7]	0	0	0	0
腱炎	1 (0.7) [0.8]	0	0	0	1 (0.2) [0.2]
腱鞘炎	1 (0.7) [0.8]	0	0	0	0
弾発指	0	0	0	1 (0.2) [0.3]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (2.2) [2.5]	5 (2.5) [2.6]	9 (4.1) [4.1]	11 (2.7) [2.5]	21 (4.9) [4.9]
結腸腺癌	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
基底細胞癌	0	0	3 (1.4) [1.4]	0	7 (1.6) [1.5]
肺の良性新生物	0	0	0	1 (0.2) [0.2]	0
良性脾腫瘍	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
ボーエン病	0	0	0	0	1 (0.2) [0.2]
気管支の良性新生物	0	0	0	1 (0.2) [0.2]	0
大腸腺腫	1 (0.7) [0.8]	0	0	0	0
線維腫	0	0	0	0	1 (0.2) [0.2]
線維性組織球腫	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
血管腫	0	0	0	1 (0.2) [0.3]	0
皮膚血管腫	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
浸潤性乳癌	1 (0.7) [0.8]	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
メラノサイト性母斑	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
髄膜腫	0	0	0	0	1 (0.2) [0.2]
卵巣胚細胞良性奇形腫	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
脂漏性角化症	1 (0.7) [0.8]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	2 (0.5) [0.4]
皮膚乳頭腫	0	0	2 (0.9) [0.9]	0	3 (0.7) [0.6]
小細胞癌	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
皮膚有棘細胞癌	0	0	0	0	1 (0.2) [0.2]
子宮頚部扁平上皮癌	0	0	0	0	1 (0.2) [0.4]
甲状腺腺腫	0	0	0	2 (0.5) [0.5]	0
子宮平滑筋腫	0	0	0	1 (0.2) [0.3]	0
神経系障害	29 (21.5) [21.6]	20 (10.0) [10.0]	22 (10.1) [10.0]	44 (10.6) [10.2]	55 (12.9) [13.4]
脳損傷	0	0	0	1 (0.2) [0.2]	0
灼熱感	0	0	0	1 (0.2) [0.2]	0
頚動脈硬化症	0	0	0	0	1 (0.2) [0.2]
手根管症候群	1 (0.7) [0.7]	1 (0.5) [0.5]	2 (0.9) [0.9]	2 (0.5) [0.4]	2 (0.5) [0.5]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)					
脳血管発作	0	0	0	0	1 (0.2) [0.2]
頚髄圧迫	0	0	0	0	1 (0.2) [0.2]
頚髄神経根障害	1 (0.7) [0.8]	0	0	0	0
注意力障害	0	0	0	1 (0.2) [0.3]	0
浮動性めまい	3 (2.2) [2.3]	2 (1.0) [1.0]	2 (0.9) [0.9]	4 (1.0) [1.0]	6 (1.4) [1.5]
味覚不全	1 (0.7) [0.8]	0	0	0	0
てんかん	1 (0.7) [0.7]	0	0	0	0
本態性振戦	1 (0.7) [0.8]	0	0	0	0
頭痛	11 (8.2) [7.9]	8 (4.0) [3.9]	10 (4.6) [4.6]	21 (5.1) [4.8]	22 (5.2) [5.3]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)					
知覚過敏	1 (0.7) [0.8]	0	0	0	0
感覚鈍麻	1 (0.7) [0.8]	4 (2.0) [2.1]	1 (0.5) [0.5]	4 (1.0) [1.0]	2 (0.5) [0.5]
腰仙部神経根障害	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
片頭痛	4 (3.0) [3.0]	1 (0.5) [0.5]	3 (1.4) [1.4]	3 (0.7) [0.6]	3 (0.7) [0.8]
前兆を伴う片頭痛	0	0	0	1 (0.2) [0.2]	0
脊髄症	0	0	0	0	1 (0.2) [0.2]
神経圧迫	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
末梢性ニューロパチー	1 (0.7) [0.8]	0	0	0	0
後頭神経痛	0	0	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)					
錯感覚	2 (1.5) [1.5]	1 (0.5) [0.5]	1 (0.5) [0.4]	1 (0.2) [0.3]	1 (0.2) [0.4]
睡眠の質低下	0	0	0	0	1 (0.2) [0.2]
ヘルペス後神経痛	0	0	0	0	1 (0.2) [0.2]
失神寸前の状態	0	0	0	0	2 (0.5) [0.4]
坐骨神経痛	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	3 (0.7) [0.8]
傾眠	0	0	0	0	2 (0.5) [0.6]
会話障害	0	0	0	1 (0.2) [0.3]	0
脊椎炎性脊髄症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
くも膜下出血	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)					
硬膜下滲出液	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
失神	1 (0.7) [0.8]	0	0	0	1 (0.2) [0.2]
緊張性頭痛	0	0	0	0	1 (0.2) [0.2]
視野欠損	0	0	0	0	1 (0.2) [0.2]
精神障害	18 (13.3) [13.5]	7 (3.5) [3.4]	16 (7.3) [7.3]	15 (3.6) [3.5]	24 (5.6) [5.7]
不安	6 (4.4) [4.3]	1 (0.5) [0.5]	2 (0.9) [0.9]	4 (1.0) [1.0]	4 (0.9) [0.9]
不安障害	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
抑うつ気分	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
うつ病	2 (1.5) [1.5]	1 (0.5) [0.5]	4 (1.8) [1.8]	2 (0.5) [0.5]	6 (1.4) [1.5]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
精神障害 (Cont.)					
不眠症	7 (5.2) [5.3]	2 (1.0) [1.0]	9 (4.1) [4.1]	5 (1.2) [1.1]	12 (2.8) [2.8]
故意の自傷行為	0	0	0	0	1 (0.2) [0.2]
易刺激性	1 (0.7) [0.8]	0	0	0	0
精神障害	1 (0.7) [0.8]	0	0	0	0
パニック発作	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
睡眠障害	0	1 (0.5) [0.5]	0	2 (0.5) [0.4]	0
自殺念慮	1 (0.7) [0.8]	0	0	0	0
腎および尿路障害	11 (8.2) [7.9]	6 (3.0) [3.0]	14 (6.4) [6.4]	8 (1.9) [1.9]	18 (4.2) [4.2]
急性腎障害	1 (0.7) [0.8]	0	1 (0.5) [0.5]	0	2 (0.5) [0.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
腎および尿路障害 (Cont.)					
膀胱結石	0	0	0	0	1 (0.2) [0.2]
排尿困難	1 (0.7) [0.8]	0	1 (0.5) [0.5]	2 (0.5) [0.5]	1 (0.2) [0.2]
糖尿	1 (0.7) [0.7]	0	0	0	0
血尿	2 (1.5) [1.5]	1 (0.5) [0.5]	2 (0.9) [0.9]	1 (0.2) [0.3]	2 (0.5) [0.4]
水腎症	1 (0.7) [0.7]	0	0	0	0
緊張性膀胱	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
白血球尿	1 (0.7) [0.7]	0	0	0	0
排尿異常	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
腎石灰沈着症	1 (0.7) [0.7]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
腎および尿路障害 (Cont.)					
腎結石症	2 (1.5) [1.4]	3 (1.5) [1.5]	2 (0.9) [0.9]	3 (0.7) [0.7]	2 (0.5) [0.4]
頻尿	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
蛋白尿	1 (0.7) [0.7]	0	0	0	2 (0.5) [0.4]
腎仙痛	0	0	4 (1.8) [1.8]	0	4 (0.9) [1.0]
腎機能障害	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
尿管結石症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
尿閉	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
生殖系および乳房障害	9 (6.7) [6.7]	11 (5.5) [5.4]	8 (3.7) [3.7]	19 (4.6) [4.7]	15 (3.5) [3.5]
無月経	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
生殖系および乳房障害 (Cont.)					
バルトリン嚢腫	1 (0.7) [0.8]	0	0	0	0
良性前立腺肥大症	0	1 (0.5) [0.5]	2 (0.9) [0.9]	3 (0.7) [0.8]	3 (0.7) [0.7]
乳房嚢胞	1 (0.7) [0.7]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
乳房痛	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
子宮頚部上皮異形成	0	0	2 (0.9) [0.9]	0	2 (0.5) [0.6]
性交出血	0	0	0	1 (0.2) [0.3]	0
機能不全性子宮出血	1 (0.7) [0.8]	0	0	0	0
月経困難症	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	1 (0.2) [0.2]
性交困難	0	0	0	1 (0.2) [0.3]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
生殖系および乳房障害 (Cont.)					
勃起不全	0	0	0	1 (0.2) [0.2]	1 (0.2) [0.2]
閉経期症状	1 (0.7) [0.8]	0	0	0	0
月経過多	0	1 (0.5) [0.5]	0	2 (0.5) [0.5]	0
不規則月経	1 (0.7) [0.7]	0	0	1 (0.2) [0.2]	0
不正子宮出血	0	1 (0.5) [0.5]	0	2 (0.5) [0.5]	1 (0.2) [0.2]
卵巣静脈血栓症	1 (0.7) [0.8]	0	0	0	0
多嚢胞性卵巣	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
閉経後出血	0	0	0	0	1 (0.2) [0.2]
前立腺腫瘤	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
生殖系および乳房障害 (Cont.)					
前立腺炎	1 (0.7) [0.7]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.3]	2 (0.5) [0.4]
精液変色	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
腟分泌物	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	1 (0.2) [0.2]
腟出血	1 (0.7) [0.7]	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
外陰腟そう痒症	1 (0.7) [0.8]	0	0	0	0
呼吸器、胸郭および縦隔障害	24 (17.8) [17.3]	15 (7.5) [7.7]	27 (12.4) [12.3]	29 (7.0) [7.0]	38 (8.9) [9.7]
急性呼吸不全	1 (0.7) [0.8]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
失声症	0	0	0	0	2 (0.5) [0.4]
喘息	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)					
気管支拡張症	1 (0.7) [0.7]	0	0	0	0
慢性閉塞性肺疾患	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
咳嗽	3 (2.2) [2.0]	3 (1.5) [1.5]	5 (2.3) [2.3]	6 (1.4) [1.6]	5 (1.2) [1.3]
呼吸困難	0	1 (0.5) [0.5]	0	3 (0.7) [0.7]	0
労作性呼吸困難	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
肺気腫	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
鼻出血	0	0	1 (0.5) [0.5]	1 (0.2) [0.3]	3 (0.7) [0.8]
喀血	1 (0.7) [0.8]	0	0	0	0
しゃっくり	1 (0.7) [0.8]	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)					
過換気	0	0	0	0	1 (0.2) [0.2]
間質性肺疾患	1 (0.7) [0.8]	0	0	0	0
肺過膨脹	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
肺浸潤	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
鼻閉	3 (2.2) [2.1]	0	2 (0.9) [0.9]	0	2 (0.5) [0.6]
鼻潰瘍	0	0	0	2 (0.5) [0.5]	0
非感染性気管支炎	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
口腔咽頭痛	5 (3.7) [3.4]	3 (1.5) [1.6]	6 (2.7) [2.7]	6 (1.4) [1.4]	7 (1.6) [1.8]
湿性咳嗽	1 (0.7) [0.8]	2 (1.0) [1.1]	0	2 (0.5) [0.5]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)					
肺塞栓症	0	2 (1.0) [1.0]	0	3 (0.7) [0.6]	3 (0.7) [0.7]
肺出血	1 (0.7) [0.8]	0	0	0	0
アレルギー性鼻炎	2 (1.5) [1.5]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]
鼻漏	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
副鼻腔うっ血	2 (1.5) [1.4]	0	1 (0.5) [0.4]	1 (0.2) [0.2]	1 (0.2) [0.4]
睡眠時無呼吸症候群	0	0	0	1 (0.2) [0.2]	0
咽喉刺激感	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
上気道の炎症	2 (1.5) [1.3]	1 (0.5) [0.5]	0	1 (0.2) [0.3]	1 (0.2) [0.2]
上気道咳症候群	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害	75 (55.6) [54.9]	45 (22.6) [22.3]	65 (29.7) [29.7]	78 (18.8) [18.4]	102 (24.0) [24.6]
ざ瘡	8 (5.9) [5.8]	7 (3.5) [3.4]	10 (4.6) [4.5]	11 (2.7) [2.6]	16 (3.8) [4.1]
嚢胞性ざ瘡	0	0	0	1 (0.2) [0.2]	0
光線角化症	0	0	0	0	2 (0.5) [0.6]
脱毛症	0	2 (1.0) [1.0]	3 (1.4) [1.4]	4 (1.0) [0.9]	5 (1.2) [1.2]
皮脂欠乏症	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
皮膚嚢腫	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]
皮膚炎	3 (2.2) [2.1]	2 (1.0) [0.9]	3 (1.4) [1.4]	2 (0.5) [0.5]	3 (0.7) [0.7]
ざ瘡様皮膚炎	0	0	0	2 (0.5) [0.5]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
アレルギー性皮膚炎	0	0	0	0	1 (0.2) [0.2]
アトピー性皮膚炎	3 (2.2) [2.1]	3 (1.5) [1.4]	1 (0.5) [0.5]	3 (0.7) [0.7]	1 (0.2) [0.2]
接触皮膚炎	2 (1.5) [1.5]	1 (0.5) [0.5]	1 (0.5) [0.5]	2 (0.5) [0.4]	1 (0.2) [0.2]
びまん性脱毛症	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
皮膚乾燥	5 (3.7) [3.9]	0	1 (0.5) [0.5]	2 (0.5) [0.4]	1 (0.2) [0.2]
異汗性湿疹	2 (1.5) [1.3]	0	0	0	2 (0.5) [0.4]
斑状出血	1 (0.7) [0.8]	0	1 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
湿疹	5 (3.7) [3.6]	2 (1.0) [1.0]	5 (2.3) [2.3]	4 (1.0) [1.0]	7 (1.6) [1.5]
皮脂欠乏性湿疹	1 (0.7) [0.8]	0	1 (0.5) [0.5]	0	4 (0.9) [0.9]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
紅斑	3 (2.2) [2.3]	3 (1.5) [1.5]	1 (0.5) [0.5]	3 (0.7) [0.7]	3 (0.7) [0.8]
結節性紅斑	1 (0.7) [0.7]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
多汗症	0	0	0	1 (0.2) [0.2]	0
間擦疹	0	0	0	1 (0.2) [0.2]	0
瘢痕そう痒感	0	0	0	0	1 (0.2) [0.2]
黒子	0	0	0	0	1 (0.2) [0.2]
機械性蕁麻疹	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
汗疹	0	0	0	1 (0.2) [0.3]	0
神経皮膚炎	1 (0.7) [0.7]	0	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events(E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
寝汗	1 (0.7) [0.7]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.3]	2 (0.5) [0.4]
爪破損	1 (0.7) [0.8]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
爪甲剥離症	0	0	1 (0.5) [0.4]	0	1 (0.2) [0.4]
掌蹠膿疱症	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
脂肪織炎	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
丘疹	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
口囲皮膚炎	0	0	0	1 (0.2) [0.2]	0
光線性皮膚症	1 (0.7) [0.7]	0	0	0	0
光線過敏性反応	1 (0.7) [0.7]	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
そう痒症	8 (5.9) [6.2]	2 (1.0) [1.0]	1 (0.5) [0.5]	3 (0.7) [0.6]	2 (0.5) [0.4]
壊疽性膿皮症	1 (0.7) [0.8]	0	0	0	0
発疹	9 (6.7) [6.9]	8 (4.0) [4.0]	11 (5.0) [5.0]	14 (3.4) [3.4]	15 (3.5) [3.7]
紅斑性皮疹	1 (0.7) [0.8]	1 (0.5) [0.5]	0	3 (0.7) [0.7]	0
毛孔性皮疹	0	1 (0.5) [0.5]	0	2 (0.5) [0.4]	0
斑状皮疹	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.2) [0.3]	2 (0.5) [0.6]
斑状丘疹状皮疹	1 (0.7) [0.7]	1 (0.5) [0.5]	4 (1.8) [1.9]	1 (0.2) [0.2]	4 (0.9) [0.9]
丘疹性皮疹	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0
そう痒性皮疹	0	0	1 (0.5) [0.4]	0	2 (0.5) [0.6]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
酒さ	1 (0.7) [0.7]	2 (1.0) [1.1]	1 (0.5) [0.5]	2 (0.5) [0.5]	1 (0.2) [0.2]
脂漏性皮膚炎	7 (5.2) [4.9]	2 (1.0) [1.0]	2 (0.9) [0.9]	2 (0.5) [0.4]	2 (0.5) [0.5]
皮膚灼熱感	1 (0.7) [0.8]	0	0	0	0
皮膚びらん	1 (0.7) [0.7]	0	0	0	0
皮膚剥脱	1 (0.7) [0.7]	0	0	1 (0.2) [0.3]	1 (0.2) [0.2]
皮膚亀裂	1 (0.7) [0.8]	0	0	1 (0.2) [0.2]	0
皮膚色素過剰	1 (0.7) [0.7]	0	0	0	0
皮膚病変	0	0	2 (0.9) [0.9]	1 (0.2) [0.3]	5 (1.2) [1.2]
皮膚腫瘤	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245) (PYs=135.0)	UPA 15 mg QD (N=250) (PYs=199.4)	UPA 30 mg QD (N=251) (PYs=218.5)	UPA 15 mg QD (N=285) (PYs=413.8)	UPA 30 mg QD (N=291) (PYs=425.2)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
皮膚潰瘍	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
蕁麻疹	3 (2.2) [2.0]	0	5 (2.3) [2.3]	0	6 (1.4) [1.4]
乾皮症	0	0	0	0	1 (0.2) [0.2]
社会環境	0	0	0	0	1 (0.2) [0.2]
閉経後	0	0	0	0	1 (0.2) [0.2]
外科および内科処置	0	2 (1.0) [1.1]	0	3 (0.7) [0.8]	2 (0.5) [0.4]
人工流産	0	2 (1.0) [1.1]	0	2 (0.5) [0.5]	0
歯科インプラント埋込み	0	0	0	0	1 (0.2) [0.2]
抜歯	0	0	0	1 (0.2) [0.2]	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
血管障害	4 (3.0) [3.0]	9 (4.5) [4.7]	12 (5.5) [5.5]	16 (3.9) [4.2]	23 (5.4) [5.4]
大動脈瘤	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
大動脈硬化症	0	0	1 (0.5) [0.5]	1 (0.2) [0.3]	1 (0.2) [0.2]
出血性静脈瘤	0	1 (0.5) [0.5]	0	1 (0.2) [0.3]	0
深部静脈血栓症	0	0	2 (0.9) [0.9]	0	3 (0.7) [0.7]
血腫	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
高血圧	2 (1.5) [1.5]	7 (3.5) [3.6]	7 (3.2) [3.2]	11 (2.7) [2.8]	12 (2.8) [3.0]
低血圧	1 (0.7) [0.7]	0	0	0	1 (0.2) [0.2]
起立性低血圧	0	0	0	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=135.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=199.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=218.5) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=413.8) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=425.2) Events (E/100 PYs) [SSA E/100 PYs]
血管障害 (Cont.)					
末梢動脈閉塞性疾患	0	0	1 (0.5) [0.5]	0	1 (0.2) [0.2]
静脈炎	0	0	0	0	1 (0.2) [0.2]
レイノー現象	0	0	0	1 (0.2) [0.3]	0
静脈血栓症	1 (0.7) [0.8]	0	0	1 (0.2) [0.3]	0
白衣性高血圧	0	0	0	0	2 (0.5) [0.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-97.

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UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
Any adverse event	35 (85.4) [85.1]	34 (75.6) [75.7]	41 (91.1) [91.2]	38 (82.6) [83.1]	51 (94.4) [94.7]
血液およびリンパ系障害	7 (17.1) [16.9]	1 (2.2) [2.5]	7 (15.6) [15.5]	3 (6.5) [6.7]	9 (16.7) [16.3]
貧血	2 (4.9) [4.9]	1 (2.2) [2.5]	2 (4.4) [4.4]	1 (2.2) [2.5]	2 (3.7) [3.6]
鉄欠乏性貧血	3 (7.3) [7.4]	0	0	1 (2.2) [2.5]	0
白血球減少症	1 (2.4) [2.3]	0	0	1 (2.2) [1.8]	1 (1.9) [1.7]
リンパ球減少症	1 (2.4) [2.3]	0	0	0	0
小球性貧血	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.

SSA = Study-size adjusted.

Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
血液およびリンパ系障害 (Cont.)					
好中球減少症	1 (2.4) [2.3]	0	4 (8.9) [8.6]	0	6 (11.1) [10.4]
血小板減少症	1 (2.4) [2.5]	0	0	0	0
心臓障害	0	1 (2.2) [2.1]	0	2 (4.3) [4.5]	3 (5.6) [5.3]
不整脈	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
完全房室ブロック	0	0	0	1 (2.2) [2.5]	0
僧帽弁閉鎖不全症	0	0	0	0	1 (1.9) [2.0]
心室性期外収縮	0	0	0	0	2 (3.7) [3.4]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
耳および迷路障害	0	2 (4.4) [4.6]	1 (2.2) [2.3]	3 (6.5) [7.0]	3 (5.6) [5.6]
感音性難聴	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
片耳難聴	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
メニエール病	0	0	0	0	1 (1.9) [1.7]
耳漏	0	0	0	0	1 (1.9) [2.0]
回転性めまい	0	1 (2.2) [2.5]	0	2 (4.3) [4.9]	1 (1.9) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
内分泌障害	0	0	0	0	1 (1.9) [2.0]
甲状腺腫瘤	0	0	0	0	1 (1.9) [2.0]
眼障害	3 (7.3) [7.4]	2 (4.4) [4.2]	3 (6.7) [6.9]	4 (8.7) [8.4]	4 (7.4) [7.6]
眼瞼炎	1 (2.4) [2.5]	0	0	0	0
白内障	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
霰粒腫	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
アレルギー性結膜炎	1 (2.4) [2.5]	1 (2.2) [2.1]	1 (2.2) [2.1]	1 (2.2) [2.0]	1 (1.9) [1.7]
ドライアイ	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
眼障害 (Cont.)					
緑内障	0	0	0	0	1 (1.9) [1.7]
角膜炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
黄斑浮腫	0	0	0	1 (2.2) [2.5]	0
網膜静脈閉塞	0	0	0	1 (2.2) [2.5]	0
潰瘍性角膜炎	1 (2.4) [2.3]	0	0	0	0
硝子体浮遊物	0	0	0	1 (2.2) [1.8]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
胃腸障害	21 (51.2) [51.5]	8 (17.8) [16.9]	7 (15.6) [15.5]	14 (30.4) [28.5]	13 (24.1) [23.8]
腹部膨満	1 (2.4) [2.3]	0	0	0	0
腹痛	0	1 (2.2) [2.0]	0	2 (4.3) [3.6]	1 (1.9) [2.0]
下腹部痛	0	0	0	1 (2.2) [1.8]	0
上腹部痛	1 (2.4) [2.5]	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.3]
肛門ポリープ	0	0	0	0	1 (1.9) [1.7]
肛門そう痒症	1 (2.4) [2.5]	0	0	0	0
アフタ性潰瘍	1 (2.4) [2.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
胃腸障害 (Cont.)					
虚血性大腸炎	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0
潰瘍性大腸炎	13 (31.7) [31.5]	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [1.7]
便秘	0	1 (2.2) [2.1]	3 (6.7) [6.7]	1 (2.2) [2.0]	5 (9.3) [9.0]
齲歯	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [2.0]
歯嚢胞	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
消化不良	0	0	0	1 (2.2) [1.8]	0
腸炎	0	0	0	0	2 (3.7) [3.6]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
胃腸障害 (Cont.)					
胃食道逆流性疾患	1 (2.4) [2.3]	0	0	1 (2.2) [2.0]	0
歯肉腫脹	1 (2.4) [2.5]	0	0	0	0
舌痛	1 (2.4) [2.5]	0	0	0	0
痔出血	1 (2.4) [2.3]	0	0	0	0
痔核	1 (2.4) [2.3]	1 (2.2) [2.1]	0	2 (4.3) [4.5]	0
血栓性痔核	1 (2.4) [2.5]	0	0	0	0
鼠径ヘルニア	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
胃腸障害 (Cont.)					
腸管ポリープ	0	0	0	1 (2.2) [1.8]	0
大腸ポリープ	0	0	0	2 (4.3) [3.8]	0
口唇障害	0	0	0	1 (2.2) [2.5]	0
口腔嚢胞	1 (2.4) [2.5]	0	0	0	0
悪心	1 (2.4) [2.5]	0	0	2 (4.3) [3.8]	0
膵炎	1 (2.4) [2.5]	0	0	0	0
歯周病	1 (2.4) [2.5]	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
胃腸障害 (Cont.)					
直腸炎	1 (2.4) [2.3]	0	0	0	0
口内炎	2 (4.9) [4.9]	1 (2.2) [2.1]	2 (4.4) [4.4]	1 (2.2) [2.0]	2 (3.7) [3.6]
埋伏歯	0	0	0	0	1 (1.9) [1.7]
歯の脱落	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
歯痛	0	0	0	0	1 (1.9) [2.0]
一般・全身障害および投与部位の状態	3 (7.3) [7.4]	2 (4.4) [4.6]	9 (20.0) [20.6]	7 (15.2) [15.6]	12 (22.2) [23.5]
胸痛	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
一般・全身障害および投与部位の状態 (Cont.)					
疲労	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
炎症	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
注射部位疼痛	0	0	1 (2.2) [2.3]	3 (6.5) [6.6]	4 (7.4) [7.3]
倦怠感	1 (2.4) [2.3]	0	0	0	0
非心臓性胸痛	1 (2.4) [2.5]	0	0	0	0
末梢性浮腫	1 (2.4) [2.3]	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]
発熱	1 (2.4) [2.5]	2 (4.4) [4.6]	7 (15.6) [15.8]	4 (8.7) [9.5]	8 (14.8) [15.7]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
一般・全身障害および投与部位の状態 (Cont.)					
腫脹	0	0	0	1 (2.2) [2.0]	0
肝胆道系障害	2 (4.9) [5.0]	1 (2.2) [2.1]	0	2 (4.3) [3.8]	1 (1.9) [1.7]
肝機能異常	1 (2.4) [2.5]	0	0	1 (2.2) [1.8]	1 (1.9) [1.7]
脂肪肝	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
肝損傷	1 (2.4) [2.5]	0	0	0	0
免疫系障害	0	1 (2.2) [2.1]	1 (2.2) [2.1]	1 (2.2) [2.0]	2 (3.7) [3.6]
アナフィラキシー反応	0	0	0	0	1 (1.9) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
免疫系障害 (Cont.)					
季節性アレルギー	0	1 (2.2) [2.1]	1 (2.2) [2.1]	1 (2.2) [2.0]	1 (1.9) [1.7]
感染症および寄生虫症	16 (39.0) [38.8]	22 (48.9) [49.2]	26 (57.8) [57.8]	24 (52.2) [52.6]	36 (66.7) [67.0]
ダニ皮膚炎	0	2 (4.4) [4.2]	0	2 (4.3) [4.1]	0
虫垂炎	0	0	0	0	1 (1.9) [2.0]
細菌性関節炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
細菌性膣症	1 (2.4) [2.5]	0	0	0	0
カンピロバクター胃腸炎	0	0	0	1 (2.2) [2.5]	1 (1.9) [1.7]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
蜂巣炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
結膜炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
COVID-19肺炎	0	0	0	0	1 (1.9) [2.0]
膀胱炎	0	1 (2.2) [2.1]	2 (4.4) [4.4]	1 (2.2) [2.0]	2 (3.7) [3.6]
感染性腸炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
毛包炎	1 (2.4) [2.3]	1 (2.2) [2.1]	3 (6.7) [6.9]	1 (2.2) [2.0]	3 (5.6) [5.9]
胃腸炎	1 (2.4) [2.5]	2 (4.4) [4.6]	0	2 (4.3) [4.5]	1 (1.9) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
歯肉炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.0]
ヘリコバクター感染	0	0	0	1 (2.2) [1.8]	0
ヘルペス性皮膚炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
ヘルペス眼感染	0	0	0	0	1 (1.9) [1.7]
帯状疱疹	0	4 (8.9) [8.6]	5 (11.1) [11.3]	5 (10.9) [10.2]	9 (16.7) [16.2]
帯状疱疹性髄膜炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
麦粒腫	2 (4.9) [5.0]	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
膿痂疹	0	0	0	1 (2.2) [2.5]	0
インフルエンザ	0	1 (2.2) [2.0]	2 (4.4) [4.8]	1 (2.2) [1.8]	2 (3.7) [4.2]
大腸感染	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [1.7]
潜伏結核	0	0	1 (2.2) [2.1]	0	2 (3.7) [3.6]
伝染性軟属腫	1 (2.4) [2.3]	0	0	0	0
上咽頭炎	5 (12.2) [11.8]	8 (17.8) [18.9]	11 (24.4) [24.0]	10 (21.7) [22.9]	13 (24.1) [24.1]
口腔カンジダ症	1 (2.4) [2.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	0	2 (4.4) [4.2]	4 (8.9) [9.0]	2 (4.3) [4.1]	5 (9.3) [9.8]
外耳炎	1 (2.4) [2.5]	0	0	0	0
歯周炎	1 (2.4) [2.5]	0	1 (2.2) [2.3]	0	2 (3.7) [3.6]
扁桃周囲炎	0	0	0	1 (2.2) [2.0]	0
咽頭炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	2 (3.7) [3.9]
胸膜感染	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]
ニューモシスチス・イロベチイ肺炎	1 (2.4) [2.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
肺炎	1 (2.4) [2.3]	0	0	0	1 (1.9) [2.0]
副鼻腔炎	0	0	0	1 (2.2) [2.5]	0
白癬感染	1 (2.4) [2.3]	0	0	0	0
足部白癬	1 (2.4) [2.3]	1 (2.2) [2.5]	0	2 (4.3) [4.9]	1 (1.9) [1.7]
扁桃炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
上気道感染	0	3 (6.7) [6.7]	1 (2.2) [2.1]	3 (6.5) [6.6]	1 (1.9) [1.7]
創傷感染	0	0	0	0	1 (1.9) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
傷害、中毒および処置合併症	3 (7.3) [7.0]	2 (4.4) [4.6]	1 (2.2) [2.3]	6 (13.0) [13.1]	2 (3.7) [3.6]
節足動物咬傷	0	0	0	1 (2.2) [2.0]	1 (1.9) [1.7]
骨挫傷	1 (2.4) [2.3]	0	0	0	0
挫傷	0	0	1 (2.2) [2.3]	1 (2.2) [2.0]	1 (1.9) [2.0]
足骨折	0	0	0	0	1 (1.9) [1.7]
熱中症	1 (2.4) [2.3]	0	0	0	0
熱射病	0	0	0	1 (2.2) [2.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
傷害、中毒および処置合併症 (Cont.)					
関節損傷	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
過量投与	0	0	0	1 (2.2) [2.5]	0
肺挫傷	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
肋骨骨折	1 (2.4) [2.3]	0	0	0	0
ストレス骨折	0	0	0	1 (2.2) [2.0]	0
皮下血腫	1 (2.4) [2.3]	0	0	0	0
胸椎骨折	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
臨床検査	4 (9.8) [9.7]	12 (26.7) [26.8]	16 (35.6) [35.7]	14 (30.4) [31.1]	23 (42.6) [42.9]
アラニンアミノトランスフェラーゼ増加	0	1 (2.2) [2.5]	4 (8.9) [9.0]	1 (2.2) [2.5]	5 (9.3) [9.2]
アミラーゼ増加	1 (2.4) [2.5]	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (4.4) [4.9]	3 (6.7) [6.7]	2 (4.3) [4.9]	4 (7.4) [7.3]
血中コレステロール増加	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
血中クレアチンホスホキナーゼ増加	1 (2.4) [2.3]	5 (11.1) [11.0]	6 (13.3) [13.2]	5 (10.9) [10.6]	10 (18.5) [18.5]
血中クレアチニン増加	1 (2.4) [2.3]	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
臨床検査 (Cont.)					
γ-グルタミルトランスフェラーゼ増加	0	3 (6.7) [7.0]	0	3 (6.5) [7.0]	0
高比重リポ蛋白増加	0	2 (4.4) [4.6]	0	3 (6.5) [6.3]	0
リパーゼ増加	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
リンパ球数減少	0	0	2 (4.4) [4.4]	0	4 (7.4) [7.6]
リンパ球数増加	1 (2.4) [2.5]	0	0	0	0
リンパ球百分率増加	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
好中球数減少	1 (2.4) [2.5]	1 (2.2) [2.5]	4 (8.9) [9.0]	3 (6.5) [7.4]	6 (11.1) [10.9]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
臨床検査 (Cont.)					
好中球数増加	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
尿中白血球エステラーゼ陽性	0	0	0	1 (2.2) [1.8]	0
体重増加	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
白血球数減少	1 (2.4) [2.5]	2 (4.4) [4.6]	1 (2.2) [2.5]	4 (8.7) [9.5]	3 (5.6) [5.9]
代謝および栄養障害	2 (4.9) [5.1]	4 (8.9) [8.6]	1 (2.2) [2.1]	6 (13.0) [12.9]	4 (7.4) [7.6]
糖尿病	0	0	0	0	1 (1.9) [1.7]
脂質異常症	0	3 (6.7) [6.2]	0	3 (6.5) [5.9]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
代謝および栄養障害 (Cont.)					
高コレステロール血症	0	1 (2.2) [2.5]	1 (2.2) [2.1]	1 (2.2) [2.5]	2 (3.7) [3.9]
高リパーゼ血症	1 (2.4) [2.5]	0	0	0	0
高脂血症	0	0	0	2 (4.3) [4.5]	1 (1.9) [2.0]
低ナトリウム血症	1 (2.4) [2.5]	0	0	0	0
筋骨格系および結合組織障害	9 (22.0) [21.9]	7 (15.6) [15.3]	3 (6.7) [6.5]	12 (26.1) [25.7]	7 (13.0) [13.2]
関節痛	4 (9.8) [9.9]	2 (4.4) [4.2]	1 (2.2) [2.3]	5 (10.9) [10.4]	1 (1.9) [2.0]
関節障害	1 (2.4) [2.3]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
背部痛	3 (7.3) [7.3]	3 (6.7) [6.9]	0	4 (8.7) [9.2]	0
椎間板突出	0	0	0	0	2 (3.7) [4.2]
腰部脊柱管狭窄症	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
筋痙縮	0	0	0	1 (2.2) [1.8]	1 (1.9) [2.0]
筋骨格系胸痛	1 (2.4) [2.3]	0	0	0	0
筋骨格痛	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
筋骨格硬直	0	0	0	1 (2.2) [1.8]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
筋肉痛	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [1.7]
変形性関節症	1 (2.4) [2.3]	0	0	1 (2.2) [1.8]	0
骨壊死	0	1 (2.2) [2.1]	0	2 (4.3) [4.1]	0
四肢痛	1 (2.4) [2.3]	0	0	0	2 (3.7) [3.9]
関節周囲炎	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
肩回旋筋腱板症候群	1 (2.4) [2.3]	0	0	0	0
腱鞘炎	1 (2.4) [2.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
弾発指	0	0	0	1 (2.2) [2.5]	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (2.4) [2.5]	0	1 (2.2) [2.1]	1 (2.2) [2.5]	2 (3.7) [3.4]
結腸腺癌	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
大腸腺腫	1 (2.4) [2.5]	0	0	0	0
線維腫	0	0	0	0	1 (1.9) [1.7]
皮膚乳頭腫	0	0	0	0	1 (1.9) [1.7]
子宮平滑筋腫	0	0	0	1 (2.2) [2.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
神経系障害	2 (4.9) [4.9]	2 (4.4) [4.6]	5 (11.1) [11.5]	3 (6.5) [6.3]	10 (18.5) [19.6]
浮動性めまい	0	0	1 (2.2) [2.1]	0	2 (3.7) [3.9]
てんかん	1 (2.4) [2.3]	0	0	0	0
頭痛	0	2 (4.4) [4.6]	2 (4.4) [4.8]	2 (4.3) [4.5]	5 (9.3) [9.8]
感覚鈍麻	0	1 (2.2) [2.5]	1 (2.2) [2.3]	1 (2.2) [2.5]	2 (3.7) [3.9]
片頭痛	1 (2.4) [2.5]	0	0	0	0
末梢性ニューロパチー	1 (2.4) [2.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
神経系障害 (Cont.)					
後頭神経痛	0	0	0	1 (2.2) [1.8]	0
ヘルペス後神経痛	0	0	0	0	1 (1.9) [1.7]
傾眠	0	0	0	0	1 (1.9) [2.3]
くも膜下出血	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
精神障害	3 (7.3) [7.2]	1 (2.2) [2.1]	2 (4.4) [4.4]	2 (4.3) [4.5]	3 (5.6) [5.3]
不安	0	0	0	1 (2.2) [2.5]	0
不安障害	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
精神障害 (Cont.)					
抑うつ気分	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
不眠症	3 (7.3) [7.2]	0	2 (4.4) [4.4]	0	3 (5.6) [5.3]
腎および尿路障害	0	0	2 (4.4) [4.2]	0	2 (3.7) [3.4]
急性腎障害	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
尿管結石症	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
生殖系および乳房障害	2 (4.9) [4.9]	2 (4.4) [4.5]	0	2 (4.3) [4.3]	0
機能不全性子宮出血	1 (2.4) [2.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
生殖系および乳房障害 (Cont.)					
月経困難症	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0
不規則月経	1 (2.4) [2.3]	0	0	0	0
前立腺炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
呼吸器、胸郭および縦隔障害	3 (7.3) [7.2]	3 (6.7) [7.0]	3 (6.7) [6.7]	4 (8.7) [9.5]	6 (11.1) [11.2]
咳嗽	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
しゃっくり	1 (2.4) [2.5]	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]
過換気	0	0	0	0	1 (1.9) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)					
口腔咽頭痛	0	0	2 (4.4) [4.2]	1 (2.2) [2.5]	3 (5.6) [5.0]
アレルギー性鼻炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
上気道の炎症	2 (4.9) [4.7]	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.0]
皮膚および皮下組織障害	13 (31.7) [31.7]	10 (22.2) [21.6]	13 (28.9) [29.0]	14 (30.4) [30.5]	19 (35.2) [35.0]
ざ瘡	3 (7.3) [7.2]	1 (2.2) [2.1]	3 (6.7) [6.9]	2 (4.3) [4.1]	4 (7.4) [7.6]
皮脂欠乏症	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
皮膚炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
ざ瘡様皮膚炎	0	0	0	1 (2.2) [2.5]	0
アトピー性皮膚炎	0	2 (4.4) [4.2]	0	2 (4.3) [4.1]	0
接触皮膚炎	1 (2.4) [2.5]	0	0	0	0
異汗性湿疹	0	0	0	0	1 (1.9) [1.7]
湿疹	1 (2.4) [2.5]	2 (4.4) [4.6]	2 (4.4) [4.2]	3 (6.5) [6.3]	4 (7.4) [6.7]
皮脂欠乏性湿疹	1 (2.4) [2.5]	0	1 (2.2) [2.1]	0	3 (5.6) [5.3]
瘢痕そう痒感	0	0	0	0	1 (1.9) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
汗疹	0	0	0	1 (2.2) [2.5]	0
掌蹠膿疱症	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
脂肪織炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
光線過敏性反応	1 (2.4) [2.3]	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
そう痒症	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0
壊疽性膿皮症	1 (2.4) [2.5]	0	0	0	0
発疹	2 (4.9) [4.7]	1 (2.2) [2.1]	1 (2.2) [2.3]	2 (4.3) [4.5]	2 (3.7) [3.6]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
紅斑性皮疹	1 (2.4) [2.5]	0	0	0	0
斑状丘疹状皮疹	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
脂漏性皮膚炎	4 (9.8) [9.7]	2 (4.4) [4.1]	1 (2.2) [2.3]	2 (4.3) [3.8]	1 (1.9) [2.0]
蕁麻疹	0	0	4 (8.9) [9.0]	0	4 (7.4) [7.6]
乾皮症	0	0	0	0	1 (1.9) [1.7]
血管障害	1 (2.4) [2.5]	1 (2.2) [2.5]	3 (6.7) [7.1]	1 (2.2) [2.5]	5 (9.3) [9.8]
大動脈瘤	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
血管障害 (Cont.)					
血腫	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
高血圧	0	0	2 (4.4) [4.8]	0	3 (5.6) [6.2]
静脈炎	0	0	0	0	1 (1.9) [1.7]
静脈血栓症	1 (2.4) [2.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

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表 2.7.4.7-98.

[redacted]20[redacted] 10:01 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] - UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
Any adverse event	35 (85.4) [85.1]	34 (75.6) [75.7]	41 (91.1) [91.2]	38 (82.6) [83.1]	51 (94.4) [94.7]		
上咽頭炎	5 (12.2) [11.8]	8 (17.8) [18.9]	11 (24.4) [24.0]	10 (21.7) [22.9]	13 (24.1) [24.1]	7.1 (-7.9, 22.0)	12.2 (-3.5, 28.0)
血中クレアチンホスホキナーゼ増加	1 (2.4) [2.3]	5 (11.1) [11.0]	6 (13.3) [13.2]	5 (10.9) [10.6]	10 (18.5) [18.5]	8.7 (-2.6, 19.9)	10.8 (-1.2, 22.9)
帯状疱疹	0	4 (8.9) [8.6]	5 (11.1) [11.3]	5 (10.9) [10.2]	9 (16.7) [16.2]	8.6 (-1.3, 18.6)	11.3 (0.6, 21.9)
発熱	1 (2.4) [2.5]	2 (4.4) [4.6]	7 (15.6) [15.8]	4 (8.7) [9.5]	8 (14.8) [15.7]	2.0 (-7.7, 11.8)	13.3 (0.9, 25.7)
好中球数減少	1 (2.4) [2.5]	1 (2.2) [2.5]	4 (8.9) [9.0]	3 (6.5) [7.4]	6 (11.1) [10.9]	-0.1 (-9.0, 8.9)	6.4 (-4.6, 17.5)
好中球減少症	1 (2.4) [2.3]	0	4 (8.9) [8.6]	0	6 (11.1) [10.4]	-2.3 (-9.9, 5.3)	6.3 (-4.5, 17.0)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
頭痛	0	2 (4.4) [4.6]	2 (4.4) [4.8]	2 (4.3) [4.5]	5 (9.3) [9.8]	4.6 (-4.1, 13.2)	4.8 (-3.8, 13.3)
口腔ヘルペス	0	2 (4.4) [4.2]	4 (8.9) [9.0]	2 (4.3) [4.1]	5 (9.3) [9.8]	4.2 (-4.1, 12.4)	9.0 (-1.1, 19.0)
アラニンアミノトランスフェラーゼ増加	0	1 (2.2) [2.5]	4 (8.9) [9.0]	1 (2.2) [2.5]	5 (9.3) [9.2]	2.5 (-5.2, 10.2)	9.0 (-1.1, 19.0)
便秘	0	1 (2.2) [2.1]	3 (6.7) [6.7]	1 (2.2) [2.0]	5 (9.3) [9.0]	2.1 (-5.3, 9.5)	6.7 (-2.7, 16.0)
湿疹	1 (2.4) [2.5]	2 (4.4) [4.6]	2 (4.4) [4.2]	3 (6.5) [6.3]	4 (7.4) [6.7]	2.0 (-7.7, 11.8)	1.7 (-7.7, 11.1)
注射部位疼痛	0	0	1 (2.2) [2.3]	3 (6.5) [6.6]	4 (7.4) [7.3]	0.0	2.3 (-5.2, 9.8)
ざ瘡	3 (7.3) [7.2]	1 (2.2) [2.1]	3 (6.7) [6.9]	2 (4.3) [4.1]	4 (7.4) [7.6]	-5.1 (-15.6, 5.4)	-0.3 (-12.3, 11.6)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] - UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (4.4) [4.9]	3 (6.7) [6.7]	2 (4.3) [4.9]	4 (7.4) [7.3]	4.9 (-3.8, 13.7)	6.7 (-2.7, 16.0)
リンパ球数減少	0	0	2 (4.4) [4.4]	0	4 (7.4) [7.6]	0.0	4.4 (-4.1, 12.9)
蕁麻疹	0	0	4 (8.9) [9.0]	0	4 (7.4) [7.6]	0.0	9.0 (-1.1, 19.0)
白血球数減少	1 (2.4) [2.5]	2 (4.4) [4.6]	1 (2.2) [2.5]	4 (8.7) [9.5]	3 (5.6) [5.9]	2.0 (-7.7, 11.8)	-0.1 (-8.8, 8.7)
毛包炎	1 (2.4) [2.3]	1 (2.2) [2.1]	3 (6.7) [6.9]	1 (2.2) [2.0]	3 (5.6) [5.9]	-0.2 (-8.7, 8.3)	4.5 (-5.7, 14.8)
口腔咽頭痛	0	0	2 (4.4) [4.2]	1 (2.2) [2.5]	3 (5.6) [5.0]	0.0	4.2 (-4.0, 12.4)
不眠症	3 (7.3) [7.2]	0	2 (4.4) [4.4]	0	3 (5.6) [5.3]	-7.2 (-16.9, 2.5)	-2.8 (-14.1, 8.4)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
皮脂欠乏性湿疹	1 (2.4) [2.5]	0	1 (2.2) [2.1]	0	3 (5.6) [5.3]	-2.5 (-10.3, 5.3)	-0.4 (-9.1, 8.2)
高血圧	0	0	2 (4.4) [4.8]	0	3 (5.6) [6.2]	0.0	4.8 (-3.8, 13.3)
発疹	2 (4.9) [4.7]	1 (2.2) [2.1]	1 (2.2) [2.3]	2 (4.3) [4.5]	2 (3.7) [3.6]	-2.6 (-12.0, 6.8)	-2.4 (-11.9, 7.2)
貧血	2 (4.9) [4.9]	1 (2.2) [2.5]	2 (4.4) [4.4]	1 (2.2) [2.5]	2 (3.7) [3.6]	-2.4 (-12.3, 7.5)	-0.5 (-11.0, 10.1)
口内炎	2 (4.9) [4.9]	1 (2.2) [2.1]	2 (4.4) [4.4]	1 (2.2) [2.0]	2 (3.7) [3.6]	-2.8 (-12.4, 6.9)	-0.5 (-11.0, 10.1)
膀胱炎	0	1 (2.2) [2.1]	2 (4.4) [4.4]	1 (2.2) [2.0]	2 (3.7) [3.6]	2.1 (-5.3, 9.5)	4.4 (-4.1, 12.9)
高コレステロール血症	0	1 (2.2) [2.5]	1 (2.2) [2.1]	1 (2.2) [2.5]	2 (3.7) [3.9]	2.5 (-5.2, 10.2)	2.1 (-5.3, 9.5)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
感覚鈍麻	0	1 (2.2) [2.5]	1 (2.2) [2.3]	1 (2.2) [2.5]	2 (3.7) [3.9]	2.5 (-5.2, 10.2)	2.3 (-5.2, 9.8)
インフルエンザ	0	1 (2.2) [2.0]	2 (4.4) [4.8]	1 (2.2) [1.8]	2 (3.7) [4.2]	2.0 (-5.1, 9.1)	4.8 (-3.8, 13.3)
咽頭炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	2 (3.7) [3.9]	2.1 (-5.3, 9.5)	0.0
四肢痛	1 (2.4) [2.3]	0	0	0	2 (3.7) [3.9]	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
歯周炎	1 (2.4) [2.5]	0	1 (2.2) [2.3]	0	2 (3.7) [3.6]	-2.5 (-10.3, 5.3)	-0.2 (-9.1, 8.6)
浮動性めまい	0	0	1 (2.2) [2.1]	0	2 (3.7) [3.9]	0.0	2.1 (-5.3, 9.5)
腸炎	0	0	0	0	2 (3.7) [3.6]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
椎間板突出	0	0	0	0	2 (3.7) [4.2]	0.0	0.0
潜伏結核	0	0	1 (2.2) [2.1]	0	2 (3.7) [3.6]	0.0	2.1 (-5.3, 9.5)
心室性期外収縮	0	0	0	0	2 (3.7) [3.4]	0.0	0.0
関節痛	4 (9.8) [9.9]	2 (4.4) [4.2]	1 (2.2) [2.3]	5 (10.9) [10.4]	1 (1.9) [2.0]	-5.7 (-17.7, 6.2)	-7.6 (-19.1, 3.8)
上気道感染	0	3 (6.7) [6.7]	1 (2.2) [2.1]	3 (6.5) [6.6]	1 (1.9) [1.7]	6.7 (-2.7, 16.0)	2.1 (-5.3, 9.5)
脂漏性皮膚炎	4 (9.8) [9.7]	2 (4.4) [4.1]	1 (2.2) [2.3]	2 (4.3) [3.8]	1 (1.9) [2.0]	-5.7 (-17.5, 6.2)	-7.4 (-18.9, 4.0)
胃腸炎	1 (2.4) [2.5]	2 (4.4) [4.6]	0	2 (4.3) [4.5]	1 (1.9) [2.0]	2.0 (-7.7, 11.8)	-2.5 (-10.3, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
足部白癬	1 (2.4) [2.3]	1 (2.2) [2.5]	0	2 (4.3) [4.9]	1 (1.9) [1.7]	0.1 (-8.7, 8.9)	-2.3 (-9.9, 5.2)
腹痛	0	1 (2.2) [2.0]	0	2 (4.3) [3.6]	1 (1.9) [2.0]	2.0 (-5.1, 9.1)	0.0
高脂血症	0	0	0	2 (4.3) [4.5]	1 (1.9) [2.0]	0.0	0.0
回転性めまい	0	1 (2.2) [2.5]	0	2 (4.3) [4.9]	1 (1.9) [2.0]	2.5 (-5.2, 10.2)	0.0
潰瘍性大腸炎	13 (31.7) [31.5]	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [1.7]	-29.4 (-44.5, -14.3)	-31.5 (-46.1, -16.9)
上気道の炎症	2 (4.9) [4.7]	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.0]	-2.2 (-11.9, 7.5)	-4.7 (-13.2, 3.9)
上腹部痛	1 (2.4) [2.5]	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.3]	-0.1 (-9.0, 8.9)	-2.5 (-10.3, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
アレルギー性結膜炎	1 (2.4) [2.5]	1 (2.2) [2.1]	1 (2.2) [2.1]	1 (2.2) [2.0]	1 (1.9) [1.7]	-0.4 (-9.1, 8.2)	-0.4 (-9.1, 8.2)
肝機能異常	1 (2.4) [2.5]	0	0	1 (2.2) [1.8]	1 (1.9) [1.7]	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
白血球減少症	1 (2.4) [2.3]	0	0	1 (2.2) [1.8]	1 (1.9) [1.7]	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
節足動物咬傷	0	0	0	1 (2.2) [2.0]	1 (1.9) [1.7]	0.0	0.0
カンピロバクター胃腸炎	0	0	0	1 (2.2) [2.5]	1 (1.9) [1.7]	0.0	0.0
挫傷	0	0	1 (2.2) [2.3]	1 (2.2) [2.0]	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
齲歯	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [2.0]	2.1 (-5.3, 9.5)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
歯肉炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.0]	2.5 (-5.2, 10.2)	0.0
大腸感染	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [1.7]	2.5 (-5.2, 10.2)	0.0
筋痙縮	0	0	0	1 (2.2) [1.8]	1 (1.9) [2.0]	0.0	0.0
筋肉痛	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [1.7]	2.1 (-5.3, 9.5)	0.0
季節性アレルギー	0	1 (2.2) [2.1]	1 (2.2) [2.1]	1 (2.2) [2.0]	1 (1.9) [1.7]	2.1 (-5.3, 9.5)	2.1 (-5.3, 9.5)
麦粒腫	2 (4.9) [5.0]	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	-5.0 (-12.8, 2.8)	-2.9 (-11.6, 5.8)
血中クレアチニン増加	1 (2.4) [2.3]	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	-2.3 (-9.9, 5.3)	-0.0 (-8.7, 8.6)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
しゃっくり	1 (2.4) [2.5]	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	-2.5 (-10.3, 5.3)	-0.1 (-8.8, 8.7)
末梢性浮腫	1 (2.4) [2.3]	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	-2.3 (-9.9, 5.3)	0.1 (-8.4, 8.7)
歯周病	1 (2.4) [2.5]	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	-2.5 (-10.3, 5.3)	-0.4 (-9.1, 8.2)
光線過敏性反応	1 (2.4) [2.3]	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	-2.3 (-9.9, 5.3)	-0.0 (-8.7, 8.6)
肺炎	1 (2.4) [2.3]	0	0	0	1 (1.9) [2.0]	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
急性腎障害	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
結腸腺癌	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
肛門ポリープ	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
アナフィラキシー反応	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
虫垂炎	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
皮脂欠乏症	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
血中コレステロール増加	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
霰粒腫	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
胸痛	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
COVID-19肺炎	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
片耳難聴	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
歯嚢胞	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
抑うつ気分	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
糖尿病	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
ドライアイ	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	0.0	2.5 (-5.0, 9.9)
異汗性湿疹	0	0	0	0	1 (1.9) [1.7]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
感染性腸炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
疲労	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
線維腫	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
足骨折	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
緑内障	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
血腫	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
ヘルペス眼感染	0	0	0	0	1 (1.9) [1.7]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
帯状疱疹性髄膜炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
過換気	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
炎症	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
瘢痕そう痒感	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
角膜炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
腰部脊柱管狭窄症	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
メニエール病	0	0	0	0	1 (1.9) [1.7]	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
小球性貧血	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	0.0	2.5 (-5.0, 9.9)
僧帽弁閉鎖不全症	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
好中球数増加	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
耳漏	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
関節周囲炎	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
静脈炎	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
胸膜感染	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	0.0	2.5 (-5.0, 9.9)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
ヘルペス後神経痛	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
斑状丘疹状皮疹	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
皮膚乳頭腫	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
傾眠	0	0	0	0	1 (1.9) [2.3]	0.0	0.0
くも膜下出血	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
甲状腺腫瘤	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
扁桃炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
埋伏歯	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
歯の脱落	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
歯痛	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
尿管結石症	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
創傷感染	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
乾皮症	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
背部痛	3 (7.3) [7.3]	3 (6.7) [6.9]	0	4 (8.7) [9.2]	0	-0.4 (-12.4, 11.6)	-7.3 (-17.1, 2.4)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
脂質異常症	0	3 (6.7) [6.2]	0	3 (6.5) [5.9]	0	6.2 (-2.7, 15.1)	0.0
γ-グルタミルトランスフェラーゼ増加	0	3 (6.7) [7.0]	0	3 (6.5) [7.0]	0	7.0 (-2.6, 16.6)	0.0
高比重リポ蛋白増加	0	2 (4.4) [4.6]	0	3 (6.5) [6.3]	0	4.6 (-4.1, 13.2)	0.0
痔核	1 (2.4) [2.3]	1 (2.2) [2.1]	0	2 (4.3) [4.5]	0	-0.2 (-8.7, 8.3)	-2.3 (-9.9, 5.2)
悪心	1 (2.4) [2.5]	0	0	2 (4.3) [3.8]	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
ダニ皮膚炎	0	2 (4.4) [4.2]	0	2 (4.3) [4.1]	0	4.2 (-4.1, 12.4)	0.0
アトピー性皮膚炎	0	2 (4.4) [4.2]	0	2 (4.3) [4.1]	0	4.2 (-4.1, 12.4)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
大腸ポリープ	0	0	0	2 (4.3) [3.8]	0	0.0	0.0
骨壊死	0	1 (2.2) [2.1]	0	2 (4.3) [4.1]	0	2.1 (-5.3, 9.5)	0.0
鉄欠乏性貧血	3 (7.3) [7.4]	0	0	1 (2.2) [2.5]	0	-7.4 (-17.3, 2.5)	-7.4 (-17.3, 2.5)
アミラーゼ増加	1 (2.4) [2.5]	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	-0.4 (-9.1, 8.2)	-2.5 (-10.3, 5.2)
胃食道逆流性疾患	1 (2.4) [2.3]	0	0	1 (2.2) [2.0]	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
変形性関節症	1 (2.4) [2.3]	0	0	1 (2.2) [1.8]	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
下腹部痛	0	0	0	1 (2.2) [1.8]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
不安	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
不安障害	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
大動脈瘤	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
不整脈	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
細菌性関節炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
完全房室ブロック	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
白内障	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
蜂巣炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
虚血性大腸炎	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0
結膜炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
咳嗽	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
感音性難聴	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
皮膚炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
ざ瘡様皮膚炎	0	0	0	1 (2.2) [2.5]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
月経困難症	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0
消化不良	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
熱射病	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
ヘリコバクター感染	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
脂肪肝	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
ヘルペス性皮膚炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
膿痂疹	0	0	0	1 (2.2) [2.5]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
単径ヘルニア	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0
腸管ポリープ	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
関節損傷	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
口唇障害	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
リパーゼ増加	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
リンパ球百分率増加	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
黄斑浮腫	0	0	0	1 (2.2) [2.5]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
汗疹	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
筋骨格痛	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
筋骨格硬直	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
後頭神経痛	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
過量投与	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
掌蹠膿疱症	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
脂肪織炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
扁桃周囲炎	0	0	0	1 (2.2) [2.0]	0	0.0	0.0
前立腺炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
そう痒症	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0
肺挫傷	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
網膜静脈閉塞	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
アレルギー性鼻炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
副鼻腔炎	0	0	0	1 (2.2) [2.5]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
ストレス骨折	0	0	0	1 (2.2) [2.0]	0	0.0	0.0
腫脹	0	0	0	1 (2.2) [2.0]	0	0.0	0.0
胸椎骨折	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
弾発指	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
尿中白血球エステラーゼ陽性	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
子宮平滑筋腫	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
硝子体浮遊物	0	0	0	1 (2.2) [1.8]	0	0.0	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
体重増加	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
腹部膨満	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
肛門そう痒症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
アフタ性潰瘍	1 (2.4) [2.5]	0	0	0	0	-2.5 (-9.9, 5.0)	-2.5 (-9.9, 5.0)
関節障害	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
細菌性膣症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
眼瞼炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
骨挫傷	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
大腸腺腫	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
接触皮膚炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
機能不全性子宮出血	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
てんかん	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
歯肉腫脹	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
舌痛	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
痔出血	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
血栓性痔核	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
熱中症	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
高リパーゼ血症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
低ナトリウム血症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
肝損傷	1 (2.4) [2.5]	0	0	0	0	-2.5 (-9.9, 5.0)	-2.5 (-9.9, 5.0)
リンパ球数増加	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
リンパ球減少症	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
倦怠感	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
不規則月経	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
片頭痛	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
伝染性軟属腫	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
口腔嚢胞	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
筋骨格系胸痛	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
末梢性ニューロパチー	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
非心臓性胸痛	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
口腔カンジダ症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
外耳炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
膵炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
ニューモシスチス・イロベチイ肺炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
直腸炎	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
壊疽性膿皮症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
紅斑性皮疹	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
肋骨骨折	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
肩回旋筋腱板症候群	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
皮下血腫	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
腱鞘炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
血小板減少症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
by Decreasing Frequency by Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
白癬感染	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
潰瘍性角膜炎	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
静脈血栓症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject on same double-blind dose.
[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

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表 2.7.4.7-99.

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UPADACITINIB (ULCERATIVE COLITIS)

INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])

R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events(E/100 PYs) [SSA E/100 PYs]
Any adverse event	122 (525.5) [520.8]	117 (283.4) [286.0]	146 (362.1) [363.4]	194 (236.6) [243.5]	264 (318.4) [321.8]
血液およびリンパ系障害	10 (43.1) [41.4]	1 (2.4) [2.8]	7 (17.4) [17.1]	4 (4.9) [4.8]	10 (12.1) [11.6]
貧血	3 (12.9) [12.3]	1 (2.4) [2.8]	2 (5.0) [4.9]	1 (1.2) [1.5]	2 (2.4) [2.3]
鉄欠乏性貧血	3 (12.9) [13.0]	0	0	1 (1.2) [1.5]	0
白血球減少症	1 (4.3) [3.9]	0	0	2 (2.4) [1.8]	1 (1.2) [1.0]
リンパ球減少症	1 (4.3) [3.9]	0	0	0	0
小球性貧血	0	0	1 (2.5) [2.5]	0	1 (1.2) [1.9]
好中球減少症	1 (4.3) [3.9]	0	4 (9.9) [9.6]	0	6 (7.2) [6.4]
血小板減少症	1 (4.3) [4.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
心臓障害	0	1 (2.4) [2.3]	0	2 (2.4) [2.7]	3 (3.6) [3.3]
不整脈	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
完全房室ブロック	0	0	0	1 (1.2) [1.5]	0
僧帽弁閉鎖不全症	0	0	0	0	1 (1.2) [1.2]
心室性期外収縮	0	0	0	0	2 (2.4) [2.0]
耳および迷路障害	0	2 (4.8) [5.0]	1 (2.5) [2.6]	4 (4.9) [5.6]	4 (4.8) [4.8]
感音性難聴	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
片耳難聴	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
メニエール病	0	0	0	0	1 (1.2) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
耳および迷路障害 (Cont.)					
耳漏	0	0	0	0	1 (1.2) [1.2]
回転性めまい	0	1 (2.4) [2.8]	0	3 (3.7) [4.5]	1 (1.2) [1.2]
内分泌障害	0	0	0	0	1 (1.2) [1.2]
甲状腺腫瘤	0	0	0	0	1 (1.2) [1.2]
眼障害	3 (12.9) [13.0]	2 (4.8) [4.5]	4 (9.9) [9.8]	5 (6.1) [6.2]	6 (7.2) [7.3]
眼瞼炎	1 (4.3) [4.5]	0	0	0	0
白内障	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
霰粒腫	0	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]
アレルギー性結膜炎	1 (4.3) [4.5]	1 (2.4) [2.3]	1 (2.5) [2.3]	1 (1.2) [1.2]	2 (2.4) [2.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events (E/100 PYs) [SSA E/100 PYs]
眼障害 (Cont.)					
ドライアイ	0	0	1 (2.5) [2.5]	0	1 (1.2) [1.9]
緑内障	0	0	0	0	1 (1.2) [1.0]
角膜炎	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
黄斑浮腫	0	0	0	1 (1.2) [1.5]	0
網膜静脈閉塞	0	0	0	1 (1.2) [1.5]	0
潰瘍性角膜炎	1 (4.3) [3.9]	0	0	0	0
硝子体浮遊物	0	0	0	1 (1.2) [0.9]	0
胃腸障害	30 (129.2) [128.5]	10 (24.2) [22.7]	10 (24.8) [24.9]	24 (29.3) [26.6]	22 (26.5) [25.6]
腹部膨満	1 (4.3) [3.9]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
腹痛	0	1 (2.4) [2.1]	0	2 (2.4) [1.8]	1 (1.2) [1.2]
下腹部痛	0	0	0	1 (1.2) [0.9]	0
上腹部痛	1 (4.3) [4.5]	1 (2.4) [2.8]	0	1 (1.2) [1.5]	1 (1.2) [1.9]
肛門ポリープ	0	0	0	0	1 (1.2) [1.0]
肛門そう痒症	1 (4.3) [4.5]	0	0	0	0
アフタ性潰瘍	1 (4.3) [5.4]	0	0	0	0
虚血性大腸炎	0	1 (2.4) [2.1]	0	1 (1.2) [0.9]	0
潰瘍性大腸炎	13 (56.0) [54.4]	1 (2.4) [2.3]	0	3 (3.7) [3.5]	2 (2.4) [2.0]
便秘	0	1 (2.4) [2.3]	3 (7.4) [7.5]	1 (1.2) [1.2]	5 (6.0) [5.6]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
齲歯	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	1 (1.2) [1.2]
歯嚢胞	0	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]
消化不良	0	0	0	1 (1.2) [0.9]	0
腸炎	0	0	0	0	2 (2.4) [2.3]
胃食道逆流性疾患	1 (4.3) [3.9]	0	0	1 (1.2) [1.2]	0
歯肉腫脹	1 (4.3) [4.5]	0	0	0	0
舌痛	1 (4.3) [4.5]	0	0	0	0
痔出血	1 (4.3) [3.9]	0	0	0	0
痔核	1 (4.3) [3.9]	2 (4.8) [4.5]	0	4 (4.9) [5.0]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
血栓性痔核	1 (4.3) [4.5]	0	0	0	0
鼠径ヘルニア	0	1 (2.4) [2.1]	0	1 (1.2) [0.9]	0
腸管ポリープ	0	0	0	1 (1.2) [0.9]	0
大腸ポリープ	0	0	0	2 (2.4) [2.1]	0
口唇障害	0	0	0	1 (1.2) [1.5]	0
口腔嚢胞	1 (4.3) [4.5]	0	0	0	0
悪心	1 (4.3) [4.5]	0	0	2 (2.4) [2.1]	0
膵炎	1 (4.3) [4.5]	0	0	0	0
歯周病	1 (4.3) [4.5]	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events(E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
直腸炎	1 (4.3) [3.9]	0	0	0	0
口内炎	2 (8.6) [8.4]	1 (2.4) [2.3]	4 (9.9) [10.1]	1 (1.2) [1.2]	4 (4.8) [4.8]
埋伏歯	0	0	0	0	1 (1.2) [1.0]
歯の脱落	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
歯痛	0	0	0	0	1 (1.2) [1.2]
一般・全身障害および投与部位の状態	4 (17.2) [16.8]	2 (4.8) [5.0]	13 (32.2) [33.4]	9 (11.0) [11.9]	20 (24.1) [25.1]
胸痛	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
疲労	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
炎症	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)					
注射部位疼痛	0	0	2 (5.0) [5.2]	4 (4.9) [5.0]	6 (7.2) [7.0]
倦怠感	1 (4.3) [3.9]	0	0	0	0
非心臓性胸痛	1 (4.3) [4.5]	0	0	0	0
末梢性浮腫	1 (4.3) [3.9]	0	1 (2.5) [2.5]	0	1 (1.2) [1.9]
発熱	1 (4.3) [4.5]	2 (4.8) [5.0]	7 (17.4) [17.9]	4 (4.9) [5.6]	10 (12.1) [12.5]
腫脹	0	0	0	1 (1.2) [1.2]	0
肝胆道系障害	2 (8.6) [10.0]	1 (2.4) [2.3]	0	2 (2.4) [2.1]	1 (1.2) [1.0]
肝機能異常	1 (4.3) [4.5]	0	0	1 (1.2) [0.9]	1 (1.2) [1.0]
脂肪肝	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events(E/100 PYs) [SSA E/100 PYs]
肝胆道系障害 (Cont.)					
肝損傷	1 (4.3) [5.4]	0	0	0	0
免疫系障害	0	1 (2.4) [2.3]	1 (2.5) [2.3]	1 (1.2) [1.2]	2 (2.4) [2.3]
アナフィラキシー反応	0	0	0	0	1 (1.2) [1.2]
季節性アレルギー	0	1 (2.4) [2.3]	1 (2.5) [2.3]	1 (1.2) [1.2]	1 (1.2) [1.0]
感染症および寄生虫症	18 (77.5) [78.4]	40 (96.9) [99.4]	40 (99.2) [100.0]	50 (61.0) [65.0]	70 (84.4) [88.1]
ダニ皮膚炎	0	2 (4.8) [4.5]	0	2 (2.4) [2.4]	0
虫垂炎	0	0	0	0	1 (1.2) [1.2]
細菌性関節炎	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	0
細菌性膣症	1 (4.3) [4.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
COVID-19肺炎	0	0	0	0	1 (1.2) [1.2]
カンピロバクター胃腸炎	0	0	0	1 (1.2) [1.5]	1 (1.2) [1.0]
蜂巣炎	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
結膜炎	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
膀胱炎	0	1 (2.4) [2.3]	3 (7.4) [7.5]	1 (1.2) [1.2]	4 (4.8) [4.8]
感染性腸炎	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
毛包炎	1 (4.3) [3.9]	1 (2.4) [2.3]	3 (7.4) [7.8]	1 (1.2) [1.2]	3 (3.6) [3.7]
胃腸炎	1 (4.3) [4.5]	2 (4.8) [5.0]	0	2 (2.4) [2.7]	1 (1.2) [1.2]
歯肉炎	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	1 (1.2) [1.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
ヘリコバクター感染	0	0	0	1 (1.2) [0.9]	0
ヘルペス性皮膚炎	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
ヘルペス眼感染	0	0	0	0	1 (1.2) [1.0]
帯状疱疹	0	4 (9.7) [9.4]	5 (12.4) [12.7]	5 (6.1) [5.6]	9 (10.9) [10.1]
帯状疱疹性髄膜炎	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
麦粒腫	2 (8.6) [10.8]	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]
膿痂疹	0	0	0	1 (1.2) [1.5]	0
インフルエンザ	0	1 (2.4) [2.1]	2 (5.0) [5.1]	1 (1.2) [0.9]	2 (2.4) [3.2]
大腸感染	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	1 (1.2) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events(E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
潜伏結核	0	0	1 (2.5) [2.3]	0	2 (2.4) [2.3]
伝染性軟属腫	1 (4.3) [3.9]	0	0	0	0
上咽頭炎	5 (21.5) [20.9]	14 (33.9) [37.5]	15 (37.2) [36.8]	17 (20.7) [23.8]	18 (21.7) [22.4]
口腔カンジダ症	1 (4.3) [4.5]	0	0	0	0
口腔ヘルペス	0	4 (9.7) [9.0]	4 (9.9) [10.1]	4 (4.9) [4.7]	11 (13.3) [15.9]
外耳炎	1 (4.3) [4.5]	0	0	0	0
歯周炎	1 (4.3) [4.5]	0	1 (2.5) [2.6]	0	3 (3.6) [3.5]
扁桃周囲炎	0	0	0	1 (1.2) [1.2]	0
咽頭炎	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	2 (2.4) [2.9]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
胸膜感染	0	0	1 (2.5) [2.5]	0	1 (1.2) [1.9]
ニューモシスチス・イロベチイ肺炎	1 (4.3) [4.5]	0	0	0	0
肺炎	1 (4.3) [3.9]	0	0	0	1 (1.2) [1.2]
副鼻腔炎	0	0	0	1 (1.2) [1.5]	0
白癬感染	1 (4.3) [3.9]	0	0	0	0
足部白癬	1 (4.3) [3.9]	1 (2.4) [2.8]	0	2 (2.4) [3.0]	1 (1.2) [1.0]
扁桃炎	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
上気道感染	0	3 (7.3) [7.3]	1 (2.5) [2.3]	3 (3.7) [3.9]	1 (1.2) [1.0]
創傷感染	0	0	0	0	1 (1.2) [1.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症	4 (17.2) [15.5]	3 (7.3) [7.3]	1 (2.5) [2.6]	8 (9.8) [10.4]	3 (3.6) [3.3]
節足動物咬傷	0	0	0	1 (1.2) [1.2]	1 (1.2) [1.0]
骨挫傷	1 (4.3) [3.9]	0	0	0	0
挫傷	0	0	1 (2.5) [2.6]	1 (1.2) [1.2]	1 (1.2) [1.2]
足骨折	0	0	0	0	1 (1.2) [1.0]
熱中症	1 (4.3) [3.9]	0	0	0	0
熱射病	0	0	0	1 (1.2) [1.5]	0
関節損傷	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	0
過量投与	0	0	0	1 (1.2) [1.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)					
肺挫傷	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
肋骨骨折	1 (4.3) [3.9]	0	0	0	0
ストレス骨折	0	0	0	1 (1.2) [1.2]	0
皮下血腫	1 (4.3) [3.9]	0	0	0	0
胸椎骨折	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
臨床検査	7 (30.2) [30.5]	20 (48.4) [50.9]	29 (71.9) [71.9]	31 (37.8) [40.1]	46 (55.5) [53.7]
アラニンアミノトランスフェラーゼ増加	0	1 (2.4) [2.8]	4 (9.9) [10.1]	1 (1.2) [1.5]	6 (7.2) [7.0]
アミラーゼ増加	1 (4.3) [4.5]	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (4.8) [5.5]	3 (7.4) [7.5]	2 (2.4) [3.0]	5 (6.0) [5.8]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
血中コレステロール増加	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
血中クレアチンホスホキナーゼ増加	1 (4.3) [3.9]	5 (12.1) [12.0]	8 (19.8) [19.5]	7 (8.5) [7.7]	13 (15.7) [14.9]
血中クレアチニン増加	1 (4.3) [3.9]	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
γ-グルタミルトランスフェラーゼ増加	0	3 (7.3) [7.8]	0	5 (6.1) [7.1]	0
高比重リポ蛋白増加	0	2 (4.8) [5.0]	0	3 (3.7) [3.6]	0
リパーゼ増加	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
リンパ球数減少	0	0	2 (5.0) [4.9]	0	4 (4.8) [5.2]
リンパ球数増加	1 (4.3) [4.5]	0	0	0	0
リンパ球百分率増加	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
好中球数減少	2 (8.6) [9.1]	1 (2.4) [2.8]	8 (19.8) [19.7]	3 (3.7) [4.5]	12 (14.5) [13.2]
好中球数増加	0	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]
尿中白血球エステラーゼ陽性	0	0	0	2 (2.4) [1.8]	0
体重増加	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	0
白血球数減少	1 (4.3) [4.5]	2 (4.8) [5.0]	1 (2.5) [2.5]	4 (4.9) [5.6]	3 (3.6) [4.2]
代謝および栄養障害	2 (8.6) [9.1]	4 (9.7) [9.4]	1 (2.5) [2.3]	6 (7.3) [7.4]	4 (4.8) [5.2]
糖尿病	0	0	0	0	1 (1.2) [1.0]
脂質異常症	0	3 (7.3) [6.6]	0	3 (3.7) [3.3]	0
高コレステロール血症	0	1 (2.4) [2.8]	1 (2.5) [2.3]	1 (1.2) [1.5]	2 (2.4) [2.9]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
代謝および栄養障害 (Cont.)					
高リパーゼ血症	1 (4.3) [4.5]	0	0	0	0
高脂血症	0	0	0	2 (2.4) [2.7]	1 (1.2) [1.2]
低ナトリウム血症	1 (4.3) [4.5]	0	0	0	0
筋骨格系および結合組織障害	14 (60.3) [59.1]	8 (19.4) [18.9]	3 (7.4) [7.3]	17 (20.7) [20.2]	11 (13.3) [14.8]
関節痛	4 (17.2) [17.5]	2 (4.8) [4.5]	1 (2.5) [2.6]	5 (6.1) [5.9]	2 (2.4) [2.5]
関節障害	1 (4.3) [3.9]	0	0	0	0
背部痛	3 (12.9) [13.8]	3 (7.3) [7.6]	0	4 (4.9) [5.4]	0
椎間板突出	0	0	0	0	2 (2.4) [3.2]
腰部脊柱管狭窄症	0	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
筋痙縮	0	0	0	1 (1.2) [0.9]	1 (1.2) [1.2]
筋骨格系胸痛	2 (8.6) [7.8]	0	0	0	0
筋骨格痛	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
筋骨格硬直	0	0	0	1 (1.2) [0.9]	0
筋肉痛	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	1 (1.2) [1.0]
変形性関節症	1 (4.3) [3.9]	0	0	1 (1.2) [0.9]	0
骨壊死	0	1 (2.4) [2.3]	0	2 (2.4) [2.4]	0
四肢痛	1 (4.3) [3.9]	0	0	0	3 (3.6) [4.8]
関節周囲炎	0	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events(E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
肩回旋筋腱板症候群	1 (4.3) [3.9]	0	0	0	0
腱鞘炎	1 (4.3) [4.5]	0	0	0	0
弾発指	0	0	0	1 (1.2) [1.5]	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (4.3) [4.5]	0	1 (2.5) [2.3]	1 (1.2) [1.5]	3 (3.6) [3.1]
結腸腺癌	0	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]
大腸腺腫	1 (4.3) [4.5]	0	0	0	0
線維腫	0	0	0	0	1 (1.2) [1.0]
皮膚乳頭腫	0	0	0	0	1 (1.2) [1.0]
子宮平滑筋腫	0	0	0	1 (1.2) [1.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
神経系障害	3 (12.9) [13.0]	3 (7.3) [7.8]	5 (12.4) [12.7]	4 (4.9) [5.0]	12 (14.5) [16.7]
浮動性めまい	0	0	1 (2.5) [2.3]	0	2 (2.4) [2.9]
てんかん	1 (4.3) [3.9]	0	0	0	0
頭痛	0	2 (4.8) [5.0]	2 (5.0) [5.1]	2 (2.4) [2.7]	5 (6.0) [7.1]
感覚鈍麻	0	1 (2.4) [2.8]	1 (2.5) [2.6]	1 (1.2) [1.5]	2 (2.4) [2.5]
片頭痛	1 (4.3) [4.5]	0	0	0	0
末梢性ニューロパチー	1 (4.3) [4.5]	0	0	0	0
後頭神経痛	0	0	0	1 (1.2) [0.9]	0
ヘルペス後神経痛	0	0	0	0	1 (1.2) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)					
傾眠	0	0	0	0	1 (1.2) [1.9]
くも膜下出血	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
精神障害	3 (12.9) [12.3]	1 (2.4) [2.3]	3 (7.4) [7.5]	2 (2.4) [2.7]	4 (4.8) [4.5]
不安	0	0	0	1 (1.2) [1.5]	0
不安障害	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
抑うつ気分	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
不眠症	3 (12.9) [12.3]	0	2 (5.0) [4.9]	0	3 (3.6) [3.3]
腎および尿路障害	0	0	2 (5.0) [4.7]	0	2 (2.4) [2.0]
急性腎障害	0	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events(E/100 PYs) [SSA E/100 PYs]
腎および尿路障害 (Cont.)					
尿管結石症	0	0	1 (2.5) [2.3]	0	1 (1.2) [1.0]
生殖系および乳房障害	2 (8.6) [8.4]	2 (4.8) [4.9]	0	2 (2.4) [2.4]	0
機能不全性子宮出血	1 (4.3) [4.5]	0	0	0	0
月経困難症	0	1 (2.4) [2.1]	0	1 (1.2) [0.9]	0
不規則月経	1 (4.3) [3.9]	0	0	0	0
前立腺炎	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	0
呼吸器、胸郭および縦隔障害	3 (12.9) [12.3]	3 (7.3) [7.8]	3 (7.4) [7.2]	4 (4.9) [5.6]	6 (7.2) [7.5]
咳嗽	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
しゃっくり	1 (4.3) [4.5]	0	1 (2.5) [2.5]	0	1 (1.2) [1.9]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)					
過換気	0	0	0	0	1 (1.2) [1.2]
口腔咽頭痛	0	0	2 (5.0) [4.7]	1 (1.2) [1.5]	3 (3.6) [3.1]
アレルギー性鼻炎	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	0
上気道の炎症	2 (8.6) [7.8]	1 (2.4) [2.8]	0	1 (1.2) [1.5]	1 (1.2) [1.2]
皮膚および皮下組織障害	15 (64.6) [63.5]	12 (29.1) [27.8]	19 (47.1) [46.9]	17 (20.7) [20.7]	29 (35.0) [33.9]
ざ瘡	3 (12.9) [12.3]	1 (2.4) [2.3]	4 (9.9) [10.0]	2 (2.4) [2.4]	5 (6.0) [7.1]
皮脂欠乏症	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
皮膚炎	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
ざ瘡様皮膚炎	0	0	0	1 (1.2) [1.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events(E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
アトピー性皮膚炎	0	2 (4.8) [4.5]	0	2 (2.4) [2.4]	0
接触皮膚炎	1 (4.3) [4.5]	0	0	0	0
異汗性湿疹	0	0	0	0	1 (1.2) [1.0]
湿疹	1 (4.3) [4.5]	2 (4.8) [5.0]	2 (5.0) [4.7]	3 (3.7) [3.6]	4 (4.8) [4.1]
皮脂欠乏性湿疹	1 (4.3) [4.5]	0	1 (2.5) [2.3]	0	4 (4.8) [4.5]
瘢痕そう痒感	0	0	0	0	1 (1.2) [1.2]
汗疹	0	0	0	1 (1.2) [1.5]	0
掌蹠膿疱症	0	1 (2.4) [2.3]	0	1 (1.2) [1.2]	0
脂肪織炎	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=23.2) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=41.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=40.3) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=82.0) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=82.9) Events(E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
光線過敏性反応	1 (4.3) [3.9]	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
そう痒症	0	1 (2.4) [2.1]	0	1 (1.2) [0.9]	0
壊疽性膿皮症	1 (4.3) [4.5]	0	0	0	0
発疹	2 (8.6) [7.8]	1 (2.4) [2.3]	1 (2.5) [2.6]	2 (2.4) [2.7]	2 (2.4) [2.3]
紅斑性皮疹	1 (4.3) [4.5]	0	0	0	0
斑状丘疹状皮疹	0	0	4 (9.9) [9.4]	0	4 (4.8) [4.1]
脂漏性皮膚炎	4 (17.2) [16.8]	2 (4.8) [4.4]	1 (2.5) [2.6]	2 (2.4) [2.1]	1 (1.2) [1.2]
蕁麻疹	0	0	4 (9.9) [10.1]	0	4 (4.8) [4.8]
乾皮症	0	0	0	0	1 (1.2) [1.0]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=23.2)	UPA 15 mg QD (N=45) (PYs=41.3)	UPA 30 mg QD (N=45) (PYs=40.3)	UPA 15 mg QD (N=46) (PYs=82.0)	UPA 30 mg QD (N=54) (PYs=82.9)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
血管障害	1 (4.3) [4.5]	1 (2.4) [2.8]	3 (7.4) [7.7]	1 (1.2) [1.5]	5 (6.0) [6.7]
大動脈瘤	0	1 (2.4) [2.8]	0	1 (1.2) [1.5]	0
血腫	0	0	1 (2.5) [2.6]	0	1 (1.2) [1.2]
高血圧	0	0	2 (5.0) [5.1]	0	3 (3.6) [4.4]
静脈炎	0	0	0	0	1 (1.2) [1.0]
静脈血栓症	1 (4.3) [4.5]	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-100.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
Any adverse event	725 (551.4)	396 (316.4)	2230 (318.8)
血液およびリンパ系障害	39 (29.7)	11 (8.8)	58 (8.3)
貧血	26 (19.8)	8 (6.4)	24 (3.4)
大球性貧血	0	0	0
失血性貧血	0	0	0
周期性好中球減少症	0	0	0
好酸球増加症	1 (0.8)	0	0
顆粒球減少症	0	0	0
内出血発生の増加傾向	0	1 (0.8)	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
Any adverse event	239 (992.5)	1851 (386.8)	1897 (304.8)	2007 (339.2)	7787 (331.3)
血液およびリンパ系障害	23 (95.5)	75 (15.7)	103 (16.5)	69 (11.7)	303 (12.9)
貧血	17 (70.6)	24 (5.0)	30 (4.8)	21 (3.5)	109 (4.6)
大球性貧血	0	0	2 (0.3)	0	2 (<0.1)
失血性貧血	0	0	0	2 (0.3)	2 (<0.1)
周期性好中球減少症	0	1 (0.2)	0	0	1 (<0.1)
好酸球増加症	0	1 (0.2)	0	0	0
顆粒球減少症	0	0	1 (0.2)	0	1 (<0.1)
内出血発生の増加傾向	0	2 (0.4)	0	2 (0.3)	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)			
鉄欠乏性貧血	1 (0.8)	0	4 (0.6)
白血球増加症	0	0	4 (0.6)
白血球減少症	1 (0.8)	0	4 (0.6)
リンパ節症	0	1 (0.8)	0
リンパ球増加症	0	0	0
リンパ球減少症	4 (3.0)	1 (0.8)	9 (1.3)
小球性貧血	0	0	0
好中球減少症	3 (2.3)	0	8 (1.1)
好中球増加症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)					
鉄欠乏性貧血	1 (4.2)	8 (1.7)	4 (0.6)	4 (0.7)	16 (0.7)
白血球増加症	0	1 (0.2)	0	1 (0.2)	5 (0.2)
白血球減少症	0	8 (1.7)	27 (4.3)	7 (1.2)	42 (1.8)
リンパ節症	0	1 (0.2)	2 (0.3)	1 (0.2)	4 (0.2)
リンパ球増加症	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
リンパ球減少症	3 (12.5)	10 (2.1)	10 (1.6)	9 (1.5)	39 (1.7)
小球性貧血	0	1 (0.2)	2 (0.3)	1 (0.2)	4 (0.2)
好中球減少症	1 (4.2)	14 (2.9)	20 (3.2)	18 (3.0)	58 (2.5)
好中球増加症	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)			
正球性貧血	1 (0.8)	0	0
汎血球減少症	0	0	0
網状赤血球増加症	0	0	1 (0.1)
脾腫	0	0	1 (0.1)
血小板減少症	1 (0.8)	0	0
血小板増加症	1 (0.8)	0	2 (0.3)
心臓障害	12 (9.1)	3 (2.4)	13 (1.9)
急性心筋梗塞	0	0	0
不安定狭心症	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)					
正球性貧血	0	0	0	0	0
汎血球減少症	0	0	2 (0.3)	0	2 (<0.1)
網状赤血球増加症	0	0	0	0	1 (<0.1)
脾腫	0	0	1 (0.2)	0	2 (<0.1)
血小板減少症	1 (4.2)	2 (0.4)	0	0	2 (<0.1)
血小板増加症	0	1 (0.2)	1 (0.2)	2 (0.3)	6 (0.3)
心臓障害	3 (12.5)	13 (2.7)	15 (2.4)	16 (2.7)	56 (2.4)
急性心筋梗塞	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
不安定狭心症	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
心臓障害 (Cont.)			
不整脈	0	0	0
心房細動	0	0	0
完全房室ブロック	0	0	0
第一度房室ブロック	0	0	0
二束ブロック	0	0	0
徐脈性不整脈	0	0	0
徐脈	0	0	1 (0.1)
脚ブロック	0	0	0
左脚ブロック	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)					
不整脈	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
心房細動	0	2 (0.4)	0	1 (0.2)	2 (<0.1)
完全房室ブロック	0	0	1 (0.2)	0	1 (<0.1)
第一度房室ブロック	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
二束ブロック	0	0	0	1 (0.2)	1 (<0.1)
徐脈性不整脈	0	0	1 (0.2)	0	1 (<0.1)
徐脈	0	0	1 (0.2)	0	2 (<0.1)
脚ブロック	0	0	1 (0.2)	0	1 (<0.1)
左脚ブロック	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
心臓障害 (Cont.)			
心不全	0	0	0
うっ血性心不全	0	0	0
心拡大	0	0	0
慢性左室不全	0	0	0
うっ血性心筋症	0	0	0
冠動脈疾患	0	1 (0.8)	1 (0.1)
期外収縮	0	0	0
虚血性心筋症	0	0	1 (0.1)
僧帽弁閉鎖不全症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)					
心不全	0	0	0	1 (0.2)	1 (<0.1)
うっ血性心不全	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
心拡大	0	0	0	1 (0.2)	1 (<0.1)
慢性左室不全	0	0	0	1 (0.2)	1 (<0.1)
うっ血性心筋症	0	0	1 (0.2)	0	1 (<0.1)
冠動脈疾患	0	0	0	0	2 (<0.1)
期外収縮	0	0	1 (0.2)	0	1 (<0.1)
虚血性心筋症	0	0	0	0	1 (<0.1)
僧帽弁閉鎖不全症	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
心臓障害 (Cont.)			
心筋梗塞	0	0	1 (0.1)
動悸	6 (4.6)	1 (0.8)	2 (0.3)
心嚢液貯留	0	0	0
心膜炎	0	0	0
洞性不整脈	1 (0.8)	0	0
洞性徐脈	0	0	0
洞性頻脈	0	0	0
上室性期外収縮	1 (0.8)	0	0
上室性頻脈	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)					
心筋梗塞	0	0	0	0	1 (<0.1)
動悸	2 (8.3)	4 (0.8)	1 (0.2)	0	7 (0.3)
心嚢液貯留	0	1 (0.2)	0	0	1 (<0.1)
心膜炎	1 (4.2)	1 (0.2)	0	1 (0.2)	3 (0.1)
洞性不整脈	0	0	0	0	0
洞性徐脈	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
洞性頻脈	0	0	0	1 (0.2)	1 (<0.1)
上室性期外収縮	0	0	1 (0.2)	0	1 (<0.1)
上室性頻脈	0	0	0	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
心臓障害 (Cont.)			
頻脈	2 (1.5)	0	1 (0.1)
心室性期外収縮	1 (0.8)	0	1 (0.1)
心室性頻脈	0	0	3 (0.4)
ウォルフ・パーキンソン・ホワイト症候群	0	0	0
先天性、家族性および遺伝性障害	0	0	3 (0.4)
先天性横隔膜ヘルニア	0	0	0
皮様嚢腫	0	0	0
胃腸管動静脈奇形	0	0	0
ジルベール症候群	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)					
頻脈	0	2 (0.4)	1 (0.2)	0	3 (0.1)
心室性期外収縮	0	0	1 (0.2)	3 (0.5)	5 (0.2)
心室性頻脈	0	0	0	0	3 (0.1)
ウォルフ・パーキンソン・ホワイト症候群	0	0	0	1 (0.2)	1 (<0.1)
先天性、家族性および遺伝性障害	0	1 (0.2)	4 (0.6)	2 (0.3)	10 (0.4)
先天性横隔膜ヘルニア	0	0	1 (0.2)	0	1 (<0.1)
皮様嚢腫	0	0	0	1 (0.2)	1 (<0.1)
胃腸管動静脈奇形	0	0	0	1 (0.2)	1 (<0.1)
ジルベール症候群	0	0	1 (0.2)	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
先天性、家族性および遺伝性障害 (Cont.)			
陰嚢水瘤	0	0	0
魚鱗癬	0	0	1 (0.1)
歯原性嚢胞	0	0	0
包茎	0	0	0
汗孔角化症	0	0	1 (0.1)
耳および迷路障害	4 (3.0)	0	16 (2.3)
耳垢栓塞	0	0	1 (0.1)
伝音難聴	0	0	1 (0.1)
感音性難聴	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
先天性、家族性および遺伝性障害 (Cont.)					
陰嚢水瘤	0	0	1 (0.2)	0	1 (<0.1)
魚鱗癬	0	0	0	0	1 (<0.1)
歯原性嚢胞	0	1 (0.2)	0	0	1 (<0.1)
包茎	0	0	1 (0.2)	0	1 (<0.1)
汗孔角化症	0	0	0	0	1 (<0.1)
耳および迷路障害	2 (8.3)	7 (1.5)	16 (2.6)	10 (1.7)	48 (2.0)
耳垢栓塞	0	0	0	0	1 (<0.1)
伝音難聴	0	0	0	0	1 (<0.1)
感音性難聴	0	0	1 (0.2)	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
耳および迷路障害 (Cont.)			
片耳難聴	0	0	0
耳不快感	0	0	0
耳痛	1 (0.8)	0	2 (0.3)
耳部腫脹	0	0	0
外耳道の外骨腫	0	0	0
外耳の炎症	0	0	0
聴力低下	0	0	0
内耳障害	0	0	1 (0.1)
メニエール病	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
耳および迷路障害 (Cont.)					
片耳難聴	0	0	0	1 (0.2)	1 (<0.1)
耳不快感	0	0	1 (0.2)	0	1 (<0.1)
耳痛	0	2 (0.4)	3 (0.5)	0	7 (0.3)
耳部腫脹	0	1 (0.2)	0	0	0
外耳道の外骨腫	0	1 (0.2)	0	0	0
外耳の炎症	0	1 (0.2)	0	0	1 (<0.1)
聴力低下	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
内耳障害	0	0	0	0	1 (<0.1)
メニエール病	0	0	0	2 (0.3)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
耳および迷路障害 (Cont.)			
中耳滲出液	0	0	0
耳漏	0	0	0
突発性難聴	1 (0.8)	0	1 (0.1)
耳鳴	0	0	5 (0.7)
回転性めまい	2 (1.5)	0	5 (0.7)
内分泌障害	1 (0.8)	1 (0.8)	7 (1.0)
アジソン病	0	0	1 (0.1)
副腎機能不全	0	0	1 (0.1)
急性副腎皮質機能不全	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
耳および迷路障害 (Cont.)					
中耳滲出液	0	1 (0.2)	0	0	0
耳漏	0	0	0	1 (0.2)	1 (<0.1)
突発性難聴	0	0	1 (0.2)	0	2 (<0.1)
耳鳴	2 (8.3)	1 (0.2)	4 (0.6)	1 (0.2)	13 (0.6)
回転性めまい	0	0	5 (0.8)	3 (0.5)	13 (0.6)
内分泌障害	0	1 (0.2)	1 (0.2)	4 (0.7)	13 (0.6)
アジソン病	0	0	0	0	1 (<0.1)
副腎機能不全	0	0	0	0	1 (<0.1)
急性副腎皮質機能不全	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
内分泌障害 (Cont.)			
クッシング症候群	0	0	0
クッシング様症状	0	0	3 (0.4)
甲状腺腫	0	0	1 (0.1)
甲状腺機能亢進症	0	1 (0.8)	0
甲状腺機能低下症	1 (0.8)	0	0
続発性副腎皮質機能不全	0	0	0
甲状腺腫瘤	0	0	1 (0.1)
眼障害	7 (5.3)	4 (3.2)	23 (3.3)
無水晶体眼	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
内分泌障害 (Cont.)					
クッシング症候群	0	1 (0.2)	0	0	0
クッシング様症状	0	0	0	1 (0.2)	4 (0.2)
甲状腺腫	0	0	1 (0.2)	0	2 (<0.1)
甲状腺機能亢進症	0	0	0	0	1 (<0.1)
甲状腺機能低下症	0	0	0	0	0
続発性副腎皮質機能不全	0	0	0	1 (0.2)	1 (<0.1)
甲状腺腫瘤	0	0	0	1 (0.2)	2 (<0.1)
眼障害	4 (16.6)	37 (7.7)	23 (3.7)	33 (5.6)	106 (4.5)
無水晶体眼	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
眼障害 (Cont.)			
眼精疲労	0	0	0
眼瞼炎	0	0	2 (0.3)
眼瞼痙攣	0	0	1 (0.1)
白内障	1 (0.8)	1 (0.8)	4 (0.6)
霰粒腫	0	0	1 (0.1)
結膜嚢胞	0	0	0
結膜出血	0	0	1 (0.1)
結膜充血	0	0	1 (0.1)
アレルギー性結膜炎	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)					
眼精疲労	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
眼瞼炎	0	4 (0.8)	0	3 (0.5)	8 (0.3)
眼瞼痙攣	0	0	0	0	1 (<0.1)
白内障	0	5 (1.0)	5 (0.8)	5 (0.8)	19 (0.8)
霰粒腫	1 (4.2)	0	0	4 (0.7)	6 (0.3)
結膜嚢胞	0	1 (0.2)	0	0	1 (<0.1)
結膜出血	0	1 (0.2)	0	2 (0.3)	4 (0.2)
結膜充血	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
アレルギー性結膜炎	0	3 (0.6)	1 (0.2)	2 (0.3)	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
眼障害 (Cont.)			
結膜弛緩症	0	0	1 (0.1)
角膜びらん	0	0	1 (0.1)
角膜浮腫	0	0	0
角膜混濁	0	0	0
後天性涙道狭窄	0	0	0
ドライアイ	0	0	2 (0.3)
上強膜炎	0	1 (0.8)	0
眼のアレルギー	1 (0.8)	0	0
眼の障害	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)					
結膜弛緩症	0	0	0	0	1 (<0.1)
角膜びらん	0	0	0	0	1 (<0.1)
角膜浮腫	0	0	0	1 (0.2)	1 (<0.1)
角膜混濁	0	1 (0.2)	0	0	0
後天性涙道狭窄	0	2 (0.4)	0	0	1 (<0.1)
ドライアイ	1 (4.2)	1 (0.2)	1 (0.2)	7 (1.2)	12 (0.5)
上強膜炎	0	2 (0.4)	1 (0.2)	0	2 (<0.1)
眼のアレルギー	0	0	0	0	0
眼の障害	0	2 (0.4)	0	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
眼障害 (Cont.)			
眼出血	0	0	0
眼刺激	0	0	1 (0.1)
眼痛	0	0	2 (0.3)
眼そう痒症	0	0	0
眼部腫脹	0	0	0
眼瞼嚢胞	0	0	0
眼瞼障害	0	0	0
眼瞼刺激	0	0	0
眼瞼発疹	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)					
眼出血	0	0	1 (0.2)	0	1 (<0.1)
眼刺激	0	0	1 (0.2)	0	2 (<0.1)
眼痛	0	0	0	0	2 (<0.1)
眼そう痒症	0	0	1 (0.2)	0	1 (<0.1)
眼部腫脹	0	0	1 (0.2)	0	1 (<0.1)
眼瞼嚢胞	0	1 (0.2)	0	0	1 (<0.1)
眼瞼障害	0	1 (0.2)	0	0	0
眼瞼刺激	0	1 (0.2)	0	0	1 (<0.1)
眼瞼発疹	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
眼障害 (Cont.)			
眼瞼肥厚	0	0	0
緑内障	0	0	0
虹彩毛様体炎	1 (0.8)	0	0
角膜炎	0	0	0
流涙増加	0	0	0
黄斑浮腫	0	0	0
近視	0	0	0
眼部不快感	1 (0.8)	0	0
眼充血	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)					
眼瞼肥厚	1 (4.2)	0	0	0	1 (<0.1)
緑内障	0	0	0	3 (0.5)	3 (0.1)
虹彩毛様体炎	0	0	0	0	0
角膜炎	0	1 (0.2)	2 (0.3)	1 (0.2)	3 (0.1)
流涙増加	0	0	1 (0.2)	0	1 (<0.1)
黄斑浮腫	0	0	1 (0.2)	0	1 (<0.1)
近視	0	0	1 (0.2)	0	1 (<0.1)
眼部不快感	0	0	0	0	0
眼充血	0	2 (0.4)	1 (0.2)	1 (0.2)	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
眼障害 (Cont.)			
高眼圧症	0	0	0
開放隅角緑内障	0	0	1 (0.1)
眼窩周囲腫脹	0	0	0
光視症	0	0	1 (0.1)
翼状片	1 (0.8)	0	0
網膜静脈閉塞	0	0	0
潰瘍性角膜炎	0	0	0
ぶどう膜炎	1 (0.8)	0	0
霧視	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)					
高眼圧症	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
開放隅角緑内障	0	0	0	0	1 (<0.1)
眼窩周囲腫脹	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
光視症	0	0	0	0	1 (<0.1)
翼状片	0	0	0	0	0
網膜静脈閉塞	0	0	1 (0.2)	0	1 (<0.1)
潰瘍性角膜炎	0	1 (0.2)	0	0	0
ぶどう膜炎	0	3 (0.6)	1 (0.2)	0	2 (<0.1)
霧視	1 (4.2)	0	0	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
眼障害 (Cont.)			
視力低下	0	1 (0.8)	0
視力障害	0	0	2 (0.3)
硝子体浮遊物	0	1 (0.8)	0
胃腸障害	162 (123.2)	69 (55.1)	357 (51.0)
腹部不快感	3 (2.3)	2 (1.6)	0
腹部膨満	2 (1.5)	1 (0.8)	13 (1.9)
腹部ヘルニア	0	0	0
腹部腫瘤	0	0	0
腹痛	4 (3.0)	2 (1.6)	23 (3.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)					
視力低下	0	1 (0.2)	0	0	0
視力障害	0	0	0	0	2 (<0.1)
硝子体浮遊物	0	0	1 (0.2)	0	2 (<0.1)
胃腸障害	48 (199.3)	335 (70.0)	252 (40.5)	285 (48.2)	1162 (49.4)
腹部不快感	0	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.2)
腹部膨満	2 (8.3)	6 (1.3)	2 (0.3)	11 (1.9)	33 (1.4)
腹部ヘルニア	0	1 (0.2)	0	0	1 (<0.1)
腹部腫瘤	0	1 (0.2)	0	0	0
腹痛	4 (16.6)	17 (3.6)	17 (2.7)	15 (2.5)	71 (3.0)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
下腹部痛	2 (1.5)	0	3 (0.4)
上腹部痛	5 (3.8)	2 (1.6)	8 (1.1)
腹部圧痛	1 (0.8)	0	8 (1.1)
異常便	0	0	0
無酸症	0	0	0
裂肛	1 (0.8)	0	3 (0.4)
痔瘻	0	0	2 (0.3)
肛門失禁	0	0	1 (0.1)
肛門の炎症	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
下腹部痛	0	7 (1.5)	3 (0.5)	2 (0.3)	11 (0.5)
上腹部痛	0	6 (1.3)	8 (1.3)	7 (1.2)	28 (1.2)
腹部圧痛	1 (4.2)	0	3 (0.5)	4 (0.7)	16 (0.7)
異常便	0	1 (0.2)	0	0	0
無酸症	0	0	0	1 (0.2)	1 (<0.1)
裂肛	1 (4.2)	3 (0.6)	3 (0.5)	2 (0.3)	11 (0.5)
痔瘻	0	0	1 (0.2)	4 (0.7)	7 (0.3)
肛門失禁	0	0	0	0	1 (<0.1)
肛門の炎症	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
肛門ポリープ	0	0	0
肛門そう痒症	0	0	0
肛門潰瘍	0	0	0
口角口唇炎	0	0	1 (0.1)
肛門直腸不快感	0	0	0
アフタ性潰瘍	4 (3.0)	1 (0.8)	7 (1.0)
口唇のひび割れ	0	0	1 (0.1)
大腸炎	7 (5.3)	0	3 (0.4)
虚血性大腸炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
肛門ポリープ	0	0	0	1 (0.2)	1 (<0.1)
肛門そう痒症	0	3 (0.6)	0	0	1 (<0.1)
肛門潰瘍	1 (4.2)	0	0	0	1 (<0.1)
口角口唇炎	0	0	0	0	1 (<0.1)
肛門直腸不快感	1 (4.2)	0	0	0	1 (<0.1)
アフタ性潰瘍	0	4 (0.8)	2 (0.3)	7 (1.2)	19 (0.8)
口唇のひび割れ	0	0	0	0	1 (<0.1)
大腸炎	0	3 (0.6)	3 (0.5)	0	6 (0.3)
虚血性大腸炎	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
潰瘍性大腸炎	77 (58.6)	18 (14.4)	104 (14.9)
結腸異形成	0	0	3 (0.4)
便秘	3 (2.3)	0	7 (1.0)
クローン病	0	0	1 (0.1)
便意切迫	2 (1.5)	0	3 (0.4)
齲歯	1 (0.8)	1 (0.8)	2 (0.3)
歯嚢胞	0	0	0
歯不快感	0	0	1 (0.1)
歯組織の壊死	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
潰瘍性大腸炎	21 (87.2)	122 (25.5)	91 (14.6)	64 (10.8)	326 (13.9)
結腸異形成	0	0	2 (0.3)	2 (0.3)	7 (0.3)
便秘	3 (12.5)	18 (3.8)	12 (1.9)	16 (2.7)	53 (2.3)
クローン病	0	0	0	0	1 (<0.1)
便意切迫	0	0	1 (0.2)	1 (0.2)	5 (0.2)
齲歯	0	5 (1.0)	1 (0.2)	3 (0.5)	11 (0.5)
歯嚢胞	0	0	0	1 (0.2)	1 (<0.1)
歯不快感	0	0	0	0	1 (<0.1)
歯組織の壊死	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
横隔膜ヘルニア	1 (0.8)	0	0
下痢	1 (0.8)	6 (4.8)	11 (1.6)
血性下痢	0	0	0
腸憩室	0	0	0
口内乾燥	0	1 (0.8)	0
十二指腸炎	0	0	0
排便困難	1 (0.8)	0	0
消化不良	3 (2.3)	0	12 (1.7)
嚥下障害	1 (0.8)	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
横隔膜ヘルニア	0	0	0	0	0
下痢	3 (12.5)	13 (2.7)	10 (1.6)	4 (0.7)	43 (1.8)
血性下痢	1 (4.2)	1 (0.2)	0	0	2 (<0.1)
腸憩室	0	0	1 (0.2)	0	1 (<0.1)
口内乾燥	0	1 (0.2)	0	2 (0.3)	4 (0.2)
十二指腸炎	0	0	0	1 (0.2)	1 (<0.1)
排便困難	0	0	0	0	0
消化不良	0	11 (2.3)	4 (0.6)	7 (1.2)	31 (1.3)
嚥下障害	0	1 (0.2)	2 (0.3)	1 (0.2)	4 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
小腸炎	0	0	1 (0.1)
腸炎	0	0	0
心窩部不快感	0	0	1 (0.1)
おくび	0	0	1 (0.1)
糞塊	1 (0.8)	0	0
変色便	0	0	0
白色便	0	0	1 (0.1)
軟便	0	0	1 (0.1)
大腿ヘルニア	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
小腸炎	0	0	1 (0.2)	2 (0.3)	4 (0.2)
腸炎	0	1 (0.2)	0	2 (0.3)	3 (0.1)
心窩部不快感	0	0	0	0	1 (<0.1)
おくび	0	0	0	1 (0.2)	2 (<0.1)
糞塊	0	1 (0.2)	0	0	0
変色便	0	0	0	1 (0.2)	1 (<0.1)
白色便	0	0	0	0	1 (<0.1)
軟便	0	0	0	0	1 (<0.1)
大腿ヘルニア	0	3 (0.6)	0	0	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
鼓腸	5 (3.8)	2 (1.6)	12 (1.7)
食中毒	3 (2.3)	0	1 (0.1)
排便回数増加	0	0	3 (0.4)
胃障害	0	0	1 (0.1)
胃ポリープ	0	0	0
胃潰瘍	0	0	0
胃炎	0	2 (1.6)	2 (0.3)
びらん性胃炎	0	0	0
胃腸障害	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
鼓腸	0	7 (1.5)	2 (0.3)	6 (1.0)	26 (1.1)
食中毒	0	2 (0.4)	0	0	3 (0.1)
排便回数増加	0	0	0	4 (0.7)	7 (0.3)
胃障害	0	0	0	0	1 (<0.1)
胃ポリープ	0	1 (0.2)	0	0	1 (<0.1)
胃潰瘍	0	0	1 (0.2)	0	1 (<0.1)
胃炎	0	3 (0.6)	5 (0.8)	1 (0.2)	11 (0.5)
びらん性胃炎	0	0	1 (0.2)	0	1 (<0.1)
胃腸障害	0	1 (0.2)	0	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
消化管運動障害	0	0	1 (0.1)
消化器痛	0	1 (0.8)	0
胃食道逆流性疾患	3 (2.3)	3 (2.4)	11 (1.6)
歯肉痛	0	0	1 (0.1)
歯肉腫脹	0	0	0
舌痛	0	0	0
血便排泄	0	1 (0.8)	0
痔出血	0	0	1 (0.1)
痔核	4 (3.0)	5 (4.0)	7 (1.0)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
消化管運動障害	0	0	0	0	1 (<0.1)
消化器痛	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
胃食道逆流性疾患	0	9 (1.9)	8 (1.3)	8 (1.4)	34 (1.4)
歯肉痛	0	0	1 (0.2)	1 (0.2)	3 (0.1)
歯肉腫脹	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
舌痛	0	1 (0.2)	0	0	0
血便排泄	0	4 (0.8)	0	0	2 (<0.1)
痔出血	1 (4.2)	3 (0.6)	1 (0.2)	0	4 (0.2)
痔核	1 (4.2)	6 (1.3)	16 (2.6)	7 (1.2)	40 (1.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
血栓性痔核	0	0	0
裂孔ヘルニア	0	0	2 (0.3)
胃酸過多	0	0	0
肛門肥大乳頭	0	0	1 (0.1)
回腸潰瘍	1 (0.8)	0	0
イレウス	0	1 (0.8)	1 (0.1)
炎症性腸疾患	0	0	1 (0.1)
単径ヘルニア	0	0	0
腸閉塞	1 (0.8)	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
血栓性痔核	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
裂孔ヘルニア	0	0	0	0	2 (<0.1)
胃酸過多	0	0	0	1 (0.2)	1 (<0.1)
肛門肥大乳頭	0	0	0	0	1 (<0.1)
回腸潰瘍	0	0	0	0	0
イレウス	0	0	0	2 (0.3)	4 (0.2)
炎症性腸疾患	0	0	0	0	1 (<0.1)
単径ヘルニア	0	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.2)
腸閉塞	0	0	1 (0.2)	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
腸管ポリープ	0	0	0
過敏性腸症候群	0	0	1 (0.1)
大腸穿孔	1 (0.8)	0	1 (0.1)
大腸ポリープ	1 (0.8)	6 (4.8)	4 (0.6)
口唇水疱	0	0	0
口唇障害	0	0	0
口唇乾燥	0	0	0
口唇腫脹	0	0	0
口唇潰瘍	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
腸管ポリープ	0	0	1 (0.2)	0	1 (<0.1)
過敏性腸症候群	0	0	2 (0.3)	1 (0.2)	4 (0.2)
大腸穿孔	0	1 (0.2)	0	0	1 (<0.1)
大腸ポリープ	0	5 (1.0)	3 (0.5)	7 (1.2)	22 (0.9)
口唇水疱	0	0	0	1 (0.2)	1 (<0.1)
口唇障害	0	0	1 (0.2)	0	1 (<0.1)
口唇乾燥	1 (4.2)	0	0	0	1 (<0.1)
口唇腫脹	0	0	0	1 (0.2)	1 (<0.1)
口唇潰瘍	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
口腔嚢胞	0	0	0
口腔内潰瘍形成	1 (0.8)	2 (1.6)	3 (0.4)
粘液便	0	0	0
悪心	12 (9.1)	5 (4.0)	29 (4.1)
非感染性歯肉炎	0	0	0
嚥下痛	0	1 (0.8)	0
食道運動低下	0	0	1 (0.1)
食道痛	0	0	1 (0.1)
食道潰瘍	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
口腔嚢胞	0	1 (0.2)	0	0	0
口腔内潰瘍形成	0	4 (0.8)	1 (0.2)	2 (0.3)	9 (0.4)
粘液便	0	1 (0.2)	0	0	0
悪心	2 (8.3)	15 (3.1)	14 (2.2)	26 (4.4)	85 (3.6)
非感染性歯肉炎	0	0	0	1 (0.2)	1 (<0.1)
嚥下痛	0	2 (0.4)	0	2 (0.3)	3 (0.1)
食道運動低下	0	0	0	0	1 (<0.1)
食道痛	0	0	0	0	1 (<0.1)
食道潰瘍	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
食道炎	0	0	0
口腔障害	0	0	0
口腔知覚不全	0	0	0
口腔扁平苔癬	0	0	1 (0.1)
口腔粘膜紅斑	0	0	0
口腔内痛	0	0	0
膵臓障害	0	0	1 (0.1)
膵脂肪変性	0	0	1 (0.1)
膵炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
食道炎	0	0	1 (0.2)	0	1 (<0.1)
口腔障害	0	0	0	1 (0.2)	1 (<0.1)
口腔知覚不全	0	1 (0.2)	0	0	1 (<0.1)
口腔扁平苔癬	0	0	0	0	1 (<0.1)
口腔粘膜紅斑	0	0	0	1 (0.2)	1 (<0.1)
口腔内痛	0	0	2 (0.3)	1 (0.2)	3 (0.1)
膵臓障害	0	0	0	0	1 (<0.1)
膵脂肪変性	0	0	0	0	1 (<0.1)
膵炎	1 (4.2)	1 (0.2)	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
肛門周囲紅斑	0	0	1 (0.1)
歯周病	0	0	1 (0.1)
肛門周囲痛	0	0	4 (0.6)
直腸炎	0	0	2 (0.3)
偽性ポリポーシス	0	1 (0.8)	1 (0.1)
直腸分泌物	1 (0.8)	0	0
直腸異形成	0	0	0
直腸出血	0	2 (1.6)	5 (0.7)
直腸ポリープ	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
肛門周囲紅斑	0	0	0	0	1 (<0.1)
歯周病	0	1 (0.2)	0	2 (0.3)	3 (0.1)
肛門周囲痛	1 (4.2)	3 (0.6)	1 (0.2)	1 (0.2)	10 (0.4)
直腸炎	0	1 (0.2)	0	0	2 (<0.1)
偽性ポリポーシス	0	1 (0.2)	0	0	3 (0.1)
直腸分泌物	0	0	0	1 (0.2)	1 (<0.1)
直腸異形成	1 (4.2)	0	2 (0.3)	0	3 (0.1)
直腸出血	0	2 (0.4)	1 (0.2)	2 (0.3)	10 (0.4)
直腸ポリープ	0	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
直腸攣縮	0	0	0
直腸しぶり	0	0	1 (0.1)
口内炎	4 (3.0)	0	3 (0.4)
舌障害	0	0	1 (0.1)
舌潰瘍	0	0	0
歯の障害	0	0	1 (0.1)
埋伏歯	0	0	1 (0.1)
歯の脱落	0	0	0
歯痛	0	1 (0.8)	7 (1.0)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
直腸攣縮	0	1 (0.2)	0	0	0
直腸しぶり	1 (4.2)	1 (0.2)	1 (0.2)	0	3 (0.1)
口内炎	0	9 (1.9)	2 (0.3)	9 (1.5)	20 (0.9)
舌障害	0	0	0	0	1 (<0.1)
舌潰瘍	0	0	0	2 (0.3)	2 (<0.1)
歯の障害	0	0	0	1 (0.2)	2 (<0.1)
埋伏歯	0	0	1 (0.2)	1 (0.2)	3 (0.1)
歯の脱落	0	0	0	1 (0.2)	1 (<0.1)
歯痛	0	1 (0.2)	8 (1.3)	9 (1.5)	26 (1.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
臍ヘルニア	0	0	0
嘔吐	4 (3.0)	2 (1.6)	14 (2.0)
一般・全身障害および投与部位の状態	41 (31.2)	18 (14.4)	141 (20.2)
医薬品副作用	0	1 (0.8)	0
無力症	2 (1.5)	0	6 (0.9)
胸部不快感	1 (0.8)	0	0
胸痛	1 (0.8)	1 (0.8)	9 (1.3)
悪寒	3 (2.3)	1 (0.8)	7 (1.0)
医療機器に対する不耐性	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
臍ヘルニア	0	4 (0.8)	0	1 (0.2)	4 (0.2)
嘔吐	1 (4.2)	6 (1.3)	1 (0.2)	13 (2.2)	36 (1.5)
一般・全身障害および投与部位の状態	18 (74.8)	85 (17.8)	131 (21.0)	130 (22.0)	481 (20.5)
医薬品副作用	0	0	1 (0.2)	0	2 (<0.1)
無力症	2 (8.3)	0	2 (0.3)	3 (0.5)	13 (0.6)
胸部不快感	2 (8.3)	0	2 (0.3)	2 (0.3)	6 (0.3)
胸痛	0	1 (0.2)	6 (1.0)	7 (1.2)	23 (1.0)
悪寒	0	5 (1.0)	6 (1.0)	6 (1.0)	22 (0.9)
医療機器に対する不耐性	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
不快感	0	0	0
薬効欠如	0	0	1 (0.1)
異形成	0	0	1 (0.1)
顔面浮腫	0	0	0
疲労	6 (4.6)	6 (4.8)	26 (3.7)
異常感	0	0	1 (0.1)
びくびく感	0	0	0
体温変動感	0	0	1 (0.1)
全身性浮腫	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
不快感	0	0	0	1 (0.2)	1 (<0.1)
薬効欠如	0	1 (0.2)	0	0	1 (<0.1)
異形成	0	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.2)
顔面浮腫	0	1 (0.2)	0	0	1 (<0.1)
疲労	1 (4.2)	11 (2.3)	26 (4.2)	25 (4.2)	87 (3.7)
異常感	0	0	0	1 (0.2)	2 (<0.1)
びくびく感	0	0	1 (0.2)	0	1 (<0.1)
体温変動感	0	0	0	0	1 (<0.1)
全身性浮腫	0	0	1 (0.2)	0	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
宿酔	1 (0.8)	0	0
過形成	0	0	0
高体温症	0	0	3 (0.4)
治癒不良	0	0	1 (0.1)
硬結	0	1 (0.8)	0
炎症	0	0	0
インフルエンザ様疾患	1 (0.8)	2 (1.6)	13 (1.9)
注入部位反応	0	0	0
注射部位疼痛	0	2 (1.6)	9 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
宿酔	0	0	0	0	0
過形成	0	1 (0.2)	0	0	1 (<0.1)
高体温症	0	1 (0.2)	0	0	3 (0.1)
治癒不良	0	0	0	0	1 (<0.1)
硬結	0	0	0	0	0
炎症	0	0	0	1 (0.2)	1 (<0.1)
インフルエンザ様疾患	0	2 (0.4)	3 (0.5)	2 (0.3)	20 (0.9)
注入部位反応	0	1 (0.2)	0	0	1 (<0.1)
注射部位疼痛	0	9 (1.9)	30 (4.8)	20 (3.4)	68 (2.9)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
医療機器関連損傷	0	0	0
倦怠感	1 (0.8)	0	3 (0.4)
腫瘤	0	0	0
粘膜乾燥	0	0	0
小結節	0	0	1 (0.1)
非心臓性胸痛	0	0	0
浮腫	0	0	0
末梢性浮腫	2 (1.5)	1 (0.8)	2 (0.3)
疼痛	3 (2.3)	0	8 (1.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
医療機器関連損傷	0	1 (0.2)	0	0	1 (<0.1)
倦怠感	1 (4.2)	2 (0.4)	10 (1.6)	5 (0.8)	19 (0.8)
腫瘤	0	0	0	3 (0.5)	3 (0.1)
粘膜乾燥	0	1 (0.2)	0	0	0
小結節	0	0	0	2 (0.3)	3 (0.1)
非心臓性胸痛	1 (4.2)	1 (0.2)	0	0	1 (<0.1)
浮腫	0	0	1 (0.2)	0	1 (<0.1)
末梢性浮腫	0	5 (1.0)	3 (0.5)	3 (0.5)	11 (0.5)
疼痛	0	3 (0.6)	4 (0.6)	5 (0.8)	19 (0.8)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
末梢腫脹	1 (0.8)	0	2 (0.3)
ポリープ	1 (0.8)	0	1 (0.1)
偽ポリープ	0	0	3 (0.4)
発熱	14 (10.6)	3 (2.4)	38 (5.4)
異物感	0	0	0
腫脹	0	0	0
顔面腫脹	0	0	2 (0.3)
潰瘍	1 (0.8)	0	0
評価不能の事象	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
末梢腫脹	0	2 (0.4)	1 (0.2)	2 (0.3)	6 (0.3)
ポリープ	0	0	0	0	1 (<0.1)
偽ポリープ	0	0	0	2 (0.3)	5 (0.2)
発熱	11 (45.7)	32 (6.7)	29 (4.7)	35 (5.9)	136 (5.8)
異物感	0	2 (0.4)	0	0	1 (<0.1)
腫脹	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
顔面腫脹	0	0	0	2 (0.3)	4 (0.2)
潰瘍	0	0	0	0	0
評価不能の事象	0	0	1 (0.2)	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
ワクチン接種部位紅斑	1 (0.8)	0	0
ワクチン接種部位疼痛	1 (0.8)	0	0
ワクチン接種部位反応	0	0	0
乾燥症	1 (0.8)	0	0
肝胆道系障害	6 (4.6)	3 (2.4)	15 (2.1)
胆道ジスキネジア	0	0	0
胆汁性嚢胞	0	0	0
硬化性胆管炎	0	1 (0.8)	0
胆嚢炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
ワクチン接種部位紅斑	0	0	0	0	0
ワクチン接種部位疼痛	0	0	2 (0.3)	1 (0.2)	3 (0.1)
ワクチン接種部位反応	0	1 (0.2)	0	0	1 (<0.1)
乾燥症	0	0	0	0	0
肝胆道系障害	1 (4.2)	10 (2.1)	20 (3.2)	8 (1.4)	53 (2.3)
胆道ジスキネジア	0	0	1 (0.2)	0	1 (<0.1)
胆汁性嚢胞	0	0	1 (0.2)	0	1 (<0.1)
硬化性胆管炎	0	0	3 (0.5)	1 (0.2)	5 (0.2)
胆嚢炎	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
胆石症	0	0	3 (0.4)
胆汁うっ滞	1 (0.8)	0	0
薬物性肝障害	0	0	0
肝嚢胞	0	0	1 (0.1)
肝機能異常	0	0	3 (0.4)
脂肪肝	0	2 (1.6)	4 (0.6)
肝炎	0	0	1 (0.1)
肝細胞損傷	0	0	1 (0.1)
肝腫大	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
肝胆道系障害 (Cont.)					
胆石症	0	0	1 (0.2)	2 (0.3)	6 (0.3)
胆汁うっ滞	0	0	0	0	0
薬物性肝障害	0	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.1)
肝嚢胞	0	0	0	0	1 (<0.1)
肝機能異常	0	3 (0.6)	5 (0.8)	3 (0.5)	11 (0.5)
脂肪肝	0	1 (0.2)	4 (0.6)	0	11 (0.5)
肝炎	0	0	0	0	1 (<0.1)
肝細胞損傷	0	0	0	0	1 (<0.1)
肝腫大	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
高ビリルビン血症	2 (1.5)	0	0
高トランスアミナーゼ血症	0	0	0
肝障害	1 (0.8)	0	0
肝損傷	1 (0.8)	0	0
非アルコール性脂肪性肝炎	0	0	1 (0.1)
非アルコール性脂肪性肝疾患	0	0	1 (0.1)
門脈血栓症	1 (0.8)	0	0
免疫系障害	5 (3.8)	2 (1.6)	15 (2.1)
動物アレルギー	1 (0.8)	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
肝胆道系障害 (Cont.)					
高ビリルビン血症	0	0	0	0	0
高トランスアミナーゼ血症	1 (4.2)	0	1 (0.2)	0	2 (<0.1)
肝障害	0	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.2)
肝損傷	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
非アルコール性脂肪性肝炎	0	0	0	0	1 (<0.1)
非アルコール性脂肪性肝疾患	0	1 (0.2)	0	0	2 (<0.1)
門脈血栓症	0	0	0	0	0
免疫系障害	0	4 (0.8)	7 (1.1)	3 (0.5)	30 (1.3)
動物アレルギー	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
免疫系障害 (Cont.)			
アミロイドーシス	1 (0.8)	0	0
アナフィラキシー反応	0	0	0
薬物過敏症	1 (0.8)	0	1 (0.1)
粉塵アレルギー	1 (0.8)	0	1 (0.1)
食物アレルギー	0	1 (0.8)	0
過敏症	0	0	1 (0.1)
ダニアレルギー	0	0	1 (0.1)
季節性アレルギー	1 (0.8)	1 (0.8)	10 (1.4)
感染症および寄生虫症	116 (88.2)	79 (63.1)	529 (75.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
免疫系障害 (Cont.)					
アミロイドーシス	0	0	0	0	0
アナフィラキシー反応	0	0	0	1 (0.2)	1 (<0.1)
薬物過敏症	0	1 (0.2)	3 (0.5)	0	4 (0.2)
粉塵アレルギー	0	0	0	0	1 (<0.1)
食物アレルギー	0	0	0	0	1 (<0.1)
過敏症	0	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.2)
ダニアレルギー	0	0	0	0	1 (<0.1)
季節性アレルギー	0	2 (0.4)	3 (0.5)	1 (0.2)	17 (0.7)
感染症および寄生虫症	39 (162.0)	398 (83.2)	426 (68.4)	457 (77.2)	1774 (75.5)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
腹部膿瘍	0	0	1 (0.1)
腹壁膿瘍	0	0	0
膿瘍	1 (0.8)	0	0
頚部膿瘍	0	0	1 (0.1)
ダニ皮膚炎	0	0	2 (0.3)
急性心内膜炎	0	0	0
急性副鼻腔炎	0	0	1 (0.1)
アデノウイルス感染	0	0	0
歯槽骨炎	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
腹部膿瘍	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
腹壁膿瘍	0	0	1 (0.2)	0	1 (<0.1)
膿瘍	0	1 (0.2)	0	0	1 (<0.1)
頚部膿瘍	0	0	0	0	1 (<0.1)
ダニ皮膚炎	0	1 (0.2)	2 (0.3)	0	5 (0.2)
急性心内膜炎	0	1 (0.2)	0	0	0
急性副鼻腔炎	0	2 (0.4)	0	0	3 (0.1)
アデノウイルス感染	0	1 (0.2)	0	0	1 (<0.1)
歯槽骨炎	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
肛門膿瘍	1 (0.8)	0	3 (0.4)
肛門直腸感染	0	0	0
虫垂炎	0	0	0
細菌性関節炎	0	0	0
無症候性COVID-19	0	0	2 (0.3)
無症候性細菌尿	0	0	0
異型肺炎	0	0	1 (0.1)
細菌感染	0	0	0
細菌性膣症	1 (0.8)	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
肛門膿瘍	0	1 (0.2)	5 (0.8)	3 (0.5)	12 (0.5)
肛門直腸感染	0	2 (0.4)	0	0	0
虫垂炎	0	0	4 (0.6)	1 (0.2)	5 (0.2)
細菌性関節炎	0	0	1 (0.2)	0	1 (<0.1)
無症候性COVID-19	0	1 (0.2)	1 (0.2)	3 (0.5)	6 (0.3)
無症候性細菌尿	0	0	1 (0.2)	0	1 (<0.1)
異型肺炎	0	0	0	1 (0.2)	2 (<0.1)
細菌感染	0	3 (0.6)	0	1 (0.2)	4 (0.2)
細菌性膣症	0	1 (0.2)	1 (0.2)	0	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
細菌尿	0	1 (0.8)	0
バルトリン腺炎	0	0	0
ブラストシスティス感染	0	0	0
体部白癬	0	0	0
ボレリア感染	0	0	0
乳房膿瘍	0	0	0
気管支炎	4 (3.0)	1 (0.8)	24 (3.4)
感染性滑液包炎	0	0	0
COVID-19	4 (3.0)	2 (1.6)	23 (3.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
細菌尿	0	0	0	0	1 (<0.1)
バルトリン腺炎	0	1 (0.2)	0	0	1 (<0.1)
ブラストシスティス感染	0	0	1 (0.2)	0	1 (<0.1)
体部白癬	1 (4.2)	0	0	0	1 (<0.1)
ボレリア感染	0	0	1 (0.2)	0	1 (<0.1)
乳房膿瘍	0	0	1 (0.2)	0	1 (<0.1)
気管支炎	2 (8.3)	10 (2.1)	9 (1.4)	6 (1.0)	49 (2.1)
感染性滑液包炎	0	0	0	1 (0.2)	1 (<0.1)
COVID-19	1 (4.2)	32 (6.7)	26 (4.2)	38 (6.4)	112 (4.8)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
COVID-19肺炎	0	0	4 (0.6)
カンピロバクター胃腸炎	0	0	1 (0.1)
カンピロバクター感染	0	0	0
カンジダ感染	0	0	0
蜂巣炎	8 (6.1)	1 (0.8)	4 (0.6)
条虫感染	0	0	0
感染性胆嚢炎	0	0	0
慢性副鼻腔炎	0	0	1 (0.1)
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
COVID-19肺炎	0	5 (1.0)	10 (1.6)	9 (1.5)	27 (1.1)
カンピロバクター胃腸炎	0	0	1 (0.2)	1 (0.2)	3 (0.1)
カンピロバクター感染	0	0	4 (0.6)	0	4 (0.2)
カンジダ感染	0	1 (0.2)	1 (0.2)	2 (0.3)	3 (0.1)
蜂巣炎	0	1 (0.2)	6 (1.0)	3 (0.5)	14 (0.6)
条虫感染	1 (4.2)	0	0	0	1 (<0.1)
感染性胆嚢炎	0	0	1 (0.2)	0	1 (<0.1)
慢性副鼻腔炎	0	0	0	0	1 (<0.1)
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.2)	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
クロストリジウム・ディフィシレ感染	3 (2.3)	2 (1.6)	9 (1.3)
結腸膿瘍	0	0	0
結膜炎	2 (1.5)	0	1 (0.1)
ウイルス性結膜炎	1 (0.8)	0	0
コロナウイルス感染	0	0	0
サイクロスポリジウム感染	0	0	0
膀胱炎	0	3 (2.4)	16 (2.3)
サイトメガロウイルス性大腸炎	0	0	0
サイトメガロウイルス感染	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
クロストリジウム・ディフィシレ感染	0	2 (0.4)	4 (0.6)	7 (1.2)	22 (0.9)
結腸膿瘍	0	0	1 (0.2)	0	1 (<0.1)
結膜炎	0	0	4 (0.6)	3 (0.5)	8 (0.3)
ウイルス性結膜炎	0	1 (0.2)	0	0	1 (<0.1)
コロナウイルス感染	0	2 (0.4)	1 (0.2)	0	3 (0.1)
サイクロスポリジウム感染	0	1 (0.2)	0	0	1 (<0.1)
膀胱炎	1 (4.2)	5 (1.0)	10 (1.6)	4 (0.7)	38 (1.6)
サイトメガロウイルス性大腸炎	0	0	0	2 (0.3)	2 (<0.1)
サイトメガロウイルス感染	1 (4.2)	1 (0.2)	2 (0.3)	0	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
毛嚢虫症	0	1 (0.8)	2 (0.3)
デング熱	0	0	0
感染性皮膚炎	0	0	0
皮膚糸状菌症	0	0	1 (0.1)
爪の皮膚糸状菌症	0	0	1 (0.1)
医療機器関連敗血症	0	0	0
感染性下痢	0	0	0
憩室炎	0	0	2 (0.3)
耳感染	2 (1.5)	0	9 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
毛嚢虫症	0	0	4 (0.6)	4 (0.7)	11 (0.5)
デング熱	0	0	0	1 (0.2)	1 (<0.1)
感染性皮膚炎	0	1 (0.2)	0	0	1 (<0.1)
皮膚糸状菌症	0	1 (0.2)	0	0	1 (<0.1)
爪の皮膚糸状菌症	0	0	0	3 (0.5)	4 (0.2)
医療機器関連敗血症	0	0	0	1 (0.2)	1 (<0.1)
感染性下痢	0	1 (0.2)	1 (0.2)	2 (0.3)	4 (0.2)
憩室炎	0	0	0	1 (0.2)	3 (0.1)
耳感染	0	1 (0.2)	5 (0.8)	4 (0.7)	19 (0.8)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
感染性腸炎	0	0	1 (0.1)
蟯虫症	0	0	1 (0.1)
腸球菌感染	1 (0.8)	0	0
エンテロウイルス感染	0	0	0
丹毒	0	0	2 (0.3)
遊走性紅斑	0	0	1 (0.1)
大腸菌感染	2 (1.5)	0	1 (0.1)
大腸菌性敗血症	0	0	1 (0.1)
大腸菌性尿路感染	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
感染性腸炎	0	0	0	1 (0.2)	2 (<0.1)
蟯虫症	0	0	0	0	1 (<0.1)
腸球菌感染	0	0	0	0	0
エンテロウイルス感染	0	0	0	1 (0.2)	1 (<0.1)
丹毒	0	0	0	0	2 (<0.1)
遊走性紅斑	0	0	0	0	1 (<0.1)
大腸菌感染	0	1 (0.2)	2 (0.3)	0	4 (0.2)
大腸菌性敗血症	0	0	0	0	1 (<0.1)
大腸菌性尿路感染	0	1 (0.2)	1 (0.2)	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
眼感染	0	0	0
眼瞼感染	0	0	0
毛包炎	2 (1.5)	0	6 (0.9)
真菌感染	1 (0.8)	0	0
皮膚真菌感染	2 (1.5)	0	2 (0.3)
せつ	0	0	2 (0.3)
胃腸炎	4 (3.0)	2 (1.6)	15 (2.1)
ノロウイルス性胃腸炎	1 (0.8)	0	0
ウイルス性胃腸炎	0	1 (0.8)	6 (0.9)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
眼感染	0	0	1 (0.2)	0	1 (<0.1)
眼瞼感染	0	0	0	1 (0.2)	1 (<0.1)
毛包炎	2 (8.3)	7 (1.5)	11 (1.8)	23 (3.9)	45 (1.9)
真菌感染	0	0	0	1 (0.2)	1 (<0.1)
皮膚真菌感染	0	2 (0.4)	1 (0.2)	2 (0.3)	7 (0.3)
せつ	0	0	1 (0.2)	2 (0.3)	5 (0.2)
胃腸炎	1 (4.2)	10 (2.1)	9 (1.4)	11 (1.9)	44 (1.9)
ノロウイルス性胃腸炎	1 (4.2)	0	0	0	1 (<0.1)
ウイルス性胃腸炎	0	2 (0.4)	4 (0.6)	5 (0.8)	18 (0.8)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
消化管内細菌過剰増殖	0	0	1 (0.1)
消化管感染	0	0	1 (0.1)
性器カンジダ症	0	0	1 (0.1)
陰部ヘルペス	0	0	1 (0.1)
陰部単純ヘルペス	0	0	0
真菌性性器感染	0	0	0
歯肉膿瘍	0	0	0
歯肉炎	1 (0.8)	0	0
鼡径部膿瘍	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
消化管内細菌過剰増殖	0	0	0	0	1 (<0.1)
消化管感染	0	0	0	1 (0.2)	2 (<0.1)
性器カンジダ症	0	0	0	0	1 (<0.1)
陰部ヘルペス	0	2 (0.4)	1 (0.2)	2 (0.3)	6 (0.3)
陰部単純ヘルペス	0	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.2)
真菌性性器感染	0	1 (0.2)	0	0	1 (<0.1)
歯肉膿瘍	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
歯肉炎	0	5 (1.0)	1 (0.2)	1 (0.2)	7 (0.3)
肛径部膿瘍	0	1 (0.2)	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ヘモフィルス感染	0	0	0
手足口病	0	0	0
ヘリコバクター性胃炎	0	0	0
ヘリコバクター感染	0	0	1 (0.1)
伝染性単核症肝炎	0	0	1 (0.1)
ヘルペス性皮膚炎	0	0	0
ヘルペス眼感染	0	0	0
単純ヘルペス	0	6 (4.8)	4 (0.6)
単純ヘルペス性咽頭炎	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ヘモフィルス感染	0	1 (0.2)	0	0	0
手足口病	0	0	0	1 (0.2)	1 (<0.1)
ヘリコバクター性胃炎	0	1 (0.2)	0	0	1 (<0.1)
ヘリコバクター感染	0	0	1 (0.2)	0	2 (<0.1)
伝染性単核症肝炎	0	0	0	0	1 (<0.1)
ヘルペス性皮膚炎	0	0	1 (0.2)	0	1 (<0.1)
ヘルペス眼感染	0	0	0	1 (0.2)	1 (<0.1)
単純ヘルペス	0	5 (1.0)	4 (0.6)	2 (0.3)	21 (0.9)
単純ヘルペス性咽頭炎	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
帯状疱疹	0	4 (3.2)	24 (3.4)
播種性帯状疱疹	0	0	0
神経合併症を伴う帯状疱疹感染	0	0	1 (0.1)
帯状疱疹性髄膜炎	0	0	0
耳帯状疱疹	0	0	0
麦粒腫	1 (0.8)	3 (2.4)	4 (0.6)
膿痂疹	0	0	2 (0.3)
咬傷感染	0	0	0
感染性嚢腫	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
帯状疱疹	7 (29.1)	11 (2.3)	32 (5.1)	31 (5.2)	107 (4.6)
播種性帯状疱疹	0	1 (0.2)	0	0	1 (<0.1)
神経合併症を伴う帯状疱疹感染	0	0	0	0	1 (<0.1)
帯状疱疹性髄膜炎	0	0	0	1 (0.2)	1 (<0.1)
耳帯状疱疹	0	0	1 (0.2)	0	1 (<0.1)
麦粒腫	0	4 (0.8)	5 (0.8)	4 (0.7)	17 (0.7)
膿痂疹	0	1 (0.2)	2 (0.3)	1 (0.2)	5 (0.2)
咬傷感染	0	0	0	1 (0.2)	1 (<0.1)
感染性嚢腫	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
感染性皮膚嚢腫	0	0	0
感染	0	1 (0.8)	1 (0.1)
伝染性単核症	0	0	2 (0.3)
インフルエンザ	1 (0.8)	2 (1.6)	24 (3.4)
クレブシエラ感染	0	0	1 (0.1)
大腸感染	0	0	0
喉頭炎	0	0	2 (0.3)
潜伏結核	0	1 (0.8)	4 (0.6)
限局性感染	1 (0.8)	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
感染性皮膚嚢腫	0	0	1 (0.2)	0	1 (<0.1)
感染	0	0	0	0	1 (<0.1)
伝染性単核症	0	0	0	0	2 (<0.1)
インフルエンザ	3 (12.5)	10 (2.1)	19 (3.1)	19 (3.2)	72 (3.1)
クレブシエラ感染	0	0	0	0	1 (<0.1)
大腸感染	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
喉頭炎	0	2 (0.4)	1 (0.2)	2 (0.3)	6 (0.3)
潜伏結核	0	2 (0.4)	3 (0.5)	4 (0.7)	14 (0.6)
限局性感染	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
下気道感染	2 (1.5)	0	1 (0.1)
ライム病	0	1 (0.8)	0
乳腺炎	0	0	0
伝染性軟属腫	0	0	0
筋膿瘍	1 (0.8)	0	0
上咽頭炎	18 (13.7)	12 (9.6)	69 (9.9)
食道カンジダ症	0	0	0
爪真菌症	0	0	3 (0.4)
口腔カンジダ症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
下気道感染	0	3 (0.6)	2 (0.3)	1 (0.2)	6 (0.3)
ライム病	0	0	0	1 (0.2)	2 (<0.1)
乳腺炎	0	0	1 (0.2)	0	1 (<0.1)
伝染性軟属腫	0	1 (0.2)	0	0	0
筋膿瘍	0	0	0	0	0
上咽頭炎	2 (8.3)	61 (12.7)	67 (10.8)	74 (12.5)	259 (11.0)
食道カンジダ症	0	0	1 (0.2)	0	1 (<0.1)
爪真菌症	0	7 (1.5)	2 (0.3)	1 (0.2)	11 (0.5)
口腔カンジダ症	1 (4.2)	2 (0.4)	1 (0.2)	3 (0.5)	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
口腔真菌感染	0	0	1 (0.1)
口腔ヘルペス	3 (2.3)	7 (5.6)	24 (3.4)
精巣炎	0	0	2 (0.3)
骨髄炎	1 (0.8)	0	0
外耳炎	0	0	0
真菌性外耳炎	0	0	0
中耳炎	0	0	0
急性中耳炎	0	0	0
乳頭腫ウイルス感染	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
口腔真菌感染	1 (4.2)	0	0	0	2 (<0.1)
口腔ヘルペス	1 (4.2)	31 (6.5)	15 (2.4)	21 (3.5)	92 (3.9)
精巣炎	0	0	0	0	2 (<0.1)
骨髄炎	0	1 (0.2)	0	0	1 (<0.1)
外耳炎	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
真菌性外耳炎	0	1 (0.2)	0	0	1 (<0.1)
中耳炎	0	1 (0.2)	2 (0.3)	0	3 (0.1)
急性中耳炎	0	1 (0.2)	0	0	1 (<0.1)
乳頭腫ウイルス感染	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
爪囲炎	0	0	1 (0.1)
歯冠周囲炎	0	0	0
歯周炎	0	0	2 (0.3)
直腸周囲膿瘍	0	0	0
扁桃周囲炎	0	0	0
咽頭炎	3 (2.3)	0	4 (0.6)
レンサ球菌性咽頭炎	0	0	2 (0.3)
毛巣嚢胞	0	0	4 (0.6)
胸膜感染	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
爪囲炎	0	1 (0.2)	2 (0.3)	1 (0.2)	5 (0.2)
歯冠周囲炎	0	2 (0.4)	0	0	2 (<0.1)
歯周炎	0	4 (0.8)	0	4 (0.7)	9 (0.4)
直腸周囲膿瘍	0	2 (0.4)	0	0	2 (<0.1)
扁桃周囲炎	0	0	1 (0.2)	0	1 (<0.1)
咽頭炎	1 (4.2)	7 (1.5)	4 (0.6)	8 (1.4)	20 (0.9)
レンサ球菌性咽頭炎	1 (4.2)	1 (0.2)	2 (0.3)	1 (0.2)	6 (0.3)
毛巣嚢胞	0	0	2 (0.3)	0	6 (0.3)
胸膜感染	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ニューモシスチス・イロベチイ感染	0	0	1 (0.1)
ニューモシスチス・イロベチイ肺炎	0	0	0
肺炎	2 (1.5)	2 (1.6)	11 (1.6)
細菌性肺炎	0	0	1 (0.1)
クリプトコッカス性肺炎	0	0	0
肺炎球菌性肺炎	0	0	1 (0.1)
ウイルス性肺炎	0	0	1 (0.1)
処置後感染	2 (1.5)	0	0
術後創感染	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ニューモシスチス・イロベチイ感染	0	0	0	0	1 (<0.1)
ニューモシスチス・イロベチイ肺炎	0	1 (0.2)	0	0	0
肺炎	1 (4.2)	5 (1.0)	1 (0.2)	7 (1.2)	23 (1.0)
細菌性肺炎	0	0	0	0	1 (<0.1)
クリプトコッカス性肺炎	0	0	0	2 (0.3)	2 (<0.1)
肺炎球菌性肺炎	0	0	0	0	1 (<0.1)
ウイルス性肺炎	0	0	0	1 (0.2)	2 (<0.1)
処置後感染	0	0	0	0	0
術後創感染	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
歯髄炎	1 (0.8)	0	1 (0.1)
膿疱	0	0	2 (0.3)
腎盂腎炎	0	1 (0.8)	1 (0.1)
膿皮症	0	0	0
膿尿	1 (0.8)	0	0
膿疱性皮疹	0	0	0
直腸膿瘍	0	0	0
RSウイルス感染	0	0	0
気道感染	1 (0.8)	0	6 (0.9)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
歯髄炎	0	1 (0.2)	2 (0.3)	1 (0.2)	5 (0.2)
膿疱	1 (4.2)	1 (0.2)	2 (0.3)	2 (0.3)	7 (0.3)
腎盂腎炎	0	2 (0.4)	1 (0.2)	0	4 (0.2)
膿皮症	0	0	0	1 (0.2)	1 (<0.1)
膿尿	0	0	0	1 (0.2)	1 (<0.1)
膿疱性皮疹	0	1 (0.2)	2 (0.3)	0	3 (0.1)
直腸膿瘍	0	0	1 (0.2)	0	1 (<0.1)
RSウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
気道感染	0	2 (0.4)	2 (0.3)	0	10 (0.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ウイルス性気道感染	1 (0.8)	0	2 (0.3)
鼻炎	2 (1.5)	0	3 (0.4)
根管感染	0	0	1 (0.1)
敗血症	0	0	2 (0.3)
セラチア感染	0	0	0
副鼻腔炎	8 (6.1)	1 (0.8)	20 (2.9)
皮膚カンジダ	0	0	1 (0.1)
皮膚感染	0	0	0
ブドウ球菌感染	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ウイルス性気道感染	1 (4.2)	1 (0.2)	6 (1.0)	2 (0.3)	11 (0.5)
鼻炎	0	5 (1.0)	1 (0.2)	2 (0.3)	7 (0.3)
根管感染	0	0	0	0	1 (<0.1)
敗血症	0	0	1 (0.2)	0	3 (0.1)
セラチア感染	0	1 (0.2)	0	0	0
副鼻腔炎	1 (4.2)	10 (2.1)	9 (1.4)	8 (1.4)	45 (1.9)
皮膚カンジダ	0	0	0	0	1 (<0.1)
皮膚感染	0	0	0	3 (0.5)	3 (0.1)
ブドウ球菌感染	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
レンサ球菌性尿路感染	0	0	1 (0.1)
皮下組織膿瘍	0	0	1 (0.1)
細菌重複感染	0	0	0
股部白癬	0	0	1 (0.1)
白癬感染	0	0	0
手白癬	0	1 (0.8)	0
足部白癬	0	1 (0.8)	1 (0.1)
癜風	0	1 (0.8)	0
扁桃炎	0	0	5 (0.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
レンサ球菌性尿路感染	0	0	0	0	1 (<0.1)
皮下組織膿瘍	0	0	0	1 (0.2)	2 (<0.1)
細菌重複感染	0	0	1 (0.2)	0	1 (<0.1)
股部白癬	0	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.2)
白癬感染	1 (4.2)	2 (0.4)	0	1 (0.2)	2 (<0.1)
手白癬	0	0	0	0	0
足部白癬	0	4 (0.8)	4 (0.6)	5 (0.8)	12 (0.5)
癜風	0	0	2 (0.3)	1 (0.2)	4 (0.2)
扁桃炎	0	1 (0.2)	4 (0.6)	4 (0.7)	13 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
細菌性扁桃炎	0	0	0
歯膿瘍	1 (0.8)	1 (0.8)	5 (0.7)
歯感染	0	0	4 (0.6)
気管気管支炎	0	0	0
トリコモナス症	0	0	0
結核	0	0	1 (0.1)
上気道感染	9 (6.8)	12 (9.6)	60 (8.6)
尿路感染	11 (8.4)	4 (3.2)	34 (4.9)
尿路性敗血症	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
細菌性扁桃炎	0	0	0	1 (0.2)	1 (<0.1)
歯膿瘍	0	1 (0.2)	3 (0.5)	2 (0.3)	11 (0.5)
歯感染	0	4 (0.8)	2 (0.3)	3 (0.5)	10 (0.4)
気管気管支炎	0	1 (0.2)	0	0	1 (<0.1)
トリコモナス症	0	1 (0.2)	0	0	0
結核	0	0	0	0	1 (<0.1)
上気道感染	3 (12.5)	35 (7.3)	32 (5.1)	38 (6.4)	169 (7.2)
尿路感染	1 (4.2)	20 (4.2)	20 (3.2)	12 (2.0)	82 (3.5)
尿路性敗血症	0	0	0	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
膣膿瘍	1 (0.8)	0	0
膣感染	0	0	4 (0.6)
ガードネレラ菌性膣炎	0	0	0
水痘	0	0	1 (0.1)
水痘帯状疱疹ウイルス感染	0	0	0
ウイルス血症	0	0	0
ウイルス性下痢	0	0	0
ウイルス感染	1 (0.8)	0	2 (0.3)
ウイルス性心膜炎	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
膣膿瘍	0	0	0	0	0
膣感染	0	0	0	0	4 (0.2)
ガードネレラ菌性膣炎	0	0	0	1 (0.2)	1 (<0.1)
水痘	0	0	0	0	1 (<0.1)
水痘帯状疱疹ウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
ウイルス血症	0	1 (0.2)	0	0	0
ウイルス性下痢	0	1 (0.2)	0	0	1 (<0.1)
ウイルス感染	1 (4.2)	3 (0.6)	1 (0.2)	3 (0.5)	10 (0.4)
ウイルス性心膜炎	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ウイルス性咽頭炎	0	0	0
ウイルス性上気道感染	0	1 (0.8)	4 (0.6)
女性外陰部蜂巣炎	0	0	1 (0.1)
外陰部腟カンジダ症	1 (0.8)	0	4 (0.6)
外陰腟真菌感染	0	0	2 (0.3)
外陰腟炎	0	1 (0.8)	0
創傷感染	1 (0.8)	0	0
傷害、中毒および処置合併症	12 (9.1)	19 (15.2)	91 (13.0)
偶発的過量投与	3 (2.3)	2 (1.6)	5 (0.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ウイルス性咽頭炎	1 (4.2)	0	1 (0.2)	0	2 (<0.1)
ウイルス性上気道感染	0	5 (1.0)	2 (0.3)	5 (0.8)	13 (0.6)
女性外陰部蜂巣炎	0	0	0	0	1 (<0.1)
外陰部腟カンジダ症	0	4 (0.8)	2 (0.3)	8 (1.4)	17 (0.7)
外陰腟真菌感染	0	2 (0.4)	1 (0.2)	1 (0.2)	5 (0.2)
外陰腟炎	0	0	0	0	1 (<0.1)
創傷感染	0	0	0	1 (0.2)	1 (<0.1)
傷害、中毒および処置合併症	7 (29.1)	71 (14.8)	45 (7.2)	39 (6.6)	254 (10.8)
偶発的過量投与	0	0	1 (0.2)	2 (0.3)	10 (0.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
吻合部漏出	1 (0.8)	0	0
動物咬傷	0	0	0
動物による引っかき傷	0	0	1 (0.1)
足関節部骨折	0	1 (0.8)	0
節足動物咬傷	0	0	3 (0.4)
節足動物刺傷	0	0	0
骨挫傷	0	0	1 (0.1)
第2度熱傷	0	0	0
胸部損傷	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
吻合部漏出	0	0	0	0	0
動物咬傷	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
動物による引っかき傷	0	1 (0.2)	0	0	1 (<0.1)
足関節部骨折	0	0	1 (0.2)	1 (0.2)	3 (0.1)
節足動物咬傷	0	1 (0.2)	1 (0.2)	1 (0.2)	6 (0.3)
節足動物刺傷	0	0	1 (0.2)	0	1 (<0.1)
骨挫傷	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
第2度熱傷	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
胸部損傷	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
挫傷	2 (1.5)	2 (1.6)	2 (0.3)
角膜擦過傷	0	0	0
上顆炎	0	1 (0.8)	2 (0.3)
毒性物質曝露	0	0	0
眼外傷	0	1 (0.8)	1 (0.1)
転倒	0	1 (0.8)	6 (0.9)
腓骨骨折	0	0	0
足骨折	0	0	5 (0.7)
骨折	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
挫傷	2 (8.3)	9 (1.9)	2 (0.3)	5 (0.8)	21 (0.9)
角膜擦過傷	0	0	1 (0.2)	0	1 (<0.1)
上顆炎	0	0	0	1 (0.2)	4 (0.2)
毒性物質曝露	0	0	1 (0.2)	0	1 (<0.1)
眼外傷	0	0	0	1 (0.2)	3 (0.1)
転倒	0	10 (2.1)	0	1 (0.2)	18 (0.8)
腓骨骨折	0	1 (0.2)	0	0	1 (<0.1)
足骨折	0	0	3 (0.5)	3 (0.5)	11 (0.5)
骨折	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
仙骨骨折	0	0	0
消化管ストーマ壊死	1 (0.8)	0	0
手骨折	0	0	0
頭部損傷	0	0	1 (0.1)
熱疲労	0	0	0
熱中症	0	0	0
熱射病	1 (0.8)	0	0
股関節部骨折	1 (0.8)	0	0
瘢痕ヘルニア	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
仙骨骨折	0	0	1 (0.2)	0	1 (<0.1)
消化管ストーマ壊死	0	0	0	0	0
手骨折	0	1 (0.2)	2 (0.3)	1 (0.2)	4 (0.2)
頭部損傷	0	0	0	0	1 (<0.1)
熱疲労	0	0	0	1 (0.2)	1 (<0.1)
熱中症	0	1 (0.2)	0	0	0
熱射病	0	0	1 (0.2)	0	1 (<0.1)
股関節部骨折	0	0	0	0	0
瘢痕ヘルニア	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
損傷	0	0	1 (0.1)
企図的過量投与	0	0	0
関節脱臼	0	0	1 (0.1)
関節損傷	0	2 (1.6)	1 (0.1)
靱帯断裂	0	0	0
靱帯捻挫	2 (1.5)	1 (0.8)	4 (0.6)
四肢損傷	0	0	2 (0.3)
四肢外傷性切断	0	0	0
腰椎骨折	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
損傷	1 (4.2)	1 (0.2)	0	1 (0.2)	3 (0.1)
企図的過量投与	0	1 (0.2)	0	0	1 (<0.1)
関節脱臼	0	0	0	0	1 (<0.1)
関節損傷	0	1 (0.2)	3 (0.5)	0	6 (0.3)
靱帯断裂	0	0	1 (0.2)	0	1 (<0.1)
靱帯捻挫	1 (4.2)	4 (0.8)	1 (0.2)	4 (0.7)	12 (0.5)
四肢損傷	0	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.2)
四肢外傷性切断	0	0	0	1 (0.2)	1 (<0.1)
腰椎骨折	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
つち指	0	0	0
半月板損傷	0	1 (0.8)	1 (0.1)
筋断裂	0	0	4 (0.6)
肉離れ	0	0	8 (1.1)
筋骨格内異物	0	0	0
過量投与	0	0	2 (0.3)
膝蓋骨骨折	0	0	1 (0.1)
骨盤骨折	0	0	0
処置後血尿	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
つち指	0	1 (0.2)	0	0	1 (<0.1)
半月板損傷	0	0	1 (0.2)	0	2 (<0.1)
筋断裂	0	1 (0.2)	1 (0.2)	1 (0.2)	7 (0.3)
肉離れ	0	1 (0.2)	2 (0.3)	3 (0.5)	13 (0.6)
筋骨格内異物	0	0	1 (0.2)	0	1 (<0.1)
過量投与	1 (4.2)	0	2 (0.3)	0	5 (0.2)
膝蓋骨骨折	0	0	0	0	1 (<0.1)
骨盤骨折	0	1 (0.2)	0	0	1 (<0.1)
処置後血尿	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
処置後出血	0	0	3 (0.4)
外傷後頚部症候群	0	0	0
外傷後疼痛	0	0	1 (0.1)
術後イレウス	0	0	1 (0.1)
処置による腸管穿孔	0	0	1 (0.1)
処置による疼痛	0	1 (0.8)	2 (0.3)
肺挫傷	0	0	1 (0.1)
橈骨骨折	0	0	1 (0.1)
肋骨骨折	0	0	4 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
処置後出血	0	0	0	1 (0.2)	4 (0.2)
外傷後頚部症候群	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
外傷後疼痛	0	0	2 (0.3)	0	3 (0.1)
術後イレウス	0	0	0	0	1 (<0.1)
処置による腸管穿孔	0	0	0	0	1 (<0.1)
処置による疼痛	0	0	1 (0.2)	0	4 (0.2)
肺挫傷	0	0	1 (0.2)	0	2 (<0.1)
橈骨骨折	0	1 (0.2)	0	0	2 (<0.1)
肋骨骨折	1 (4.2)	3 (0.6)	1 (0.2)	1 (0.2)	9 (0.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
交通事故	0	1 (0.8)	3 (0.4)
瘢痕	0	0	1 (0.1)
陰嚢血腫	0	0	1 (0.1)
皮膚擦過傷	1 (0.8)	3 (2.4)	1 (0.1)
皮膚裂傷	0	1 (0.8)	3 (0.4)
軟部組織損傷	0	0	0
脊柱損傷	0	0	0
脊椎圧迫骨折	0	0	1 (0.1)
スポーツ損傷	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
交通事故	0	2 (0.4)	0	0	5 (0.2)
瘢痕	0	0	0	0	1 (<0.1)
陰嚢血腫	0	0	0	0	1 (<0.1)
皮膚擦過傷	0	5 (1.0)	0	0	9 (0.4)
皮膚裂傷	1 (4.2)	3 (0.6)	4 (0.6)	0	11 (0.5)
軟部組織損傷	0	1 (0.2)	0	0	1 (<0.1)
脊柱損傷	0	1 (0.2)	0	0	1 (<0.1)
脊椎圧迫骨折	0	1 (0.2)	0	0	1 (<0.1)
スポーツ損傷	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
ストレス骨折	0	0	3 (0.4)
皮下血腫	0	0	1 (0.1)
腱損傷	0	0	1 (0.1)
腱断裂	0	0	1 (0.1)
熱傷	0	0	1 (0.1)
胸椎骨折	0	0	0
脛骨骨折	0	0	1 (0.1)
歯牙破折	0	0	3 (0.4)
上肢骨折	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
ストレス骨折	0	2 (0.4)	1 (0.2)	0	6 (0.3)
皮下血腫	0	2 (0.4)	0	0	2 (<0.1)
腱損傷	0	0	0	0	1 (<0.1)
腱断裂	0	0	0	0	1 (<0.1)
熱傷	0	0	1 (0.2)	0	2 (<0.1)
胸椎骨折	0	0	1 (0.2)	0	1 (<0.1)
脛骨骨折	0	1 (0.2)	1 (0.2)	0	3 (0.1)
歯牙破折	0	2 (0.4)	0	2 (0.3)	6 (0.3)
上肢骨折	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
子宮穿孔	0	0	1 (0.1)
ワクチン接種合併症	0	0	0
創傷	0	0	1 (0.1)
創合併症	0	1 (0.8)	0
手首関節骨折	0	0	1 (0.1)
臨床検査	57 (43.4)	33 (26.4)	196 (28.0)
アラニンアミノトランスフェラーゼ増加	6 (4.6)	2 (1.6)	10 (1.4)
αヒドロキシ酪酸脱水素酵素増加	0	0	0
アミラーゼ増加	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
子宮穿孔	0	0	0	0	1 (<0.1)
ワクチン接種合併症	0	1 (0.2)	0	0	1 (<0.1)
創傷	0	3 (0.6)	1 (0.2)	1 (0.2)	6 (0.3)
創合併症	0	1 (0.2)	0	0	2 (<0.1)
手首関節骨折	0	0	0	1 (0.2)	2 (<0.1)
臨床検査	27 (112.1)	145 (30.3)	270 (43.4)	291 (49.2)	924 (39.3)
アラニンアミノトランスフェラーゼ増加	0	8 (1.7)	17 (2.7)	19 (3.2)	54 (2.3)
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.2)	0	0	1 (<0.1)
アミラーゼ増加	1 (4.2)	1 (0.2)	2 (0.3)	0	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
抗好中球細胞質抗体陽性	0	0	0
抗核抗体増加	0	0	0
大動脈雑音	0	0	0
関節鏡検査	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	7 (5.3)	2 (1.6)	10 (1.4)
細菌検査陽性	0	0	0
好塩基球数増加	0	0	1 (0.1)
血中アルブミン減少	0	0	0
血中アルブミン増加	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
抗好中球細胞質抗体陽性	0	0	0	1 (0.2)	1 (<0.1)
抗核抗体増加	0	1 (0.2)	0	0	0
大動脈雑音	0	0	0	1 (0.2)	1 (<0.1)
関節鏡検査	0	1 (0.2)	0	0	1 (<0.1)
アスパラギン酸アミノトランスフェラーゼ増加	1 (4.2)	10 (2.1)	18 (2.9)	17 (2.9)	56 (2.4)
細菌検査陽性	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
好塩基球数増加	0	0	0	0	1 (<0.1)
血中アルブミン減少	0	0	2 (0.3)	0	2 (<0.1)
血中アルブミン増加	0	0	1 (0.2)	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血中アルカリホスファターゼ減少	0	0	0
血中アルカリホスファターゼ増加	1 (0.8)	1 (0.8)	0
血中重炭酸塩減少	0	0	1 (0.1)
血中ビリルビン増加	0	0	2 (0.3)
血中非抱合ビリルビン増加	0	0	0
血中カルシウム増加	0	0	0
血中クロール減少	0	0	0
血中コレステロール減少	0	0	1 (0.1)
血中コレステロール増加	0	1 (0.8)	5 (0.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血中アルカリホスファターゼ減少	0	0	0	1 (0.2)	1 (<0.1)
血中アルカリホスファターゼ増加	0	0	2 (0.3)	1 (0.2)	4 (0.2)
血中重炭酸塩減少	0	0	1 (0.2)	0	2 (<0.1)
血中ビリルビン増加	0	0	9 (1.4)	8 (1.4)	19 (0.8)
血中非抱合ビリルビン増加	0	0	0	1 (0.2)	1 (<0.1)
血中カルシウム増加	0	0	2 (0.3)	0	2 (<0.1)
血中クロール減少	0	1 (0.2)	0	0	1 (<0.1)
血中コレステロール減少	0	1 (0.2)	1 (0.2)	0	3 (0.1)
血中コレステロール増加	0	2 (0.4)	3 (0.5)	12 (2.0)	23 (1.0)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血中クレアチン増加	0	0	1 (0.1)
血中クレアチンホスホキナーゼMB増加	0	0	0
血中クレアチンホスホキナーゼ増加	6 (4.6)	12 (9.6)	40 (5.7)
血中クレアチニン増加	1 (0.8)	0	2 (0.3)
血中葉酸減少	0	1 (0.8)	0
血中ブドウ糖	1 (0.8)	0	0
血中ブドウ糖減少	0	0	0
血中ブドウ糖増加	3 (2.3)	0	4 (0.6)
血中鉄減少	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血中クレアチン増加	0	0	0	1 (0.2)	2 (<0.1)
血中クレアチンホスホキナーゼMB増加	0	1 (0.2)	0	0	1 (<0.1)
血中クレアチンホスホキナーゼ増加	8 (33.2)	33 (6.9)	56 (9.0)	72 (12.2)	213 (9.1)
血中クレアチニン増加	0	2 (0.4)	1 (0.2)	8 (1.4)	11 (0.5)
血中葉酸減少	0	0	1 (0.2)	0	2 (<0.1)
血中ブドウ糖	0	0	0	0	0
血中ブドウ糖減少	0	0	0	1 (0.2)	1 (<0.1)
血中ブドウ糖増加	0	0	1 (0.2)	1 (0.2)	6 (0.3)
血中鉄減少	0	1 (0.2)	1 (0.2)	1 (0.2)	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血中乳酸脱水素酵素増加	0	0	0
血中マグネシウム減少	0	0	0
血中リン減少	0	0	1 (0.1)
血中カリウム減少	0	0	2 (0.3)
血中カリウム増加	0	0	1 (0.1)
血圧上昇	0	0	0
血中ナトリウム増加	0	0	0
血中トリグリセリド異常	0	0	0
血中トリグリセリド減少	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血中乳酸脱水素酵素増加	0	1 (0.2)	0	0	1 (<0.1)
血中マグネシウム減少	0	1 (0.2)	0	0	1 (<0.1)
血中リン減少	0	2 (0.4)	1 (0.2)	2 (0.3)	6 (0.3)
血中カリウム減少	0	0	2 (0.3)	0	4 (0.2)
血中カリウム増加	0	0	1 (0.2)	0	2 (<0.1)
血圧上昇	0	1 (0.2)	2 (0.3)	1 (0.2)	4 (0.2)
血中ナトリウム増加	0	0	1 (0.2)	0	1 (<0.1)
血中トリグリセリド異常	0	0	1 (0.2)	0	1 (<0.1)
血中トリグリセリド減少	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血中トリグリセリド増加	0	2 (1.6)	2 (0.3)
血中尿素増加	0	0	1 (0.1)
血中尿酸増加	0	0	0
尿中血陽性	0	0	3 (0.4)
体温上昇	0	0	0
骨密度減少	0	0	0
炭水化物耐性低下	0	0	0
心雑音	1 (0.8)	1 (0.8)	0
クロストリジウム検査陽性	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血中トリグリセリド増加	0	0	1 (0.2)	1 (0.2)	6 (0.3)
血中尿素増加	0	0	1 (0.2)	0	2 (<0.1)
血中尿酸増加	0	1 (0.2)	0	0	1 (<0.1)
尿中血陽性	0	0	0	6 (1.0)	9 (0.4)
体温上昇	0	0	1 (0.2)	2 (0.3)	3 (0.1)
骨密度減少	0	0	1 (0.2)	0	1 (<0.1)
炭水化物耐性低下	0	0	0	1 (0.2)	1 (<0.1)
心雑音	0	0	0	0	1 (<0.1)
クロストリジウム検査陽性	1 (4.2)	0	2 (0.3)	0	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
凝固時間延長	0	0	1 (0.1)
尿中結晶陽性	1 (0.8)	0	0
心電図QT延長	0	0	1 (0.1)
心電図再分極異常	0	0	1 (0.1)
便中カルプロテクチン増加	0	0	3 (0.4)
γ-グルタミルトランスフェラーゼ増加	6 (4.6)	2 (1.6)	5 (0.7)
糸球体濾過率減少	0	0	0
尿中ブドウ糖陽性	1 (0.8)	0	0
顆粒球数減少	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
凝固時間延長	0	0	0	0	1 (<0.1)
尿中結晶陽性	0	1 (0.2)	0	0	1 (<0.1)
心電図QT延長	0	0	0	0	1 (<0.1)
心電図再分極異常	0	0	0	0	1 (<0.1)
便中カルプロテクチン増加	0	0	0	1 (0.2)	4 (0.2)
γ-グルタミルトランスフェラーゼ増加	0	5 (1.0)	12 (1.9)	6 (1.0)	28 (1.2)
糸球体濾過率減少	1 (4.2)	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.1)
尿中ブドウ糖陽性	0	0	1 (0.2)	0	1 (<0.1)
顆粒球数減少	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
握力低下	0	0	0
ヘマトクリット減少	0	0	1 (0.1)
ヘモグロビン減少	4 (3.0)	1 (0.8)	5 (0.7)
尿中ヘモグロビン陽性	0	0	0
肝酵素上昇	0	0	10 (1.4)
B型肝炎DNA測定陽性	1 (0.8)	0	2 (0.3)
高比重リポ蛋白増加	0	0	1 (0.1)
ヒト乳頭腫ウイルス検査陽性	0	0	0
眼圧上昇	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
握力低下	0	0	1 (0.2)	0	1 (<0.1)
ヘマトクリット減少	0	0	1 (0.2)	0	2 (<0.1)
ヘモグロビン減少	1 (4.2)	3 (0.6)	7 (1.1)	5 (0.8)	21 (0.9)
尿中ヘモグロビン陽性	0	0	0	1 (0.2)	1 (<0.1)
肝酵素上昇	4 (16.6)	1 (0.2)	7 (1.1)	5 (0.8)	27 (1.1)
B型肝炎DNA測定陽性	0	0	0	1 (0.2)	3 (0.1)
高比重リポ蛋白増加	0	1 (0.2)	4 (0.6)	3 (0.5)	9 (0.4)
ヒト乳頭腫ウイルス検査陽性	0	1 (0.2)	0	0	1 (<0.1)
眼圧上昇	0	1 (0.2)	0	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
臨床検査異常	0	0	1 (0.1)
リパーゼ増加	0	0	0
肝機能検査異常	0	1 (0.8)	0
肝機能検査値上昇	1 (0.8)	0	2 (0.3)
低比重リポ蛋白減少	0	0	2 (0.3)
低比重リポ蛋白増加	0	1 (0.8)	0
リンパ球数減少	1 (0.8)	0	11 (1.6)
リンパ球数増加	0	0	1 (0.1)
リンパ球百分率減少	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
臨床検査異常	0	0	0	0	1 (<0.1)
リパーゼ増加	1 (4.2)	0	2 (0.3)	0	3 (0.1)
肝機能検査異常	0	0	0	0	1 (<0.1)
肝機能検査値上昇	0	1 (0.2)	0	2 (0.3)	5 (0.2)
低比重リポ蛋白減少	0	1 (0.2)	1 (0.2)	0	4 (0.2)
低比重リポ蛋白増加	0	0	1 (0.2)	7 (1.2)	9 (0.4)
リンパ球数減少	0	6 (1.3)	16 (2.6)	11 (1.9)	42 (1.8)
リンパ球数増加	1 (4.2)	2 (0.4)	1 (0.2)	4 (0.7)	8 (0.3)
リンパ球百分率減少	0	0	6 (1.0)	2 (0.3)	8 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
リンパ球百分率増加	0	0	0
平均赤血球容積異常	0	0	0
平均赤血球容積増加	0	0	0
単球数増加	0	0	3 (0.4)
結核菌群検査陽性	0	0	0
好中球数減少	0	1 (0.8)	5 (0.7)
好中球数増加	1 (0.8)	0	7 (1.0)
好中球百分率増加	0	0	0
尿中亜硝酸塩陽性	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
リンパ球百分率増加	0	0	2 (0.3)	0	2 (<0.1)
平均赤血球容積異常	0	0	0	1 (0.2)	1 (<0.1)
平均赤血球容積増加	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
単球数増加	0	0	2 (0.3)	0	5 (0.2)
結核菌群検査陽性	0	1 (0.2)	0	0	1 (<0.1)
好中球数減少	4 (16.6)	18 (3.8)	23 (3.7)	27 (4.6)	74 (3.1)
好中球数増加	0	2 (0.4)	4 (0.6)	6 (1.0)	17 (0.7)
好中球百分率増加	0	0	0	2 (0.3)	2 (<0.1)
尿中亜硝酸塩陽性	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血小板数減少	0	0	1 (0.1)
血小板数増加	0	1 (0.8)	0
プレアルブミン減少	0	0	0
前立腺特異性抗原増加	0	0	0
総蛋白減少	0	0	0
総蛋白増加	0	0	0
尿蛋白	0	0	0
尿中蛋白陽性	5 (3.8)	0	4 (0.6)
赤血球数減少	0	0	3 (0.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血小板数減少	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
血小板数増加	0	1 (0.2)	1 (0.2)	3 (0.5)	6 (0.3)
プレアルブミン減少	0	0	1 (0.2)	0	1 (<0.1)
前立腺特異性抗原増加	1 (4.2)	0	1 (0.2)	0	2 (<0.1)
総蛋白減少	0	0	1 (0.2)	0	1 (<0.1)
総蛋白増加	0	0	0	1 (0.2)	1 (<0.1)
尿蛋白	0	1 (0.2)	0	0	1 (<0.1)
尿中蛋白陽性	0	1 (0.2)	3 (0.5)	3 (0.5)	10 (0.4)
赤血球数減少	0	0	2 (0.3)	5 (0.8)	10 (0.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
赤血球数増加	0	0	1 (0.1)
血沈亢進	0	0	0
網状赤血球数減少	0	0	0
網状赤血球数増加	0	0	2 (0.3)
血清フェリチン減少	0	1 (0.8)	1 (0.1)
尿比重増加	0	0	1 (0.1)
ブドウ球菌検査陽性	0	0	0
トランスアミナーゼ上昇	0	0	0
トランスフェリン増加	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
赤血球数増加	0	0	0	0	1 (<0.1)
血沈亢進	0	0	1 (0.2)	0	1 (<0.1)
網状赤血球数減少	0	0	1 (0.2)	0	1 (<0.1)
網状赤血球数増加	0	0	1 (0.2)	0	3 (0.1)
血清フェリチン減少	0	0	0	0	1 (<0.1)
尿比重増加	0	0	0	0	1 (<0.1)
ブドウ球菌検査陽性	0	0	1 (0.2)	0	1 (<0.1)
トランスアミナーゼ上昇	0	1 (0.2)	4 (0.6)	1 (0.2)	6 (0.3)
トランスフェリン増加	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
尿検査異常	1 (0.8)	0	1 (0.1)
尿中ケトン体陽性	1 (0.8)	0	3 (0.4)
尿中白血球エステラーゼ陽性	0	0	3 (0.4)
尿量減少	0	0	1 (0.1)
ビタミンB12減少	0	0	0
ビタミンD減少	1 (0.8)	0	0
ビタミンD増加	0	0	0
体重減少	2 (1.5)	0	1 (0.1)
体重増加	1 (0.8)	0	5 (0.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
尿検査異常	0	0	1 (0.2)	0	2 (<0.1)
尿中ケトン体陽性	0	0	0	1 (0.2)	4 (0.2)
尿中白血球エステラーゼ陽性	0	1 (0.2)	2 (0.3)	0	6 (0.3)
尿量減少	0	0	0	0	1 (<0.1)
ビタミンB12減少	0	1 (0.2)	0	0	1 (<0.1)
ビタミンD減少	0	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.1)
ビタミンD増加	0	0	1 (0.2)	0	1 (<0.1)
体重減少	0	1 (0.2)	0	2 (0.3)	4 (0.2)
体重増加	0	2 (0.4)	2 (0.3)	5 (0.8)	13 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
白血球数減少	3 (2.3)	1 (0.8)	6 (0.9)
白血球数増加	1 (0.8)	1 (0.8)	4 (0.6)
尿中白血球陽性	0	0	4 (0.6)
代謝および栄養障害	34 (25.9)	9 (7.2)	67 (9.6)
食欲障害	0	0	1 (0.1)
乳製品不耐症	0	0	1 (0.1)
食欲減退	4 (3.0)	1 (0.8)	4 (0.6)
脱水	2 (1.5)	0	2 (0.3)
糖尿病	2 (1.5)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
白血球数減少	2 (8.3)	16 (3.3)	17 (2.7)	17 (2.9)	55 (2.3)
白血球数増加	1 (4.2)	0	1 (0.2)	3 (0.5)	10 (0.4)
尿中白血球陽性	0	2 (0.4)	1 (0.2)	1 (0.2)	8 (0.3)
代謝および栄養障害	1 (4.2)	41 (8.6)	56 (9.0)	50 (8.4)	208 (8.9)
食欲障害	0	0	0	0	1 (<0.1)
乳製品不耐症	0	0	0	0	1 (<0.1)
食欲減退	0	2 (0.4)	2 (0.3)	1 (0.2)	9 (0.4)
脱水	0	0	0	1 (0.2)	3 (0.1)
糖尿病	0	0	0	2 (0.3)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
糖尿病性代謝代償不全	0	0	1 (0.1)
脂質異常症	0	0	2 (0.3)
体液貯留	0	0	1 (0.1)
葉酸欠乏	0	0	1 (0.1)
耐糖能障害	0	0	0
痛風	0	1 (0.8)	0
ヒスタミン不耐性	0	0	1 (0.1)
高カルシウム血症	0	0	0
高コレステロール血症	2 (1.5)	2 (1.6)	8 (1.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
糖尿病性代謝代償不全	0	0	0	0	1 (<0.1)
脂質異常症	0	2 (0.4)	4 (0.6)	2 (0.3)	10 (0.4)
体液貯留	0	0	0	0	1 (<0.1)
葉酸欠乏	0	0	3 (0.5)	1 (0.2)	5 (0.2)
耐糖能障害	0	2 (0.4)	0	0	1 (<0.1)
痛風	0	1 (0.2)	3 (0.5)	1 (0.2)	6 (0.3)
ヒスタミン不耐性	0	0	0	0	1 (<0.1)
高カルシウム血症	0	0	0	1 (0.2)	1 (<0.1)
高コレステロール血症	0	8 (1.7)	7 (1.1)	10 (1.7)	33 (1.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
高血糖	6 (4.6)	0	8 (1.1)
高ホモシステイン血症	0	0	1 (0.1)
高カリウム血症	0	0	0
高リパーゼ血症	0	0	0
高脂血症	2 (1.5)	0	7 (1.0)
高ナトリウム血症	0	0	0
高トリグリセリド血症	2 (1.5)	0	2 (0.3)
高尿酸血症	1 (0.8)	1 (0.8)	0
低アルブミン血症	1 (0.8)	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
高血糖	0	2 (0.4)	8 (1.3)	4 (0.7)	21 (0.9)
高ホモシステイン血症	0	1 (0.2)	0	0	2 (<0.1)
高カリウム血症	0	1 (0.2)	0	0	1 (<0.1)
高リパーゼ血症	0	1 (0.2)	0	0	0
高脂血症	0	1 (0.2)	13 (2.1)	3 (0.5)	24 (1.0)
高ナトリウム血症	0	0	0	2 (0.3)	2 (<0.1)
高トリグリセリド血症	0	0	0	1 (0.2)	3 (0.1)
高尿酸血症	0	1 (0.2)	0	2 (0.3)	4 (0.2)
低アルブミン血症	0	0	1 (0.2)	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
低カリウム血症	2 (1.5)	0	6 (0.9)
低マグネシウム血症	0	0	3 (0.4)
低ナトリウム血症	1 (0.8)	0	0
低リン酸血症	2 (1.5)	1 (0.8)	4 (0.6)
低蛋白血症	0	0	0
食欲亢進	0	1 (0.8)	0
鉄欠乏	4 (3.0)	0	4 (0.6)
ラクトース不耐性	0	0	2 (0.3)
栄養障害	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
低カリウム血症	0	5 (1.0)	2 (0.3)	1 (0.2)	11 (0.5)
低マグネシウム血症	0	0	0	0	3 (0.1)
低ナトリウム血症	0	3 (0.6)	1 (0.2)	1 (0.2)	3 (0.1)
低リン酸血症	0	2 (0.4)	1 (0.2)	4 (0.7)	11 (0.5)
低蛋白血症	1 (4.2)	1 (0.2)	0	0	2 (<0.1)
食欲亢進	0	1 (0.2)	0	0	2 (<0.1)
鉄欠乏	0	2 (0.4)	1 (0.2)	3 (0.5)	9 (0.4)
ラクトース不耐性	0	0	0	0	2 (<0.1)
栄養障害	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
代謝性アシドーシス	0	0	1 (0.1)
代謝症候群	0	0	0
肥満	0	0	0
テタニー	0	0	1 (0.1)
2型糖尿病	1 (0.8)	0	0
過少体重	0	0	0
ビタミンB群欠乏	0	0	0
ビタミンB1欠乏	1 (0.8)	0	0
ビタミンB12欠乏	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
代謝性アシドーシス	0	0	1 (0.2)	0	2 (<0.1)
代謝症候群	0	0	0	1 (0.2)	1 (<0.1)
肥満	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
テタニー	0	0	0	0	1 (<0.1)
2型糖尿病	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
過少体重	0	0	1 (0.2)	0	1 (<0.1)
ビタミンB群欠乏	0	0	1 (0.2)	0	1 (<0.1)
ビタミンB1欠乏	0	0	0	0	0
ビタミンB12欠乏	0	0	1 (0.2)	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
ビタミンD欠乏	1 (0.8)	2 (1.6)	4 (0.6)
筋骨格系および結合組織障害	69 (52.5)	39 (31.2)	179 (25.6)
強直性脊椎炎	0	0	0
関節痛	15 (11.4)	7 (5.6)	49 (7.0)
関節炎	1 (0.8)	3 (2.4)	4 (0.6)
腸炎性関節炎	0	0	0
関節障害	8 (6.1)	1 (0.8)	12 (1.7)
腋窩腫瘤	0	0	1 (0.1)
背部痛	7 (5.3)	7 (5.6)	19 (2.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
ビタミンD欠乏	0	4 (0.8)	4 (0.6)	6 (1.0)	18 (0.8)
筋骨格系および結合組織障害	13 (54.0)	176 (36.8)	143 (23.0)	116 (19.6)	570 (24.3)
強直性脊椎炎	0	1 (0.2)	0	0	0
関節痛	3 (12.5)	38 (7.9)	41 (6.6)	30 (5.1)	141 (6.0)
関節炎	2 (8.3)	2 (0.4)	2 (0.3)	0	11 (0.5)
腸炎性関節炎	0	3 (0.6)	0	1 (0.2)	1 (<0.1)
関節障害	2 (8.3)	10 (2.1)	8 (1.3)	3 (0.5)	29 (1.2)
腋窩腫瘤	0	0	0	0	1 (<0.1)
背部痛	0	21 (4.4)	17 (2.7)	13 (2.2)	63 (2.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
骨痛	0	0	0
滑液包炎	1 (0.8)	0	4 (0.6)
軟骨萎縮	0	0	0
頚部脊柱管狭窄症	0	0	0
軟骨軟化症	0	0	0
ばち状指	0	0	0
尾骨痛	0	0	0
コンパートメント症候群	0	0	1 (0.1)
肋軟骨炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
骨痛	0	0	0	1 (0.2)	1 (<0.1)
滑液包炎	0	1 (0.2)	0	2 (0.3)	7 (0.3)
軟骨萎縮	0	0	1 (0.2)	0	1 (<0.1)
頚部脊柱管狭窄症	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
軟骨軟化症	0	0	0	2 (0.3)	2 (<0.1)
ばち状指	0	0	1 (0.2)	0	1 (<0.1)
尾骨痛	0	3 (0.6)	0	0	2 (<0.1)
コンパートメント症候群	0	0	0	0	1 (<0.1)
肋軟骨炎	0	2 (0.4)	0	2 (0.3)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
指炎	0	0	0
腱付着部症	0	0	1 (0.1)
外骨腫	0	0	1 (0.1)
四肢拘縮	0	0	0
線維筋痛	0	0	0
側腹部痛	1 (0.8)	0	1 (0.1)
尺骨部痛	0	0	2 (0.3)
出血性関節症	0	0	0
椎間板変性症	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
指炎	0	1 (0.2)	0	0	1 (<0.1)
腱付着部症	0	0	0	0	1 (<0.1)
外骨腫	0	0	1 (0.2)	0	2 (<0.1)
四肢拘縮	0	0	1 (0.2)	0	1 (<0.1)
線維筋痛	0	0	1 (0.2)	0	1 (<0.1)
側腹部痛	0	3 (0.6)	1 (0.2)	1 (0.2)	5 (0.2)
尺骨部痛	0	0	0	0	2 (<0.1)
出血性関節症	0	1 (0.2)	0	0	0
椎間板変性症	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
椎間板障害	0	1 (0.8)	0
椎間板突出	0	1 (0.8)	5 (0.7)
関節滲出液	0	0	0
関節弛緩	0	0	0
関節ロック	0	0	0
関節雑音	0	0	1 (0.1)
関節硬直	1 (0.8)	0	2 (0.3)
関節腫脹	2 (1.5)	0	2 (0.3)
腰部脊柱管狭窄症	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
椎間板障害	0	0	0	0	1 (<0.1)
椎間板突出	0	5 (1.0)	3 (0.5)	3 (0.5)	15 (0.6)
関節滲出液	0	0	1 (0.2)	0	1 (<0.1)
関節弛緩	0	0	0	1 (0.2)	1 (<0.1)
関節ロック	0	0	0	2 (0.3)	2 (<0.1)
関節雑音	0	0	0	0	1 (<0.1)
関節硬直	0	0	1 (0.2)	0	3 (0.1)
関節腫脹	0	1 (0.2)	2 (0.3)	1 (0.2)	6 (0.3)
腰部脊柱管狭窄症	0	1 (0.2)	0	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
脛骨内側過労性症候群	0	0	1 (0.1)
筋拘縮	0	0	0
筋不快感	1 (0.8)	0	0
筋障害	0	0	0
筋痙縮	5 (3.8)	0	8 (1.1)
筋緊張	0	0	0
筋攣縮	0	0	1 (0.1)
筋力低下	0	0	0
筋骨格系胸痛	1 (0.8)	2 (1.6)	4 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
脛骨内側過労性症候群	0	0	0	0	1 (<0.1)
筋拘縮	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
筋不快感	0	0	0	0	0
筋障害	0	1 (0.2)	0	0	1 (<0.1)
筋痙縮	2 (8.3)	5 (1.0)	4 (0.6)	5 (0.8)	23 (1.0)
筋緊張	1 (4.2)	0	0	0	1 (<0.1)
筋攣縮	0	0	0	0	1 (<0.1)
筋力低下	0	1 (0.2)	0	0	0
筋骨格系胸痛	0	6 (1.3)	2 (0.3)	0	11 (0.5)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
筋骨格不快感	0	0	0
筋骨格痛	1 (0.8)	2 (1.6)	4 (0.6)
筋骨格硬直	1 (0.8)	1 (0.8)	3 (0.4)
筋肉痛	5 (3.8)	0	14 (2.0)
筋膜疼痛症候群	0	1 (0.8)	0
ミオパチー	0	1 (0.8)	0
筋炎	1 (0.8)	0	0
頚部痛	1 (0.8)	5 (4.0)	2 (0.3)
骨炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
筋骨格不快感	0	0	1 (0.2)	0	1 (<0.1)
筋骨格痛	0	5 (1.0)	4 (0.6)	3 (0.5)	15 (0.6)
筋骨格硬直	0	1 (0.2)	2 (0.3)	1 (0.2)	7 (0.3)
筋肉痛	1 (4.2)	9 (1.9)	17 (2.7)	13 (2.2)	52 (2.2)
筋膜疼痛症候群	0	0	0	0	1 (<0.1)
ミオパチー	0	0	0	0	1 (<0.1)
筋炎	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
頚部痛	0	3 (0.6)	3 (0.5)	3 (0.5)	13 (0.6)
骨炎	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
変形性関節症	1 (0.8)	0	1 (0.1)
骨端症	0	0	0
骨壊死	0	0	2 (0.3)
骨減少症	1 (0.8)	0	1 (0.1)
骨粗鬆症	0	0	1 (0.1)
四肢痛	7 (5.3)	2 (1.6)	11 (1.6)
顎痛	0	0	2 (0.3)
膝蓋大腿関節痛症候群	0	0	1 (0.1)
病的骨折	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
変形性関節症	0	5 (1.0)	3 (0.5)	0	7 (0.3)
骨端症	0	1 (0.2)	0	0	1 (<0.1)
骨壊死	0	1 (0.2)	2 (0.3)	0	5 (0.2)
骨減少症	0	2 (0.4)	1 (0.2)	2 (0.3)	6 (0.3)
骨粗鬆症	0	3 (0.6)	4 (0.6)	2 (0.3)	9 (0.4)
四肢痛	1 (4.2)	19 (4.0)	5 (0.8)	11 (1.9)	44 (1.9)
顎痛	0	0	0	0	2 (<0.1)
膝蓋大腿関節痛症候群	0	0	0	0	1 (<0.1)
病的骨折	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
関節周囲炎	0	0	0
足底筋膜炎	0	0	3 (0.4)
多発性関節炎	1 (0.8)	0	0
姿勢異常	0	0	0
横紋筋融解症	0	0	1 (0.1)
関節リウマチ	0	1 (0.8)	0
肩回旋筋腱板症候群	0	0	1 (0.1)
仙腸骨炎	1 (0.8)	0	0
軟部組織腫瘤	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
関節周囲炎	0	2 (0.4)	0	2 (0.3)	4 (0.2)
足底筋膜炎	0	2 (0.4)	2 (0.3)	3 (0.5)	10 (0.4)
多発性関節炎	0	0	0	0	0
姿勢異常	0	1 (0.2)	0	0	0
横紋筋融解症	0	0	1 (0.2)	0	2 (<0.1)
関節リウマチ	0	0	0	0	0
肩回旋筋腱板症候群	0	2 (0.4)	2 (0.3)	1 (0.2)	4 (0.2)
仙腸骨炎	0	0	0	0	0
軟部組織腫瘤	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
脊柱変形	0	1 (0.8)	0
変形性脊椎症	0	0	2 (0.3)
脊椎痛	1 (0.8)	0	0
脊椎炎	0	0	1 (0.1)
脊椎関節障害	4 (3.0)	1 (0.8)	0
軟骨下機能不全骨折	0	0	0
滑液嚢腫	1 (0.8)	0	0
滑膜炎	0	0	2 (0.3)
顎関節症候群	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
脊柱変形	0	0	0	0	1 (<0.1)
変形性脊椎症	0	3 (0.6)	0	0	4 (0.2)
脊椎痛	0	1 (0.2)	0	0	1 (<0.1)
脊椎炎	0	0	0	0	1 (<0.1)
脊椎関節障害	0	1 (0.2)	5 (0.8)	0	6 (0.3)
軟骨下機能不全骨折	0	0	1 (0.2)	0	1 (<0.1)
滑液嚢腫	0	0	0	0	0
滑膜炎	0	0	0	0	2 (<0.1)
顎関節症候群	0	1 (0.2)	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
腱痛	0	0	0
腱炎	0	1 (0.8)	3 (0.4)
腱鞘炎	0	0	0
狭窄性腱鞘炎	0	0	1 (0.1)
弾発指	0	0	1 (0.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	4 (3.0)	10 (8.0)	24 (3.4)
アクロコルドン	0	0	1 (0.1)
結腸腺癌	0	1 (0.8)	0
膵腺癌	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
腱痛	0	1 (0.2)	0	0	0
腱炎	0	2 (0.4)	0	2 (0.3)	6 (0.3)
腱鞘炎	0	1 (0.2)	0	0	0
狭窄性腱鞘炎	0	0	0	0	1 (<0.1)
弾発指	1 (4.2)	1 (0.2)	1 (0.2)	0	4 (0.2)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)	1 (4.2)	15 (3.1)	21 (3.4)	27 (4.6)	93 (4.0)
アクロコルドン	0	0	0	0	1 (<0.1)
結腸腺癌	0	0	0	1 (0.2)	2 (<0.1)
膵腺癌	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
エナメル上皮腫	1 (0.8)	0	1 (0.1)
血管肉腫	0	0	0
肛門性器疣贅	0	0	0
基底細胞癌	0	3 (2.4)	1 (0.1)
肺の良性新生物	0	0	0
精巣の良性新生物	0	0	0
良性脾腫瘍	0	0	0
ボーエン病	0	1 (0.8)	1 (0.1)
乳癌	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
エナメル上皮腫	0	0	0	0	1 (<0.1)
血管肉腫	0	1 (0.2)	0	0	1 (<0.1)
肛門性器疣贅	0	1 (0.2)	0	0	1 (<0.1)
基底細胞癌	0	2 (0.4)	0	7 (1.2)	13 (0.6)
肺の良性新生物	0	0	1 (0.2)	0	1 (<0.1)
精巣の良性新生物	0	0	1 (0.2)	0	1 (<0.1)
良性脾腫瘍	0	0	0	1 (0.2)	1 (<0.1)
ボーエン病	0	0	0	1 (0.2)	3 (0.1)
乳癌	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
気管支の良性新生物	0	0	0
大腸腺腫	1 (0.8)	2 (1.6)	2 (0.3)
線維腫	0	0	0
線維性組織球腫	0	0	1 (0.1)
神経節腫	0	0	0
血管腫	0	0	0
皮膚血管腫	0	0	0
浸潤性乳癌	0	0	0
喉頭扁平上皮癌	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
気管支の良性新生物	0	0	1 (0.2)	0	1 (<0.1)
大腸腺腫	0	2 (0.4)	1 (0.2)	0	5 (0.2)
線維腫	0	0	0	1 (0.2)	1 (<0.1)
線維性組織球腫	0	0	0	1 (0.2)	2 (<0.1)
神経節腫	1 (4.2)	0	0	0	1 (<0.1)
血管腫	0	0	1 (0.2)	0	1 (<0.1)
皮膚血管腫	0	0	1 (0.2)	0	1 (<0.1)
浸潤性乳癌	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
喉頭扁平上皮癌	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
脂肪腫	0	0	0
悪性黒色腫	0	0	1 (0.1)
メラノサイト性母斑	0	0	4 (0.6)
髄膜腫	0	0	0
口腔線維腫	0	1 (0.8)	0
皮膚骨腫	0	0	0
卵巣胚細胞良性奇形腫	0	0	0
前立腺癌	0	0	0
直腸腺腫	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
脂肪腫	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
悪性黒色腫	0	0	0	0	1 (<0.1)
メラノサイト性母斑	0	0	1 (0.2)	0	5 (0.2)
髄膜腫	0	0	0	1 (0.2)	1 (<0.1)
口腔線維腫	0	0	0	0	0
皮膚骨腫	0	0	0	1 (0.2)	1 (<0.1)
卵巣胚細胞良性奇形腫	0	0	1 (0.2)	0	1 (<0.1)
前立腺癌	0	1 (0.2)	0	0	1 (<0.1)
直腸腺腫	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
脂漏性角化症	2 (1.5)	0	0
皮膚乳頭腫	0	1 (0.8)	5 (0.7)
小細胞癌	0	0	0
扁平上皮癌	0	0	1 (0.1)
皮膚有棘細胞癌	0	0	2 (0.3)
子宮頚部扁平上皮癌	0	0	0
舌扁平上皮癌	0	0	1 (0.1)
精巣（純粋）セミノーマ	0	0	0
精巣癌	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
脂漏性角化症	0	3 (0.6)	1 (0.2)	2 (0.3)	5 (0.2)
皮膚乳頭腫	0	1 (0.2)	4 (0.6)	6 (1.0)	17 (0.7)
小細胞癌	0	0	0	1 (0.2)	1 (<0.1)
扁平上皮癌	0	0	0	0	1 (<0.1)
皮膚有棘細胞癌	0	1 (0.2)	0	1 (0.2)	4 (0.2)
子宮頚部扁平上皮癌	0	0	0	1 (0.2)	1 (<0.1)
舌扁平上皮癌	0	0	0	0	1 (<0.1)
精巣（純粋）セミノーマ	0	0	1 (0.2)	0	1 (<0.1)
精巣癌	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
甲状腺腺腫	0	0	0
子宮平滑筋腫	0	0	1 (0.1)
神経系障害	33 (25.1)	26 (20.8)	96 (13.7)
健忘	0	0	1 (0.1)
脳損傷	0	0	0
灼熱感	0	0	0
頚動脈硬化症	0	0	0
手根管症候群	2 (1.5)	0	3 (0.4)
大脳障害	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
甲状腺腺腫	0	0	2 (0.3)	0	2 (<0.1)
子宮平滑筋腫	0	1 (0.2)	3 (0.5)	0	5 (0.2)
神経系障害	11 (45.7)	75 (15.7)	70 (11.2)	104 (17.6)	343 (14.6)
健忘	0	0	0	0	1 (<0.1)
脳損傷	0	0	1 (0.2)	0	1 (<0.1)
灼熱感	1 (4.2)	0	1 (0.2)	0	2 (<0.1)
頚動脈硬化症	0	0	0	1 (0.2)	1 (<0.1)
手根管症候群	0	2 (0.4)	2 (0.3)	2 (0.3)	8 (0.3)
大脳障害	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
脳虚血	0	0	0
脳血管発作	0	0	0
頚髄圧迫	0	0	0
頚髄神経根障害	0	0	1 (0.1)
注意力障害	0	0	2 (0.3)
浮動性めまい	1 (0.8)	4 (3.2)	11 (1.6)
異常感覚	0	0	1 (0.1)
構語障害	0	0	1 (0.1)
味覚不全	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
脳虚血	0	0	2 (0.3)	0	2 (<0.1)
脳血管発作	0	0	0	1 (0.2)	1 (<0.1)
頚髄圧迫	0	0	0	1 (0.2)	1 (<0.1)
頚髄神経根障害	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
注意力障害	0	0	1 (0.2)	0	3 (0.1)
浮動性めまい	0	6 (1.3)	8 (1.3)	15 (2.5)	40 (1.7)
異常感覚	0	0	0	0	1 (<0.1)
構語障害	0	0	0	0	1 (<0.1)
味覚不全	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
てんかん	0	0	0
本態性振戦	0	0	0
頭痛	21 (16.0)	11 (8.8)	42 (6.0)
知覚過敏	0	0	2 (0.3)
感覚鈍麻	0	1 (0.8)	3 (0.4)
頭蓋内動脈瘤	0	0	1 (0.1)
ラクナ梗塞	0	0	0
腰仙部神経根障害	0	0	0
記憶障害	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
てんかん	0	1 (0.2)	0	0	0
本態性振戦	0	1 (0.2)	0	0	0
頭痛	6 (24.9)	37 (7.7)	36 (5.8)	47 (7.9)	162 (6.9)
知覚過敏	0	1 (0.2)	0	0	2 (<0.1)
感覚鈍麻	0	2 (0.4)	4 (0.6)	4 (0.7)	13 (0.6)
頭蓋内動脈瘤	0	0	0	0	1 (<0.1)
ラクナ梗塞	0	0	0	1 (0.2)	1 (<0.1)
腰仙部神経根障害	0	0	1 (0.2)	0	1 (<0.1)
記憶障害	0	0	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
片頭痛	3 (2.3)	0	8 (1.1)
前兆を伴う片頭痛	0	0	0
脊髄症	0	0	0
神経圧迫	0	0	0
神経痛	0	0	1 (0.1)
神経炎	0	0	0
末梢性ニューロパチー	0	0	1 (0.1)
後頭神経痛	0	0	0
起立不耐性	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
片頭痛	2 (8.3)	9 (1.9)	4 (0.6)	4 (0.7)	23 (1.0)
前兆を伴う片頭痛	0	0	1 (0.2)	0	1 (<0.1)
脊髄症	0	0	0	1 (0.2)	1 (<0.1)
神経圧迫	0	0	0	1 (0.2)	1 (<0.1)
神経痛	0	1 (0.2)	0	1 (0.2)	3 (0.1)
神経炎	0	0	0	1 (0.2)	1 (<0.1)
末梢性ニューロパチー	1 (4.2)	1 (0.2)	0	1 (0.2)	3 (0.1)
後頭神経痛	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
起立不耐性	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
錯感覚	2 (1.5)	2 (1.6)	4 (0.6)
末梢性感覚ニューロパチー	0	1 (0.8)	0
睡眠の質低下	0	0	0
ヘルペス後神経痛	0	0	0
失神寸前の状態	1 (0.8)	0	1 (0.1)
回内筋症候群	0	0	1 (0.1)
橈骨神経麻痺	0	0	1 (0.1)
神経根痛	0	0	1 (0.1)
下肢静止不能症候群	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
錯感覚	0	4 (0.8)	1 (0.2)	2 (0.3)	11 (0.5)
末梢性感覚ニューロパチー	0	0	0	0	0
睡眠の質低下	0	0	0	1 (0.2)	1 (<0.1)
ヘルペス後神経痛	1 (4.2)	0	0	1 (0.2)	2 (<0.1)
失神寸前の状態	0	1 (0.2)	0	2 (0.3)	4 (0.2)
回内筋症候群	0	0	0	0	1 (<0.1)
橈骨神経麻痺	0	0	0	0	1 (<0.1)
神経根痛	0	0	0	0	1 (<0.1)
下肢静止不能症候群	0	0	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
坐骨神経痛	0	2 (1.6)	3 (0.4)
発作様現象	0	0	1 (0.1)
副鼻腔炎に伴う頭痛	0	0	1 (0.1)
傾眠	0	0	0
会話障害	0	0	0
脊椎炎性脊髄症	0	0	0
くも膜下出血	0	0	0
硬膜下滲出液	0	0	0
失神	1 (0.8)	2 (1.6)	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
坐骨神経痛	0	1 (0.2)	3 (0.5)	4 (0.7)	11 (0.5)
発作様現象	0	0	0	0	1 (<0.1)
副鼻腔炎に伴う頭痛	0	0	0	0	1 (<0.1)
傾眠	0	0	0	3 (0.5)	3 (0.1)
会話障害	0	0	1 (0.2)	0	1 (<0.1)
脊椎炎性脊髄症	0	0	0	1 (0.2)	1 (<0.1)
くも膜下出血	0	0	0	1 (0.2)	1 (<0.1)
硬膜下滲出液	0	0	1 (0.2)	0	1 (<0.1)
失神	0	3 (0.6)	0	2 (0.3)	8 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
味覚障害	0	0	0
緊張性頭痛	2 (1.5)	1 (0.8)	0
振戦	0	1 (0.8)	1 (0.1)
視野欠損	0	0	0
妊娠、産褥および周産期の状態	0	0	0
自然流産	0	0	0
精神障害	19 (14.5)	10 (8.0)	44 (6.3)
異常な夢	0	0	1 (0.1)
急性精神病	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
味覚障害	0	0	0	1 (0.2)	1 (<0.1)
緊張性頭痛	0	0	0	1 (0.2)	2 (<0.1)
振戦	0	1 (0.2)	1 (0.2)	1 (0.2)	5 (0.2)
視野欠損	0	0	0	1 (0.2)	1 (<0.1)
妊娠、産褥および周産期の状態	0	0	1 (0.2)	0	1 (<0.1)
自然流産	0	0	1 (0.2)	0	1 (<0.1)
精神障害	3 (12.5)	45 (9.4)	28 (4.5)	37 (6.3)	145 (6.2)
異常な夢	0	0	0	0	1 (<0.1)
急性精神病	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
精神障害 (Cont.)			
急性ストレス反応	0	0	0
感情障害	0	0	0
激越	0	0	1 (0.1)
不安	8 (6.1)	7 (5.6)	2 (0.3)
不安障害	0	0	0
注意欠如・多動性障害	0	0	1 (0.1)
自閉症スペクトラム障害	0	0	1 (0.1)
双極1型障害	0	0	0
双極性障害	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)					
急性ストレス反応	0	0	1 (0.2)	0	1 (<0.1)
感情障害	0	1 (0.2)	0	0	1 (<0.1)
激越	0	0	0	0	1 (<0.1)
不安	1 (4.2)	13 (2.7)	8 (1.3)	7 (1.2)	30 (1.3)
不安障害	0	0	2 (0.3)	0	2 (<0.1)
注意欠如・多動性障害	0	0	0	0	1 (<0.1)
自閉症スペクトラム障害	0	0	0	0	1 (<0.1)
双極1型障害	0	0	1 (0.2)	0	1 (<0.1)
双極性障害	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
精神障害 (Cont.)			
抑うつ気分	0	0	1 (0.1)
うつ病	3 (2.3)	1 (0.8)	16 (2.3)
薬物依存	0	0	0
全般性不安障害	0	0	1 (0.1)
初期不眠症	0	0	1 (0.1)
不眠症	6 (4.6)	1 (0.8)	12 (1.7)
故意の自傷行為	0	0	0
易刺激性	0	1 (0.8)	2 (0.3)
リビドー減退	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)					
抑うつ気分	0	1 (0.2)	0	1 (0.2)	3 (0.1)
うつ病	0	5 (1.0)	3 (0.5)	10 (1.7)	33 (1.4)
薬物依存	0	0	1 (0.2)	0	1 (<0.1)
全般性不安障害	0	0	0	0	1 (<0.1)
初期不眠症	0	0	0	0	1 (<0.1)
不眠症	2 (8.3)	16 (3.3)	5 (0.8)	16 (2.7)	45 (1.9)
故意の自傷行為	0	0	0	1 (0.2)	1 (<0.1)
易刺激性	0	1 (0.2)	0	0	2 (<0.1)
リビドー減退	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
精神障害 (Cont.)			
精神障害	0	0	0
気分変化	0	0	1 (0.1)
悪夢	0	0	0
パニック発作	1 (0.8)	0	0
心的外傷後ストレス障害	0	0	0
落ち着きのなさ	0	0	0
睡眠障害	1 (0.8)	0	2 (0.3)
社交不安障害	0	0	1 (0.1)
ストレス	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)					
精神障害	0	1 (0.2)	0	0	0
気分変化	0	0	0	0	1 (<0.1)
悪夢	0	0	0	1 (0.2)	1 (<0.1)
パニック発作	0	0	1 (0.2)	0	1 (<0.1)
心的外傷後ストレス障害	0	0	1 (0.2)	0	1 (<0.1)
落ち着きのなさ	0	1 (0.2)	0	0	1 (<0.1)
睡眠障害	0	2 (0.4)	3 (0.5)	0	6 (0.3)
社交不安障害	0	0	0	0	1 (<0.1)
ストレス	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
精神障害 (Cont.)			
自殺念慮	0	0	0
自殺企図	0	0	1 (0.1)
腎および尿路障害	12 (9.1)	5 (4.0)	41 (5.9)
急性腎障害	0	0	0
膀胱痛	1 (0.8)	0	0
膀胱タンポナーデ	0	0	1 (0.1)
膀胱結石	0	0	0
尿路結石	0	0	0
着色尿	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)					
自殺念慮	0	2 (0.4)	0	0	1 (<0.1)
自殺企図	0	1 (0.2)	0	0	2 (<0.1)
腎および尿路障害	3 (12.5)	26 (5.4)	19 (3.1)	35 (5.9)	115 (4.9)
急性腎障害	0	1 (0.2)	1 (0.2)	2 (0.3)	3 (0.1)
膀胱痛	0	0	0	0	0
膀胱タンポナーデ	0	0	0	0	1 (<0.1)
膀胱結石	0	0	0	1 (0.2)	1 (<0.1)
尿路結石	0	0	1 (0.2)	0	1 (<0.1)
着色尿	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
慢性腎臓病	0	0	0
肋骨脊柱角圧痛	0	0	1 (0.1)
出血性膀胱炎	0	0	1 (0.1)
非感染性膀胱炎	0	0	2 (0.3)
排尿困難	2 (1.5)	0	8 (1.1)
糖尿	0	0	0
血尿	1 (0.8)	0	2 (0.3)
水腎症	0	0	0
緊張性膀胱	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
慢性腎臓病	1 (4.2)	0	0	1 (0.2)	2 (<0.1)
肋骨脊柱角圧痛	0	0	0	0	1 (<0.1)
出血性膀胱炎	0	0	0	0	1 (<0.1)
非感染性膀胱炎	0	0	0	0	2 (<0.1)
排尿困難	1 (4.2)	5 (1.0)	3 (0.5)	4 (0.7)	20 (0.9)
糖尿	0	1 (0.2)	0	0	0
血尿	0	3 (0.6)	2 (0.3)	6 (1.0)	11 (0.5)
水腎症	0	1 (0.2)	0	0	0
緊張性膀胱	0	1 (0.2)	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
ケトン尿	0	0	0
白血球尿	0	0	0
排尿異常	0	0	0
尿意切迫	0	0	2 (0.3)
腎炎	0	0	0
腎石灰沈着症	0	0	0
腎結石症	1 (0.8)	3 (2.4)	4 (0.6)
夜間頻尿	0	0	3 (0.4)
頻尿	2 (1.5)	1 (0.8)	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
ケトン尿	0	1 (0.2)	0	0	0
白血球尿	1 (4.2)	1 (0.2)	0	0	1 (<0.1)
排尿異常	0	0	0	1 (0.2)	1 (<0.1)
尿意切迫	0	0	0	1 (0.2)	3 (0.1)
腎炎	0	0	0	1 (0.2)	1 (<0.1)
腎石灰沈着症	0	1 (0.2)	0	0	0
腎結石症	0	5 (1.0)	5 (0.8)	4 (0.7)	19 (0.8)
夜間頻尿	0	0	0	0	3 (0.1)
頻尿	0	1 (0.2)	0	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
多尿	0	0	1 (0.1)
蛋白尿	4 (3.0)	0	7 (1.0)
腎萎縮	0	1 (0.8)	0
腎仙痛	0	0	2 (0.3)
腎嚢胞	0	0	0
腎機能障害	0	0	1 (0.1)
腎臓痛	0	0	1 (0.1)
腎尿細管機能障害	0	0	0
尿管閉塞	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
多尿	0	0	0	0	1 (<0.1)
蛋白尿	0	4 (0.8)	1 (0.2)	4 (0.7)	14 (0.6)
腎萎縮	0	0	0	0	1 (<0.1)
腎仙痛	0	0	0	6 (1.0)	8 (0.3)
腎嚢胞	0	0	1 (0.2)	0	1 (<0.1)
腎機能障害	0	0	3 (0.5)	0	4 (0.2)
腎臓痛	0	1 (0.2)	0	0	2 (<0.1)
腎尿細管機能障害	0	0	0	1 (0.2)	1 (<0.1)
尿管閉塞	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
尿管結石症	0	0	3 (0.4)
尿閉	0	0	0
生殖系および乳房障害	0	5 (4.0)	21 (3.0)
無月経	0	0	0
萎縮性外陰腟炎	0	0	1 (0.1)
バルトリン嚢腫	0	0	0
良性前立腺肥大症	0	0	2 (0.3)
乳房嚢胞	0	0	0
乳房障害	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
尿管結石症	0	0	1 (0.2)	1 (0.2)	5 (0.2)
尿閉	0	0	1 (0.2)	0	1 (<0.1)
生殖系および乳房障害	0	22 (4.6)	22 (3.5)	21 (3.5)	82 (3.5)
無月経	0	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.2)
萎縮性外陰腟炎	0	0	0	0	1 (<0.1)
バルトリン嚢腫	0	1 (0.2)	0	0	0
良性前立腺肥大症	0	0	3 (0.5)	4 (0.7)	9 (0.4)
乳房嚢胞	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
乳房障害	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
乳房腫大	0	0	1 (0.1)
乳房腫瘤	0	0	0
乳房痛	0	0	0
子宮頚部上皮異形成	0	0	1 (0.1)
子宮頚管ポリープ	0	0	1 (0.1)
子宮頚部障害	0	1 (0.8)	0
子宮頚部の炎症	0	0	0
性交出血	0	0	1 (0.1)
機能不全性子宮出血	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
乳房腫大	0	0	0	0	1 (<0.1)
乳房腫瘤	0	1 (0.2)	0	0	1 (<0.1)
乳房痛	0	0	1 (0.2)	0	1 (<0.1)
子宮頚部上皮異形成	0	1 (0.2)	0	2 (0.3)	4 (0.2)
子宮頚管ポリープ	0	0	0	0	1 (<0.1)
子宮頚部障害	0	0	0	0	1 (<0.1)
子宮頚部の炎症	0	0	1 (0.2)	0	1 (<0.1)
性交出血	0	0	1 (0.2)	0	2 (<0.1)
機能不全性子宮出血	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
月経困難症	0	0	1 (0.1)
性交困難	0	0	0
子宮内膜症	0	0	0
勃起不全	0	1 (0.8)	1 (0.1)
性器びらん	0	0	1 (0.1)
閉経期症状	0	0	0
月経過多	0	0	0
不規則月経	0	0	1 (0.1)
不正子宮出血	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
月経困難症	0	0	1 (0.2)	2 (0.3)	4 (0.2)
性交困難	0	0	1 (0.2)	0	1 (<0.1)
子宮内膜症	0	1 (0.2)	0	0	1 (<0.1)
勃起不全	0	0	1 (0.2)	1 (0.2)	4 (0.2)
性器びらん	0	0	0	0	1 (<0.1)
閉経期症状	0	2 (0.4)	0	0	1 (<0.1)
月経過多	0	0	2 (0.3)	0	2 (<0.1)
不規則月経	0	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.2)
不正子宮出血	0	0	2 (0.3)	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
卵巣嚢胞	0	0	1 (0.1)
卵巣静脈血栓症	0	0	0
多嚢胞性卵巣	0	0	0
閉経後出血	0	0	0
月経前頭痛	0	0	0
月経前症候群	0	1 (0.8)	0
前立腺腫瘤	0	0	0
前立腺炎	0	1 (0.8)	4 (0.6)
精液変色	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
卵巣嚢胞	0	1 (0.2)	0	0	2 (<0.1)
卵巣静脈血栓症	0	1 (0.2)	0	0	0
多嚢胞性卵巣	0	0	1 (0.2)	0	1 (<0.1)
閉経後出血	0	0	0	1 (0.2)	1 (<0.1)
月経前頭痛	0	0	0	1 (0.2)	1 (<0.1)
月経前症候群	0	0	0	0	1 (<0.1)
前立腺腫瘤	0	0	0	1 (0.2)	1 (<0.1)
前立腺炎	0	2 (0.4)	1 (0.2)	2 (0.3)	9 (0.4)
精液変色	0	1 (0.2)	0	2 (0.3)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
精嚢腺炎	0	0	0
子宮ポリープ	0	0	1 (0.1)
子宮脱	0	1 (0.8)	0
腟分泌物	0	0	1 (0.1)
腟出血	0	0	0
精索静脈瘤	0	0	0
外陰腟不快感	0	0	1 (0.1)
外陰腟の炎症	0	0	1 (0.1)
外陰腟痛	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
精嚢腺炎	0	0	1 (0.2)	0	1 (<0.1)
子宮ポリープ	0	0	0	0	1 (<0.1)
子宮脱	0	0	0	0	1 (<0.1)
腟分泌物	0	0	1 (0.2)	1 (0.2)	3 (0.1)
腟出血	0	2 (0.4)	1 (0.2)	0	2 (<0.1)
精索静脈瘤	0	0	1 (0.2)	0	1 (<0.1)
外陰腟不快感	0	0	0	1 (0.2)	2 (<0.1)
外陰腟の炎症	0	0	0	0	1 (<0.1)
外陰腟痛	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
外陰腟そう痒症	0	0	0
呼吸器、胸郭および縦隔障害	31 (23.6)	9 (7.2)	123 (17.6)
急性呼吸不全	0	0	0
胞隔炎	0	0	0
失声症	0	0	0
喘息	0	0	8 (1.1)
無気肺	0	0	1 (0.1)
気管支反応性亢進	0	0	0
気管支拡張症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
外陰腟そう痒症	0	2 (0.4)	0	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	14 (58.1)	70 (14.6)	55 (8.8)	65 (11.0)	310 (13.2)
急性呼吸不全	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
胞隔炎	1 (4.2)	0	0	0	1 (<0.1)
失声症	0	0	0	2 (0.3)	2 (<0.1)
喘息	0	1 (0.2)	1 (0.2)	1 (0.2)	11 (0.5)
無気肺	0	1 (0.2)	0	0	2 (<0.1)
気管支反応性亢進	0	0	0	1 (0.2)	1 (<0.1)
気管支拡張症	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
カタル	1 (0.8)	0	0
慢性閉塞性肺疾患	1 (0.8)	0	1 (0.1)
咳嗽	7 (5.3)	2 (1.6)	29 (4.1)
嚢胞性肺疾患	0	0	0
横隔膜痛	1 (0.8)	0	0
咽喉乾燥	0	0	0
発声障害	0	0	1 (0.1)
呼吸困難	0	0	12 (1.7)
労作性呼吸困難	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
カタル	0	0	0	0	0
慢性閉塞性肺疾患	0	0	3 (0.5)	0	4 (0.2)
咳嗽	4 (16.6)	14 (2.9)	14 (2.2)	10 (1.7)	69 (2.9)
嚢胞性肺疾患	0	0	1 (0.2)	0	1 (<0.1)
横隔膜痛	0	0	0	0	0
咽喉乾燥	0	0	1 (0.2)	0	1 (<0.1)
発声障害	0	1 (0.2)	0	0	2 (<0.1)
呼吸困難	2 (8.3)	2 (0.4)	3 (0.5)	2 (0.3)	21 (0.9)
労作性呼吸困難	0	0	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
肺気腫	0	0	0
鼻出血	0	1 (0.8)	8 (1.1)
喀血	0	0	0
しゃっくり	0	0	0
過換気	0	0	0
上気道分泌増加	0	0	0
間質性肺疾患	0	0	0
肺過膨脹	0	0	0
肺浸潤	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
肺気腫	0	0	0	1 (0.2)	1 (<0.1)
鼻出血	0	1 (0.2)	1 (0.2)	4 (0.7)	15 (0.6)
喀血	0	1 (0.2)	0	0	0
しゃっくり	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
過換気	0	0	0	1 (0.2)	1 (<0.1)
上気道分泌増加	0	1 (0.2)	0	0	1 (<0.1)
間質性肺疾患	0	1 (0.2)	0	0	0
肺過膨脹	0	0	0	1 (0.2)	1 (<0.1)
肺浸潤	0	0	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
鼻閉	1 (0.8)	1 (0.8)	6 (0.9)
鼻中隔弯曲	0	0	0
鼻中隔障害	0	0	0
鼻中隔穿孔	0	0	1 (0.1)
鼻甲介肥大	0	0	0
鼻潰瘍	0	0	0
非感染性気管支炎	0	0	0
口腔咽頭不快感	0	0	1 (0.1)
口腔咽頭痛	3 (2.3)	2 (1.6)	25 (3.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
鼻閉	1 (4.2)	3 (0.6)	1 (0.2)	4 (0.7)	13 (0.6)
鼻中隔弯曲	0	0	1 (0.2)	0	1 (<0.1)
鼻中隔障害	0	0	0	1 (0.2)	1 (<0.1)
鼻中隔穿孔	0	0	0	0	1 (<0.1)
鼻甲介肥大	0	0	1 (0.2)	0	1 (<0.1)
鼻潰瘍	0	0	3 (0.5)	0	3 (0.1)
非感染性気管支炎	0	0	0	1 (0.2)	1 (<0.1)
口腔咽頭不快感	0	1 (0.2)	0	0	2 (<0.1)
口腔咽頭痛	3 (12.5)	14 (2.9)	11 (1.8)	10 (1.7)	60 (2.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
呼吸時疼痛	0	0	1 (0.1)
副鼻腔不快感	1 (0.8)	0	0
副鼻腔分泌過多	0	0	1 (0.1)
咽頭紅斑	0	0	0
咽頭病変	0	0	1 (0.1)
胸膜障害	1 (0.8)	0	0
胸水	0	0	2 (0.3)
胸膜痛	0	0	1 (0.1)
肺臓炎	2 (1.5)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
呼吸時疼痛	0	0	0	0	1 (<0.1)
副鼻腔不快感	0	0	0	0	0
副鼻腔分泌過多	0	0	0	0	1 (<0.1)
咽頭紅斑	0	0	0	1 (0.2)	1 (<0.1)
咽頭病変	0	0	0	0	1 (<0.1)
胸膜障害	0	0	0	0	0
胸水	0	1 (0.2)	1 (0.2)	0	4 (0.2)
胸膜痛	0	0	0	0	1 (<0.1)
肺臓炎	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
気胸	1 (0.8)	0	0
湿性咳嗽	0	0	1 (0.1)
肺塞栓症	1 (0.8)	0	3 (0.4)
肺出血	0	0	0
肺腫瘤	2 (1.5)	0	3 (0.4)
逆流性喉頭炎	0	1 (0.8)	0
気道うっ血	0	0	2 (0.3)
鼻痛	0	0	1 (0.1)
アレルギー性鼻炎	1 (0.8)	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
気胸	0	0	0	0	0
湿性咳嗽	0	3 (0.6)	2 (0.3)	3 (0.5)	8 (0.3)
肺塞栓症	1 (4.2)	0	4 (0.6)	3 (0.5)	11 (0.5)
肺出血	0	1 (0.2)	0	0	0
肺腫瘤	1 (4.2)	1 (0.2)	0	0	5 (0.2)
逆流性喉頭炎	0	0	0	0	1 (<0.1)
気道うっ血	0	1 (0.2)	0	0	3 (0.1)
鼻痛	1 (4.2)	0	0	0	2 (<0.1)
アレルギー性鼻炎	0	7 (1.5)	2 (0.3)	1 (0.2)	10 (0.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
鼻漏	2 (1.5)	1 (0.8)	1 (0.1)
低音性連続性ラ音	0	0	0
副鼻腔うっ血	2 (1.5)	0	2 (0.3)
副鼻腔障害	0	0	0
副鼻腔痛	0	0	0
睡眠時無呼吸症候群	0	0	4 (0.6)
咽喉刺激感	0	0	1 (0.1)
扁桃肥大	0	0	1 (0.1)
上気道うっ血	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
鼻漏	0	0	0	2 (0.3)	4 (0.2)
低音性連続性ラ音	0	0	1 (0.2)	0	1 (<0.1)
副鼻腔うっ血	0	3 (0.6)	2 (0.3)	5 (0.8)	9 (0.4)
副鼻腔障害	0	0	0	1 (0.2)	1 (<0.1)
副鼻腔痛	0	1 (0.2)	0	0	1 (<0.1)
睡眠時無呼吸症候群	0	1 (0.2)	1 (0.2)	2 (0.3)	8 (0.3)
咽喉刺激感	0	0	0	1 (0.2)	2 (<0.1)
扁桃肥大	0	0	0	0	1 (<0.1)
上気道うっ血	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
上気道の炎症	2 (1.5)	0	0
上気道咳症候群	2 (1.5)	0	1 (0.1)
声帯ポリープ	0	1 (0.8)	0
喘鳴	0	0	0
皮膚および皮下組織障害	49 (37.3)	30 (24.0)	144 (20.6)
ざ瘡	3 (2.3)	3 (2.4)	23 (3.3)
嚢胞性ざ瘡	0	0	0
光線性弾性線維症	0	0	0
光線角化症	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
上気道の炎症	0	4 (0.8)	1 (0.2)	1 (0.2)	4 (0.2)
上気道咳症候群	0	1 (0.2)	0	2 (0.3)	4 (0.2)
声帯ポリープ	0	0	0	0	0
喘鳴	0	2 (0.4)	0	0	2 (<0.1)
皮膚および皮下組織障害	19 (78.9)	171 (35.7)	134 (21.5)	166 (28.1)	573 (24.4)
ざ瘡	5 (20.8)	27 (5.6)	27 (4.3)	42 (7.1)	119 (5.1)
嚢胞性ざ瘡	0	0	1 (0.2)	0	1 (<0.1)
光線性弾性線維症	0	1 (0.2)	0	0	1 (<0.1)
光線角化症	0	3 (0.6)	0	2 (0.3)	6 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
脱毛症	2 (1.5)	1 (0.8)	12 (1.7)
円形脱毛症	0	0	0
アンドロゲン性脱毛症	0	0	0
皮脂欠乏症	0	0	0
水疱	0	0	0
皮膚嚢腫	0	0	1 (0.1)
皮膚炎	2 (1.5)	1 (0.8)	3 (0.4)
ざ瘡様皮膚炎	1 (0.8)	0	5 (0.7)
アレルギー性皮膚炎	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
脱毛症	2 (8.3)	4 (0.8)	6 (1.0)	10 (1.7)	35 (1.5)
円形脱毛症	0	0	1 (0.2)	0	1 (<0.1)
アンドロゲン性脱毛症	0	0	0	1 (0.2)	1 (<0.1)
皮脂欠乏症	0	0	0	1 (0.2)	1 (<0.1)
水疱	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
皮膚嚢腫	0	0	2 (0.3)	2 (0.3)	5 (0.2)
皮膚炎	0	4 (0.8)	3 (0.5)	4 (0.7)	11 (0.5)
ざ瘡様皮膚炎	1 (4.2)	3 (0.6)	4 (0.6)	2 (0.3)	15 (0.6)
アレルギー性皮膚炎	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
アトピー性皮膚炎	1 (0.8)	0	1 (0.1)
接触皮膚炎	3 (2.3)	0	2 (0.3)
剥脱性皮膚炎	0	0	0
乾癬様皮膚炎	0	1 (0.8)	0
皮膚症	0	0	0
びまん性脱毛症	0	0	0
薬疹	0	0	1 (0.1)
皮膚乾燥	3 (2.3)	2 (1.6)	3 (0.4)
異汗性湿疹	2 (1.5)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
アトピー性皮膚炎	0	4 (0.8)	3 (0.5)	1 (0.2)	6 (0.3)
接触皮膚炎	0	3 (0.6)	2 (0.3)	2 (0.3)	7 (0.3)
剥脱性皮膚炎	0	0	1 (0.2)	0	1 (<0.1)
乾癬様皮膚炎	0	0	0	0	0
皮膚症	0	1 (0.2)	0	0	1 (<0.1)
びまん性脱毛症	0	0	1 (0.2)	0	1 (<0.1)
薬疹	0	0	0	0	1 (<0.1)
皮膚乾燥	0	5 (1.0)	2 (0.3)	2 (0.3)	8 (0.3)
異汗性湿疹	0	3 (0.6)	0	2 (0.3)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
斑状出血	0	0	1 (0.1)
湿疹	4 (3.0)	0	10 (1.4)
皮脂欠乏性湿疹	0	0	1 (0.1)
紅斑	1 (0.8)	3 (2.4)	4 (0.6)
環状紅斑	0	0	1 (0.1)
多形紅斑	0	0	0
結節性紅斑	0	1 (0.8)	0
固定疹	0	0	0
多汗症	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
斑状出血	0	3 (0.6)	1 (0.2)	1 (0.2)	5 (0.2)
湿疹	1 (4.2)	10 (2.1)	8 (1.3)	8 (1.4)	32 (1.4)
皮脂欠乏性湿疹	0	1 (0.2)	0	4 (0.7)	5 (0.2)
紅斑	0	4 (0.8)	4 (0.6)	4 (0.7)	15 (0.6)
環状紅斑	0	0	0	0	1 (<0.1)
多形紅斑	1 (4.2)	0	0	0	1 (<0.1)
結節性紅斑	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
固定疹	0	0	0	1 (0.2)	1 (<0.1)
多汗症	0	1 (0.2)	1 (0.2)	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
過角化	0	0	0
多毛症	0	1 (0.8)	0
嵌入爪	0	0	0
内方発育毛	0	0	1 (0.1)
間擦疹	0	0	0
瘢痕そう痒感	0	0	0
毛孔性角化症	0	0	1 (0.1)
黒子	0	0	0
扁平苔癬	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
過角化	0	2 (0.4)	0	1 (0.2)	3 (0.1)
多毛症	0	0	0	0	0
嵌入爪	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
内方発育毛	0	0	0	0	1 (<0.1)
間擦疹	0	0	1 (0.2)	0	1 (<0.1)
瘢痕そう痒感	0	0	0	1 (0.2)	1 (<0.1)
毛孔性角化症	0	1 (0.2)	0	0	2 (<0.1)
黒子	0	0	0	1 (0.2)	1 (<0.1)
扁平苔癬	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
機械性蕁麻疹	0	0	1 (0.1)
汗疹	0	0	1 (0.1)
爪床の炎症	0	0	1 (0.1)
爪肥厚	0	0	1 (0.1)
神経皮膚炎	0	0	0
寝汗	1 (0.8)	1 (0.8)	3 (0.4)
爪破損	0	0	1 (0.1)
爪甲剥離症	0	0	1 (0.1)
皮膚疼痛	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
機械性蕁麻疹	0	0	0	1 (0.2)	2 (<0.1)
汗疹	0	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.2)
爪床の炎症	0	0	0	0	1 (<0.1)
爪肥厚	0	0	0	0	1 (<0.1)
神経皮膚炎	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
寝汗	0	2 (0.4)	3 (0.5)	4 (0.7)	12 (0.5)
爪破損	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
爪甲剥離症	0	0	0	1 (0.2)	2 (<0.1)
皮膚疼痛	1 (4.2)	0	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
掌蹠膿疱症	0	0	0
脂肪織炎	0	0	1 (0.1)
丘疹	1 (0.8)	0	1 (0.1)
口囲皮膚炎	0	0	1 (0.1)
点状出血	0	0	1 (0.1)
光線性皮膚症	0	0	0
光線過敏性反応	0	0	0
そう痒症	10 (7.6)	3 (2.4)	11 (1.6)
乾癬	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
掌蹠膿疱症	0	0	1 (0.2)	0	1 (<0.1)
脂肪織炎	0	0	1 (0.2)	0	2 (<0.1)
丘疹	1 (4.2)	1 (0.2)	2 (0.3)	3 (0.5)	8 (0.3)
口囲皮膚炎	0	0	1 (0.2)	0	2 (<0.1)
点状出血	0	0	0	0	1 (<0.1)
光線性皮膚症	0	1 (0.2)	0	0	0
光線過敏性反応	1 (4.2)	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.2)
そう痒症	1 (4.2)	12 (2.5)	7 (1.1)	3 (0.5)	28 (1.2)
乾癬	0	1 (0.2)	0	0	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
壊疽性膿皮症	1 (0.8)	0	0
発疹	6 (4.6)	7 (5.6)	24 (3.4)
紅斑性皮疹	1 (0.8)	0	3 (0.4)
毛孔性皮疹	0	0	0
斑状皮疹	0	0	1 (0.1)
斑状丘疹状皮疹	0	2 (1.6)	0
丘疹性皮疹	0	0	1 (0.1)
そう痒性皮疹	0	0	2 (0.3)
酒さ	1 (0.8)	1 (0.8)	8 (1.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
壊疽性膿皮症	1 (4.2)	1 (0.2)	0	0	1 (<0.1)
発疹	2 (8.3)	29 (6.1)	21 (3.4)	22 (3.7)	92 (3.9)
紅斑性皮疹	0	1 (0.2)	3 (0.5)	0	6 (0.3)
毛孔性皮疹	1 (4.2)	1 (0.2)	2 (0.3)	0	4 (0.2)
斑状皮疹	0	0	2 (0.3)	2 (0.3)	5 (0.2)
斑状丘疹状皮疹	0	1 (0.2)	2 (0.3)	6 (1.0)	8 (0.3)
丘疹性皮疹	0	3 (0.6)	2 (0.3)	0	6 (0.3)
そう痒性皮疹	0	0	0	3 (0.5)	5 (0.2)
酒さ	0	3 (0.6)	3 (0.5)	1 (0.2)	15 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
脂腺過形成	0	0	0
脂漏性皮膚炎	1 (0.8)	0	1 (0.1)
皮膚灼熱感	0	0	0
皮膚変色	0	0	1 (0.1)
皮膚不快感	0	0	1 (0.1)
皮膚びらん	0	0	0
皮膚剥脱	0	0	0
皮膚亀裂	0	0	0
皮膚色素過剰	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
脂腺過形成	0	1 (0.2)	0	0	1 (<0.1)
脂漏性皮膚炎	1 (4.2)	9 (1.9)	4 (0.6)	3 (0.5)	11 (0.5)
皮膚灼熱感	0	1 (0.2)	0	0	0
皮膚変色	0	1 (0.2)	1 (0.2)	0	3 (0.1)
皮膚不快感	0	0	0	0	1 (<0.1)
皮膚びらん	0	1 (0.2)	0	0	0
皮膚剥脱	0	2 (0.4)	1 (0.2)	1 (0.2)	3 (0.1)
皮膚亀裂	0	2 (0.4)	1 (0.2)	0	2 (<0.1)
皮膚色素過剰	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
皮膚病変	0	1 (0.8)	2 (0.3)
皮膚腫瘤	0	0	0
皮膚線条	0	0	0
皮膚潰瘍	0	1 (0.8)	0
日光皮膚炎	0	1 (0.8)	0
毛細血管拡張症	0	0	0
蕁麻疹	2 (1.5)	0	2 (0.3)
尋常性白斑	1 (0.8)	0	0
乾皮症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
皮膚病変	0	2 (0.4)	2 (0.3)	7 (1.2)	14 (0.6)
皮膚腫瘤	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
皮膚線条	0	0	1 (0.2)	0	1 (<0.1)
皮膚潰瘍	0	1 (0.2)	0	3 (0.5)	4 (0.2)
日光皮膚炎	0	0	0	0	0
毛細血管拡張症	0	0	1 (0.2)	0	1 (<0.1)
蕁麻疹	0	5 (1.0)	0	6 (1.0)	10 (0.4)
尋常性白斑	0	0	0	0	0
乾皮症	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
社会環境	0	0	0
閉経	0	0	0
閉経後	0	0	0
外科および内科処置	0	2 (1.6)	1 (0.1)
人工流産	0	0	1 (0.1)
歯科インプラント埋込み	0	0	0
植込み型除細動器挿入	0	0	0
抜歯	0	1 (0.8)	0
智歯抜歯	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
社会環境	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
閉経	0	1 (0.2)	0	0	1 (<0.1)
閉経後	0	0	0	1 (0.2)	1 (<0.1)
外科および内科処置	0	2 (0.4)	7 (1.1)	2 (0.3)	14 (0.6)
人工流産	0	0	2 (0.3)	0	3 (0.1)
歯科インプラント埋込み	0	0	0	1 (0.2)	1 (<0.1)
植込み型除細動器挿入	0	0	1 (0.2)	0	1 (<0.1)
抜歯	0	1 (0.2)	2 (0.3)	1 (0.2)	5 (0.2)
智歯抜歯	0	1 (0.2)	2 (0.3)	0	4 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血管障害	12 (9.1)	9 (7.2)	26 (3.7)
大動脈瘤	0	0	0
大動脈硬化症	0	0	0
動脈硬化症	0	0	1 (0.1)
出血性静脈瘤	0	0	0
コントロール不良の血圧	0	1 (0.8)	0
深部静脈血栓症	0	3 (2.4)	2 (0.3)
本態性高血圧症	0	0	1 (0.1)
潮紅	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害	2 (8.3)	25 (5.2)	28 (4.5)	36 (6.1)	117 (5.0)
大動脈瘤	0	0	1 (0.2)	0	1 (<0.1)
大動脈硬化症	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
動脈硬化症	0	1 (0.2)	0	0	2 (<0.1)
出血性静脈瘤	0	0	1 (0.2)	0	1 (<0.1)
コントロール不良の血圧	0	0	0	0	1 (<0.1)
深部静脈血栓症	1 (4.2)	0	0	3 (0.5)	8 (0.3)
本態性高血圧症	0	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.1)
潮紅	0	0	1 (0.2)	0	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血管障害 (Cont.)			
血腫	1 (0.8)	0	1 (0.1)
出血	0	0	1 (0.1)
ほてり	0	0	3 (0.4)
高血圧	7 (5.3)	4 (3.2)	13 (1.9)
高血圧クリーゼ	0	0	1 (0.1)
低血圧	1 (0.8)	0	0
起立性低血圧	0	0	0
蒼白	0	0	0
骨盤静脈血栓症	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害 (Cont.)					
血腫	0	0	0	1 (0.2)	2 (<0.1)
出血	0	0	0	0	1 (<0.1)
ほてり	0	1 (0.2)	0	1 (0.2)	5 (0.2)
高血圧	0	15 (3.1)	19 (3.1)	22 (3.7)	70 (3.0)
高血圧クリーゼ	0	1 (0.2)	0	0	1 (<0.1)
低血圧	1 (4.2)	1 (0.2)	0	2 (0.3)	3 (0.1)
起立性低血圧	0	0	0	1 (0.2)	1 (<0.1)
蒼白	0	0	1 (0.2)	0	1 (<0.1)
骨盤静脈血栓症	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血管障害 (Cont.)			
末梢動脈閉塞性疾患	0	0	0
末梢冷感	1 (0.8)	0	0
末梢静脈疾患	0	1 (0.8)	0
静脈炎	0	0	0
レイノー現象	0	0	0
血栓性静脈炎	0	0	0
表在性血栓性静脈炎	1 (0.8)	0	0
静脈瘤	0	0	1 (0.1)
静脈血栓症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害 (Cont.)					
末梢動脈閉塞性疾患	0	0	0	1 (0.2)	1 (<0.1)
末梢冷感	0	0	0	0	0
末梢静脈疾患	0	0	1 (0.2)	0	2 (<0.1)
静脈炎	0	0	0	1 (0.2)	1 (<0.1)
レイノー現象	0	3 (0.6)	1 (0.2)	0	3 (0.1)
血栓性静脈炎	0	1 (0.2)	0	0	1 (<0.1)
表在性血栓性静脈炎	0	0	0	0	0
静脈瘤	0	0	0	0	1 (<0.1)
静脈血栓症	0	1 (0.2)	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血管障害 (Cont.)			
白衣性高血圧	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害 (Cont.)					
白衣性高血圧	0	0	0	2 (0.3)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-101.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
Any adverse event	1558 (486.7)	150 (666.1)	3663 (285.5)	2602 (297.2)	6265 (290.2)	1372 (810.9)	7787 (331.3)
血液およびリンパ系障害	75 (23.4)	3 (13.3)	121 (9.4)	86 (9.8)	207 (9.6)	93 (55.0)	303 (12.9)
貧血	41 (12.8)	2 (8.9)	46 (3.6)	24 (2.7)	70 (3.2)	37 (21.9)	109 (4.6)
大球性貧血	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
失血性貧血	0	0	0	0	0	2 (1.2)	2 (<0.1)
周期性好中球減少症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
好酸球増加症	2 (0.6)	0	0	0	0	0	0
顆粒球減少症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
内出血発生の増加傾向	1 (0.3)	0	1 (<0.1)	3 (0.3)	4 (0.2)	1 (0.6)	5 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)							
鉄欠乏性貧血	6 (1.9)	0	5 (0.4)	5 (0.6)	10 (0.5)	6 (3.5)	16 (0.7)
白血球増加症	1 (0.3)	0	2 (0.2)	2 (0.2)	4 (0.2)	1 (0.6)	5 (0.2)
白血球減少症	5 (1.6)	0	17 (1.3)	15 (1.7)	32 (1.5)	10 (5.9)	42 (1.8)
リンパ節症	1 (0.3)	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
リンパ球増加症	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
リンパ球減少症	7 (2.2)	1 (4.4)	15 (1.2)	9 (1.0)	24 (1.1)	14 (8.3)	39 (1.7)
小球性貧血	0	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
好中球減少症	6 (1.9)	0	19 (1.5)	20 (2.3)	39 (1.8)	19 (11.2)	58 (2.5)
好中球増加症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)							
正球性貧血	1 (0.3)	0	0	0	0	0	0
汎血球減少症	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
網状赤血球増加症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脾腫	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
血小板減少症	2 (0.6)	0	0	0	0	2 (1.2)	2 (<0.1)
血小板増加症	1 (0.3)	0	4 (0.3)	1 (0.1)	5 (0.2)	1 (0.6)	6 (0.3)
心臓障害	19 (5.9)	0	26 (2.0)	25 (2.9)	51 (2.4)	5 (3.0)	56 (2.4)
急性心筋梗塞	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
不安定狭心症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)							
不整脈	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
心房細動	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
完全房室ブロック	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
第一度房室ブロック	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
二束ブロック	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
徐脈性不整脈	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
徐脈	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
脚ブロック	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
左脚ブロック	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)							
心不全	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
うっ血性心不全	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
心拡大	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
慢性左室不全	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
うっ血性心筋症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
冠動脈疾患	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
期外収縮	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
虚血性心筋症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
僧帽弁閉鎖不全症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)							
心筋梗塞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
動悸	9 (2.8)	0	4 (0.3)	0	4 (0.2)	3 (1.8)	7 (0.3)
心嚢液貯留	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
心膜炎	0	0	0	2 (0.2)	2 (<0.1)	1 (0.6)	3 (0.1)
洞性不整脈	1 (0.3)	0	0	0	0	0	0
洞性徐脈	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
洞性頻脈	0	0	0	0	0	1 (0.6)	1 (<0.1)
上室性期外収縮	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
上室性頻脈	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)							
頻脈	3 (0.9)	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
心室性期外収縮	1 (0.3)	0	1 (<0.1)	4 (0.5)	5 (0.2)	0	5 (0.2)
心室性頻脈	0	0	3 (0.2)	0	3 (0.1)	0	3 (0.1)
ウォルフ・パーキンソン・ホワイト症候群	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
先天性、家族性および遺伝性障害	0	0	7 (0.5)	3 (0.3)	10 (0.5)	0	10 (0.4)
先天性横隔膜ヘルニア	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮様嚢腫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
胃腸管動静脈奇形	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
ジルベール症候群	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
先天性、家族性および遺伝性障害 (Cont.)							
陰嚢水瘤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
魚鱗癬	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
歯原性嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
包茎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
汗孔角化症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
耳および迷路障害	7 (2.2)	2 (8.9)	22 (1.7)	15 (1.7)	37 (1.7)	9 (5.3)	48 (2.0)
耳垢栓塞	0	1 (4.4)	0	0	0	0	1 (<0.1)
伝音難聴	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
感音性難聴	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
耳および迷路障害 (Cont.)							
片耳難聴	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
耳不快感	0	0	0	0	0	1 (0.6)	1 (<0.1)
耳痛	1 (0.3)	0	6 (0.5)	1 (0.1)	7 (0.3)	0	7 (0.3)
耳部腫脹	1 (0.3)	0	0	0	0	0	0
外耳道の外骨腫	1 (0.3)	0	0	0	0	0	0
外耳の炎症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
聴力低下	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
内耳障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
メニエール病	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
耳および迷路障害 (Cont.)							
中耳滲出液	1 (0.3)	0	0	0	0	0	0
耳漏	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
突発性難聴	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
耳鳴	0	1 (4.4)	5 (0.4)	4 (0.5)	9 (0.4)	3 (1.8)	13 (0.6)
回転性めまい	2 (0.6)	0	8 (0.6)	4 (0.5)	12 (0.6)	1 (0.6)	13 (0.6)
内分泌障害	2 (0.6)	2 (8.9)	6 (0.5)	4 (0.5)	10 (0.5)	1 (0.6)	13 (0.6)
アジソン病	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
副腎機能不全	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
急性副腎皮質機能不全	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
内分泌障害 (Cont.)							
クッシング症候群	1 (0.3)	0	0	0	0	0	0
クッシング様症状	0	2 (8.9)	1 (<0.1)	0	1 (<0.1)	1 (0.6)	4 (0.2)
甲状腺腫	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
甲状腺機能亢進症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
甲状腺機能低下症	1 (0.3)	0	0	0	0	0	0
続発性副腎皮質機能不全	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
甲状腺腫瘤	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
眼障害	25 (7.8)	5 (22.2)	46 (3.6)	31 (3.5)	77 (3.6)	24 (14.2)	106 (4.5)
無水晶体眼	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)							
眼精疲労	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)
眼瞼炎	1 (0.3)	0	4 (0.3)	3 (0.3)	7 (0.3)	1 (0.6)	8 (0.3)
眼瞼痙攣	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
白内障	2 (0.6)	2 (8.9)	11 (0.9)	3 (0.3)	14 (0.6)	3 (1.8)	19 (0.8)
霰粒腫	0	0	1 (<0.1)	4 (0.5)	5 (0.2)	1 (0.6)	6 (0.3)
結膜嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
結膜出血	0	1 (4.4)	1 (<0.1)	0	1 (<0.1)	2 (1.2)	4 (0.2)
結膜充血	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
アレルギー性結膜炎	2 (0.6)	0	2 (0.2)	3 (0.3)	5 (0.2)	0	5 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)							
結膜弛緩症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
角膜びらん	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
角膜浮腫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
角膜混濁	1 (0.3)	0	0	0	0	0	0
後天性涙道狭窄	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ドライアイ	0	0	5 (0.4)	3 (0.3)	8 (0.4)	4 (2.4)	12 (0.5)
上強膜炎	2 (0.6)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
眼のアレルギー	1 (0.3)	0	0	0	0	0	0
眼の障害	0	0	0	0	0	2 (1.2)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)							
眼出血	0	0	0	0	0	1 (0.6)	1 (<0.1)
眼刺激	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
眼痛	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
眼そう痒症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼部腫脹	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼瞼嚢胞	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
眼瞼障害	1 (0.3)	0	0	0	0	0	0
眼瞼刺激	0	0	0	0	0	1 (0.6)	1 (<0.1)
眼瞼発疹	1 (0.3)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)							
眼瞼肥厚	0	0	0	0	0	1 (0.6)	1 (<0.1)
緑内障	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)
虹彩毛様体炎	1 (0.3)	0	0	0	0	0	0
角膜炎	1 (0.3)	0	0	2 (0.2)	2 (<0.1)	1 (0.6)	3 (0.1)
流涙増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
黄斑浮腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
近視	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼部不快感	1 (0.3)	0	0	0	0	0	0
眼充血	0	0	3 (0.2)	1 (0.1)	4 (0.2)	1 (0.6)	5 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)							
高眼圧症	0	0	0	0	0	2 (1.2)	2 (<0.1)
開放隅角緑内障	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
眼窩周囲腫脹	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)
光視症	0	1 (4.4)	0	0	0	0	1 (<0.1)
翼状片	1 (0.3)	0	0	0	0	0	0
網膜静脈閉塞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
潰瘍性角膜炎	1 (0.3)	0	0	0	0	0	0
ぶどう膜炎	3 (0.9)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
霧視	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)							
視力低下	2 (0.6)	0	0	0	0	0	0
視力障害	0	1 (4.4)	1 (<0.1)	0	1 (<0.1)	0	2 (<0.1)
硝子体浮遊物	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
胃腸障害	346 (108.1)	25 (111.0)	579 (45.1)	356 (40.7)	935 (43.3)	202 (119.4)	1162 (49.4)
腹部不快感	4 (1.2)	0	3 (0.2)	0	3 (0.1)	1 (0.6)	4 (0.2)
腹部膨満	4 (1.2)	4 (17.8)	8 (0.6)	12 (1.4)	20 (0.9)	9 (5.3)	33 (1.4)
腹部ヘルニア	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
腹部腫瘤	1 (0.3)	0	0	0	0	0	0
腹痛	11 (3.4)	3 (13.3)	36 (2.8)	13 (1.5)	49 (2.3)	19 (11.2)	71 (3.0)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
下腹部痛	6 (1.9)	0	7 (0.5)	0	7 (0.3)	4 (2.4)	11 (0.5)
上腹部痛	8 (2.5)	0	15 (1.2)	8 (0.9)	23 (1.1)	5 (3.0)	28 (1.2)
腹部圧痛	1 (0.3)	1 (4.4)	7 (0.5)	4 (0.5)	11 (0.5)	4 (2.4)	16 (0.7)
異常便	1 (0.3)	0	0	0	0	0	0
無酸症	0	0	0	0	0	1 (0.6)	1 (<0.1)
裂肛	2 (0.6)	0	5 (0.4)	1 (0.1)	6 (0.3)	5 (3.0)	11 (0.5)
痔瘻	0	0	3 (0.2)	4 (0.5)	7 (0.3)	0	7 (0.3)
肛門失禁	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肛門の炎症	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
肛門ポリープ	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肛門そう痒症	2 (0.6)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肛門潰瘍	0	0	0	0	0	1 (0.6)	1 (<0.1)
口角口唇炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肛門直腸不快感	0	0	0	0	0	1 (0.6)	1 (<0.1)
アフタ性潰瘍	6 (1.9)	1 (4.4)	7 (0.5)	7 (0.8)	14 (0.6)	4 (2.4)	19 (0.8)
口唇のひび割れ	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
大腸炎	10 (3.1)	0	3 (0.2)	3 (0.3)	6 (0.3)	0	6 (0.3)
虚血性大腸炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
潰瘍性大腸炎	171 (53.4)	4 (17.8)	189 (14.7)	106 (12.1)	295 (13.7)	27 (16.0)	326 (13.9)
結腸異形成	0	0	3 (0.2)	3 (0.3)	6 (0.3)	1 (0.6)	7 (0.3)
便秘	6 (1.9)	2 (8.9)	21 (1.6)	15 (1.7)	36 (1.7)	15 (8.9)	53 (2.3)
クローン病	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
便意切迫	2 (0.6)	0	3 (0.2)	2 (0.2)	5 (0.2)	0	5 (0.2)
齲歯	2 (0.6)	0	6 (0.5)	4 (0.5)	10 (0.5)	1 (0.6)	11 (0.5)
歯嚢胞	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
歯不快感	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
歯組織の壊死	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
横隔膜ヘルニア	1 (0.3)	0	0	0	0	0	0
下痢	5 (1.6)	2 (8.9)	25 (1.9)	9 (1.0)	34 (1.6)	7 (4.1)	43 (1.8)
血性下痢	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
腸憩室	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
口内乾燥	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	2 (1.2)	4 (0.2)
十二指腸炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
排便困難	1 (0.3)	0	0	0	0	0	0
消化不良	6 (1.9)	0	14 (1.1)	12 (1.4)	26 (1.2)	5 (3.0)	31 (1.3)
嚥下障害	2 (0.6)	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
小腸炎	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	0	4 (0.2)
腸炎	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)
心窩部不快感	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
おくび	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
糞塊	2 (0.6)	0	0	0	0	0	0
変色便	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
白色便	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
軟便	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
大腿ヘルニア	0	0	3 (0.2)	0	3 (0.1)	0	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
鼓腸	8 (2.5)	2 (8.9)	10 (0.8)	8 (0.9)	18 (0.8)	6 (3.5)	26 (1.1)
食中毒	3 (0.9)	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.1)
排便回数増加	0	0	4 (0.3)	2 (0.2)	6 (0.3)	1 (0.6)	7 (0.3)
胃障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胃ポリープ	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胃潰瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胃炎	2 (0.6)	0	9 (0.7)	2 (0.2)	11 (0.5)	0	11 (0.5)
びらん性胃炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
胃腸障害	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
消化管運動障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
消化器痛	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
胃食道逆流性疾患	8 (2.5)	0	18 (1.4)	7 (0.8)	25 (1.2)	9 (5.3)	34 (1.4)
歯肉痛	0	0	0	1 (0.1)	1 (<0.1)	2 (1.2)	3 (0.1)
歯肉腫脹	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)
舌痛	1 (0.3)	0	0	0	0	0	0
血便排泄	3 (0.9)	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
痔出血	2 (0.6)	0	2 (0.2)	1 (0.1)	3 (0.1)	1 (0.6)	4 (0.2)
痔核	6 (1.9)	0	18 (1.4)	9 (1.0)	27 (1.3)	13 (7.7)	40 (1.7)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
血栓性痔核	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
裂孔ヘルニア	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
胃酸過多	0	0	0	0	0	1 (0.6)	1 (<0.1)
肛門肥大乳頭	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
回腸潰瘍	1 (0.3)	0	0	0	0	0	0
イレウス	0	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
炎症性腸疾患	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
鼠径ヘルニア	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	0	4 (0.2)
腸閉塞	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
腸管ポリープ	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
過敏性腸症候群	0	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)
大腸穿孔	2 (0.6)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
大腸ポリープ	4 (1.2)	0	13 (1.0)	7 (0.8)	20 (0.9)	2 (1.2)	22 (0.9)
口唇水疱	0	0	0	0	0	1 (0.6)	1 (<0.1)
口唇障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
口唇乾燥	0	0	0	0	0	1 (0.6)	1 (<0.1)
口唇腫脹	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
口唇潰瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
口腔嚢胞	1 (0.3)	0	0	0	0	0	0
口腔内潰瘍形成	4 (1.2)	0	5 (0.4)	2 (0.2)	7 (0.3)	2 (1.2)	9 (0.4)
粘液便	1 (0.3)	0	0	0	0	0	0
悪心	18 (5.6)	2 (8.9)	42 (3.3)	31 (3.5)	73 (3.4)	10 (5.9)	85 (3.6)
非感染性歯肉炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
嚥下痛	2 (0.6)	0	0	2 (0.2)	2 (<0.1)	1 (0.6)	3 (0.1)
食道運動低下	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
食道痛	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
食道潰瘍	0	0	0	0	0	1 (0.6)	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
食道炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
口腔障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
口腔知覚不全	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
口腔扁平苔癬	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
口腔粘膜紅斑	0	0	0	0	0	1 (0.6)	1 (<0.1)
口腔内痛	0	0	0	0	0	3 (1.8)	3 (0.1)
膵臓障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膵脂肪変性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膵炎	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
肛門周囲紅斑	0	1 (4.4)	0	0	0	0	1 (<0.1)
歯周病	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
肛門周囲痛	0	1 (4.4)	5 (0.4)	1 (0.1)	6 (0.3)	3 (1.8)	10 (0.4)
直腸炎	1 (0.3)	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
偽性ポリポーシス	0	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
直腸分泌物	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
直腸異形成	0	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
直腸出血	2 (0.6)	0	5 (0.4)	5 (0.6)	10 (0.5)	0	10 (0.4)
直腸ポリープ	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
直腸攣縮	1 (0.3)	0	0	0	0	0	0
直腸しぶり	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
口内炎	7 (2.2)	0	6 (0.5)	5 (0.6)	11 (0.5)	9 (5.3)	20 (0.9)
舌障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
舌潰瘍	0	0	0	0	0	2 (1.2)	2 (<0.1)
歯の障害	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
埋伏歯	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
歯の脱落	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
歯痛	0	0	11 (0.9)	14 (1.6)	25 (1.2)	1 (0.6)	26 (1.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)							
臍ヘルニア	1 (0.3)	0	2 (0.2)	1 (0.1)	3 (0.1)	1 (0.6)	4 (0.2)
嘔吐	5 (1.6)	2 (8.9)	20 (1.6)	9 (1.0)	29 (1.3)	5 (3.0)	36 (1.5)
一般・全身障害および投与部位の状態	83 (25.9)	11 (48.8)	209 (16.3)	180 (20.6)	389 (18.0)	81 (47.9)	481 (20.5)
医薬品副作用	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
無力症	2 (0.6)	1 (4.4)	6 (0.5)	0	6 (0.3)	6 (3.5)	13 (0.6)
胸部不快感	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	4 (2.4)	6 (0.3)
胸痛	2 (0.6)	0	11 (0.9)	10 (1.1)	21 (1.0)	2 (1.2)	23 (1.0)
悪寒	6 (1.9)	0	12 (0.9)	7 (0.8)	19 (0.9)	3 (1.8)	22 (0.9)
医療機器に対する不耐性	1 (0.3)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
不快感	0	0	0	0	0	1 (0.6)	1 (<0.1)
薬効欠如	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
異形成	0	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
顔面浮腫	0	0	0	0	0	1 (0.6)	1 (<0.1)
疲労	14 (4.4)	2 (8.9)	43 (3.4)	31 (3.5)	74 (3.4)	11 (6.5)	87 (3.7)
異常感	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
びくびく感	0	0	0	0	0	1 (0.6)	1 (<0.1)
体温変動感	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
全身性浮腫	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
宿酔	1 (0.3)	0	0	0	0	0	0
過形成	0	0	0	0	0	1 (0.6)	1 (<0.1)
高体温症	1 (0.3)	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)
治癒不良	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
硬結	1 (0.3)	0	0	0	0	0	0
炎症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
インフルエンザ様疾患	3 (0.9)	2 (8.9)	9 (0.7)	8 (0.9)	17 (0.8)	1 (0.6)	20 (0.9)
注入部位反応	0	0	0	0	0	1 (0.6)	1 (<0.1)
注射部位疼痛	2 (0.6)	0	27 (2.1)	41 (4.7)	68 (3.2)	0	68 (2.9)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
医療機器関連損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
倦怠感	3 (0.9)	1 (4.4)	7 (0.5)	8 (0.9)	15 (0.7)	3 (1.8)	19 (0.8)
腫瘤	0	0	0	2 (0.2)	2 (<0.1)	1 (0.6)	3 (0.1)
粘膜乾燥	1 (0.3)	0	0	0	0	0	0
小結節	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
非心臓性胸痛	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)
浮腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
末梢性浮腫	5 (1.6)	0	6 (0.5)	3 (0.3)	9 (0.4)	2 (1.2)	11 (0.5)
疼痛	4 (1.2)	1 (4.4)	10 (0.8)	6 (0.7)	16 (0.7)	2 (1.2)	19 (0.8)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
末梢腫脹	2 (0.6)	0	3 (0.2)	2 (0.2)	5 (0.2)	1 (0.6)	6 (0.3)
ポリープ	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
偽ポリープ	0	1 (4.4)	2 (0.2)	1 (0.1)	3 (0.1)	1 (0.6)	5 (0.2)
発熱	26 (8.1)	2 (8.9)	53 (4.1)	47 (5.4)	100 (4.6)	34 (20.1)	136 (5.8)
異物感	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腫脹	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
顔面腫脹	0	1 (4.4)	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	4 (0.2)
潰瘍	1 (0.3)	0	0	0	0	0	0
評価不能の事象	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
ワクチン接種部位紅斑	1 (0.3)	0	0	0	0	0	0
ワクチン接種部位疼痛	1 (0.3)	0	0	3 (0.3)	3 (0.1)	0	3 (0.1)
ワクチン接種部位反応	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乾燥症	1 (0.3)	0	0	0	0	0	0
肝胆道系障害	10 (3.1)	0	36 (2.8)	11 (1.3)	47 (2.2)	6 (3.5)	53 (2.3)
胆道ジスキネジア	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胆汁性嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
硬化性胆管炎	0	0	5 (0.4)	0	5 (0.2)	0	5 (0.2)
胆嚢炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
肝胆道系障害 (Cont.)							
胆石症	0	0	3 (0.2)	1 (0.1)	4 (0.2)	2 (1.2)	6 (0.3)
胆汁うっ滞	1 (0.3)	0	0	0	0	0	0
薬物性肝障害	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
肝嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肝機能異常	3 (0.9)	0	7 (0.5)	2 (0.2)	9 (0.4)	2 (1.2)	11 (0.5)
脂肪肝	0	0	8 (0.6)	3 (0.3)	11 (0.5)	0	11 (0.5)
肝炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肝細胞損傷	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肝腫大	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
肝胆道系障害 (Cont.)							
高ビリルビン血症	2 (0.6)	0	0	0	0	0	0
高トランスアミナーゼ血症	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
肝障害	1 (0.3)	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
肝損傷	2 (0.6)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
非アルコール性脂肪性肝炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
非アルコール性脂肪性肝疾患	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
門脈血栓症	1 (0.3)	0	0	0	0	0	0
免疫系障害	6 (1.9)	0	13 (1.0)	14 (1.6)	27 (1.3)	3 (1.8)	30 (1.3)
動物アレルギー	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
免疫系障害 (Cont.)							
アミロイドーシス	1 (0.3)	0	0	0	0	0	0
アナフィラキシー反応	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
薬物過敏症	2 (0.6)	0	0	3 (0.3)	3 (0.1)	1 (0.6)	4 (0.2)
粉塵アレルギー	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
食物アレルギー	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
過敏症	0	0	2 (0.2)	1 (0.1)	3 (0.1)	1 (0.6)	4 (0.2)
ダニアレルギー	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
季節性アレルギー	1 (0.3)	0	10 (0.8)	6 (0.7)	16 (0.7)	1 (0.6)	17 (0.7)
感染症および寄生虫症	270 (84.3)	28 (124.3)	868 (67.7)	627 (71.6)	1495 (69.3)	251 (148.4)	1774 (75.5)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
腹部膿瘍	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
腹壁膿瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膿瘍	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)
頚部膿瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ダニ皮膚炎	0	0	4 (0.3)	1 (0.1)	5 (0.2)	0	5 (0.2)
急性心内膜炎	1 (0.3)	0	0	0	0	0	0
急性副鼻腔炎	0	0	3 (0.2)	0	3 (0.1)	0	3 (0.1)
アデノウイルス感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
歯槽骨炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
肛門膿瘍	1 (0.3)	0	5 (0.4)	6 (0.7)	11 (0.5)	1 (0.6)	12 (0.5)
肛門直腸感染	2 (0.6)	0	0	0	0	0	0
虫垂炎	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	2 (1.2)	5 (0.2)
細菌性関節炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
無症候性COVID-19	1 (0.3)	0	4 (0.3)	2 (0.2)	6 (0.3)	0	6 (0.3)
無症候性細菌尿	0	0	0	0	0	1 (0.6)	1 (<0.1)
異型肺炎	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
細菌感染	0	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)
細菌性膣症	2 (0.6)	0	0	2 (0.2)	2 (<0.1)	1 (0.6)	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
細菌尿	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
バルトリン腺炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ブラストシスティス感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
体部白癬	0	0	0	0	0	1 (0.6)	1 (<0.1)
ボレリア感染	0	0	0	0	0	1 (0.6)	1 (<0.1)
乳房膿瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
気管支炎	7 (2.2)	1 (4.4)	34 (2.7)	11 (1.3)	45 (2.1)	3 (1.8)	49 (2.1)
感染性滑液包炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
COVID-19	14 (4.4)	0	55 (4.3)	56 (6.4)	111 (5.1)	1 (0.6)	112 (4.8)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
COVID-19肺炎	1 (0.3)	0	11 (0.9)	14 (1.6)	25 (1.2)	2 (1.2)	27 (1.1)
カンピロバクター胃腸炎	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
カンピロバクター感染	0	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
カンジダ感染	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
蜂巣炎	9 (2.8)	0	10 (0.8)	4 (0.5)	14 (0.6)	0	14 (0.6)
条虫感染	0	0	0	0	0	1 (0.6)	1 (<0.1)
感染性胆嚢炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
慢性副鼻腔炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
クロストリジウム・ディフィシレ大腸炎	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
クロストリジウム・ディフィシレ感染	5 (1.6)	0	9 (0.7)	12 (1.4)	21 (1.0)	1 (0.6)	22 (0.9)
結腸膿瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
結膜炎	2 (0.6)	0	5 (0.4)	3 (0.3)	8 (0.4)	0	8 (0.3)
ウイルス性結膜炎	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
コロナウイルス感染	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
サイクロスポリジウム感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膀胱炎	1 (0.3)	3 (13.3)	23 (1.8)	10 (1.1)	33 (1.5)	2 (1.2)	38 (1.6)
サイトメガロウイルス性大腸炎	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
サイトメガロウイルス感染	2 (0.6)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
毛嚢虫症	0	0	5 (0.4)	5 (0.6)	10 (0.5)	1 (0.6)	11 (0.5)
デング熱	0	0	0	0	0	1 (0.6)	1 (<0.1)
感染性皮膚炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
皮膚糸状菌症	1 (0.3)	1 (4.4)	0	0	0	0	1 (<0.1)
爪の皮膚糸状菌症	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)
医療機器関連敗血症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
感染性下痢	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	0	4 (0.2)
憩室炎	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
耳感染	2 (0.6)	1 (4.4)	9 (0.7)	7 (0.8)	16 (0.7)	2 (1.2)	19 (0.8)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
感染性腸炎	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
蟯虫症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腸球菌感染	1 (0.3)	0	0	0	0	0	0
エンテロウイルス感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
丹毒	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
遊走性紅斑	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
大腸菌感染	2 (0.6)	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)
大腸菌性敗血症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
大腸菌性尿路感染	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
眼感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼瞼感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
毛包炎	6 (1.9)	1 (4.4)	7 (0.5)	17 (1.9)	24 (1.1)	20 (11.8)	45 (1.9)
真菌感染	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
皮膚真菌感染	2 (0.6)	0	2 (0.2)	4 (0.5)	6 (0.3)	1 (0.6)	7 (0.3)
せつ	0	0	2 (0.2)	3 (0.3)	5 (0.2)	0	5 (0.2)
胃腸炎	8 (2.5)	1 (4.4)	16 (1.2)	21 (2.4)	37 (1.7)	6 (3.5)	44 (1.9)
ノロウイルス性胃腸炎	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)
ウイルス性胃腸炎	0	0	8 (0.6)	7 (0.8)	15 (0.7)	3 (1.8)	18 (0.8)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
消化管内細菌過剰増殖	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
消化管感染	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
性器カンジダ症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
陰部ヘルペス	0	0	3 (0.2)	1 (0.1)	4 (0.2)	2 (1.2)	6 (0.3)
陰部単純ヘルペス	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	2 (1.2)	4 (0.2)
真菌性性器感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
歯肉膿瘍	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
歯肉炎	1 (0.3)	0	4 (0.3)	1 (0.1)	5 (0.2)	2 (1.2)	7 (0.3)
鼠径部膿瘍	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
ヘモフィルス感染	1 (0.3)	0	0	0	0	0	0
手足口病	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
ヘリコバクター性胃炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
ヘリコバクター感染	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
伝染性単核症肝炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ヘルペス性皮膚炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ヘルペス眼感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
単純ヘルペス	0	0	12 (0.9)	4 (0.5)	16 (0.7)	5 (3.0)	21 (0.9)
単純ヘルペス性咽頭炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
帯状疱疹	2 (0.6)	0	52 (4.1)	42 (4.8)	94 (4.4)	13 (7.7)	107 (4.6)
播種性帯状疱疹	0	0	0	0	0	1 (0.6)	1 (<0.1)
神経合併症を伴う帯状疱疹感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
帯状疱疹性髄膜炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
耳帯状疱疹	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
麦粒腫	4 (1.2)	0	5 (0.4)	8 (0.9)	13 (0.6)	4 (2.4)	17 (0.7)
膿痂疹	1 (0.3)	0	3 (0.2)	1 (0.1)	4 (0.2)	1 (0.6)	5 (0.2)
咬傷感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
感染性嚢腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
感染性皮膚嚢腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
感染	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
伝染性単核症	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
インフルエンザ	6 (1.9)	2 (8.9)	33 (2.6)	23 (2.6)	56 (2.6)	14 (8.3)	72 (3.1)
クレブシエラ感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
大腸感染	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
喉頭炎	1 (0.3)	0	3 (0.2)	3 (0.3)	6 (0.3)	0	6 (0.3)
潜伏結核	0	0	9 (0.7)	5 (0.6)	14 (0.6)	0	14 (0.6)
限局性感染	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
下気道感染	3 (0.9)	0	5 (0.4)	0	5 (0.2)	1 (0.6)	6 (0.3)
ライム病	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
乳腺炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
伝染性軟属腫	1 (0.3)	0	0	0	0	0	0
筋膿瘍	1 (0.3)	0	0	0	0	0	0
上咽頭炎	44 (13.7)	1 (4.4)	127 (9.9)	88 (10.1)	215 (10.0)	43 (25.4)	259 (11.0)
食道カンジダ症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
爪真菌症	2 (0.6)	1 (4.4)	8 (0.6)	2 (0.2)	10 (0.5)	0	11 (0.5)
口腔カンジダ症	2 (0.6)	0	1 (<0.1)	3 (0.3)	4 (0.2)	1 (0.6)	5 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
口腔真菌感染	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
口腔ヘルペス	10 (3.1)	1 (4.4)	46 (3.6)	32 (3.7)	78 (3.6)	13 (7.7)	92 (3.9)
精巣炎	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
骨髄炎	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
外耳炎	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
真菌性外耳炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
中耳炎	0	0	0	1 (0.1)	1 (<0.1)	2 (1.2)	3 (0.1)
急性中耳炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
乳頭腫ウイルス感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
爪囲炎	0	0	2 (0.2)	2 (0.2)	4 (0.2)	1 (0.6)	5 (0.2)
歯冠周囲炎	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
歯周炎	1 (0.3)	0	3 (0.2)	5 (0.6)	8 (0.4)	1 (0.6)	9 (0.4)
直腸周囲膿瘍	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
扁桃周囲炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
咽頭炎	7 (2.2)	0	6 (0.5)	6 (0.7)	12 (0.6)	8 (4.7)	20 (0.9)
レンサ球菌性咽頭炎	1 (0.3)	0	2 (0.2)	3 (0.3)	5 (0.2)	1 (0.6)	6 (0.3)
毛巣嚢胞	0	0	1 (<0.1)	4 (0.5)	5 (0.2)	1 (0.6)	6 (0.3)
胸膜感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
ニューモシスチス・イロベチイ感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ニューモシスチス・イロベチイ肺炎	1 (0.3)	0	0	0	0	0	0
肺炎	6 (1.9)	0	11 (0.9)	9 (1.0)	20 (0.9)	3 (1.8)	23 (1.0)
細菌性肺炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
クリプトコッカス性肺炎	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
肺炎球菌性肺炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ウイルス性肺炎	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
処置後感染	2 (0.6)	0	0	0	0	0	0
術後創感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
歯髄炎	1 (0.3)	1 (4.4)	3 (0.2)	1 (0.1)	4 (0.2)	0	5 (0.2)
膿疱	1 (0.3)	2 (8.9)	2 (0.2)	1 (0.1)	3 (0.1)	2 (1.2)	7 (0.3)
腎盂腎炎	1 (0.3)	0	3 (0.2)	0	3 (0.1)	1 (0.6)	4 (0.2)
膿皮症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
膿尿	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
膿疱性皮疹	0	0	0	1 (0.1)	1 (<0.1)	2 (1.2)	3 (0.1)
直腸膿瘍	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
RSウイルス感染	0	0	0	0	0	1 (0.6)	1 (<0.1)
気道感染	1 (0.3)	0	6 (0.5)	2 (0.2)	8 (0.4)	2 (1.2)	10 (0.4)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
ウイルス性気道感染	2 (0.6)	1 (4.4)	7 (0.5)	1 (0.1)	8 (0.4)	2 (1.2)	11 (0.5)
鼻炎	6 (1.9)	0	5 (0.4)	2 (0.2)	7 (0.3)	0	7 (0.3)
根管感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
敗血症	0	0	0	2 (0.2)	2 (<0.1)	1 (0.6)	3 (0.1)
セラチア感染	1 (0.3)	0	0	0	0	0	0
副鼻腔炎	12 (3.7)	1 (4.4)	24 (1.9)	15 (1.7)	39 (1.8)	5 (3.0)	45 (1.9)
皮膚カンジダ	0	1 (4.4)	0	0	0	0	1 (<0.1)
皮膚感染	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
ブドウ球菌感染	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
レンサ球菌性尿路感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮下組織膿瘍	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
細菌重複感染	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
股部白癬	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)
白癬感染	2 (0.6)	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
手白癬	1 (0.3)	0	0	0	0	0	0
足部白癬	3 (0.9)	0	8 (0.6)	3 (0.3)	11 (0.5)	1 (0.6)	12 (0.5)
癜風	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)
扁桃炎	1 (0.3)	0	6 (0.5)	6 (0.7)	12 (0.6)	1 (0.6)	13 (0.6)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
細菌性扁桃炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
歯膿瘍	2 (0.6)	0	4 (0.3)	6 (0.7)	10 (0.5)	1 (0.6)	11 (0.5)
歯感染	3 (0.9)	0	2 (0.2)	6 (0.7)	8 (0.4)	2 (1.2)	10 (0.4)
気管気管支炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
トリコモナス症	1 (0.3)	0	0	0	0	0	0
結核	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
上気道感染	20 (6.2)	3 (13.3)	99 (7.7)	40 (4.6)	139 (6.4)	27 (16.0)	169 (7.2)
尿路感染	20 (6.2)	3 (13.3)	47 (3.7)	21 (2.4)	68 (3.2)	11 (6.5)	82 (3.5)
尿路性敗血症	0	1 (4.4)	1 (<0.1)	0	1 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
膣膿瘍	1 (0.3)	0	0	0	0	0	0
膣感染	0	1 (4.4)	3 (0.2)	0	3 (0.1)	0	4 (0.2)
ガードネレラ菌性膣炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
水痘	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
水痘帯状疱疹ウイルス感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ウイルス血症	1 (0.3)	0	0	0	0	0	0
ウイルス性下痢	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ウイルス感染	1 (0.3)	0	3 (0.2)	5 (0.6)	8 (0.4)	2 (1.2)	10 (0.4)
ウイルス性心膜炎	1 (0.3)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
ウイルス性咽頭炎	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
ウイルス性上気道感染	4 (1.2)	0	2 (0.2)	9 (1.0)	11 (0.5)	2 (1.2)	13 (0.6)
女性外陰部蜂巣炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
外陰部腟カンジダ症	2 (0.6)	1 (4.4)	5 (0.4)	8 (0.9)	13 (0.6)	3 (1.8)	17 (0.7)
外陰腟真菌感染	1 (0.3)	0	2 (0.2)	2 (0.2)	4 (0.2)	1 (0.6)	5 (0.2)
外陰腟炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
創傷感染	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
傷害、中毒および処置合併症	30 (9.4)	3 (13.3)	133 (10.4)	82 (9.4)	215 (10.0)	36 (21.3)	254 (10.8)
偶発的過量投与	3 (0.9)	0	2 (0.2)	5 (0.6)	7 (0.3)	3 (1.8)	10 (0.4)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
吻合部漏出	1 (0.3)	0	0	0	0	0	0
動物咬傷	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
動物による引っかき傷	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
足関節部骨折	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
節足動物咬傷	0	0	2 (0.2)	4 (0.5)	6 (0.3)	0	6 (0.3)
節足動物刺傷	0	0	0	0	0	1 (0.6)	1 (<0.1)
骨挫傷	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
第2度熱傷	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
胸部損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
挫傷	3 (0.9)	0	10 (0.8)	5 (0.6)	15 (0.7)	6 (3.5)	21 (0.9)
角膜擦過傷	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
上顆炎	0	0	3 (0.2)	0	3 (0.1)	1 (0.6)	4 (0.2)
毒性物質曝露	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼外傷	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)
転倒	0	1 (4.4)	9 (0.7)	7 (0.8)	16 (0.7)	1 (0.6)	18 (0.8)
腓骨骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
足骨折	0	0	8 (0.6)	3 (0.3)	11 (0.5)	0	11 (0.5)
骨折	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
仙骨骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
消化管ストーマ壊死	1 (0.3)	0	0	0	0	0	0
手骨折	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)
頭部損傷	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
熱疲労	0	0	0	0	0	1 (0.6)	1 (<0.1)
熱中症	1 (0.3)	0	0	0	0	0	0
熱射病	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
股関節部骨折	1 (0.3)	0	0	0	0	0	0
瘢痕ヘルニア	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
損傷	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.1)
企図的過量投与	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
関節脱臼	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
関節損傷	1 (0.3)	0	5 (0.4)	1 (0.1)	6 (0.3)	0	6 (0.3)
靱帯断裂	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
靱帯捻挫	5 (1.6)	0	4 (0.3)	4 (0.5)	8 (0.4)	4 (2.4)	12 (0.5)
四肢損傷	1 (0.3)	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)
四肢外傷性切断	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
腰椎骨折	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
つち指	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
半月板損傷	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
筋断裂	0	0	2 (0.2)	5 (0.6)	7 (0.3)	0	7 (0.3)
肉離れ	1 (0.3)	0	9 (0.7)	2 (0.2)	11 (0.5)	2 (1.2)	13 (0.6)
筋骨格内異物	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
過量投与	0	1 (4.4)	3 (0.2)	0	3 (0.1)	1 (0.6)	5 (0.2)
膝蓋骨骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
骨盤骨折	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
処置後血尿	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
処置後出血	0	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)
外傷後頚部症候群	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
外傷後疼痛	0	0	3 (0.2)	0	3 (0.1)	0	3 (0.1)
術後イレウス	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
処置による腸管穿孔	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
処置による疼痛	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	0	4 (0.2)
肺挫傷	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
橈骨骨折	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
肋骨骨折	1 (0.3)	0	5 (0.4)	3 (0.3)	8 (0.4)	1 (0.6)	9 (0.4)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
交通事故	1 (0.3)	0	2 (0.2)	3 (0.3)	5 (0.2)	0	5 (0.2)
瘢痕	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
陰嚢血腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮膚擦過傷	1 (0.3)	0	7 (0.5)	0	7 (0.3)	2 (1.2)	9 (0.4)
皮膚裂傷	1 (0.3)	0	7 (0.5)	2 (0.2)	9 (0.4)	2 (1.2)	11 (0.5)
軟部組織損傷	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
脊柱損傷	0	0	0	0	0	1 (0.6)	1 (<0.1)
脊椎圧迫骨折	1 (0.3)	1 (4.4)	0	0	0	0	1 (<0.1)
スポーツ損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
ストレス骨折	0	0	4 (0.3)	2 (0.2)	6 (0.3)	0	6 (0.3)
皮下血腫	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
腱損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腱断裂	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
熱傷	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
胸椎骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脛骨骨折	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
歯牙破折	1 (0.3)	0	2 (0.2)	4 (0.5)	6 (0.3)	0	6 (0.3)
上肢骨折	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
子宮穿孔	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ワクチン接種合併症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
創傷	0	0	2 (0.2)	0	2 (<0.1)	4 (2.4)	6 (0.3)
創合併症	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
手首関節骨折	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
臨床検査	95 (29.7)	9 (40.0)	393 (30.6)	293 (33.5)	686 (31.8)	229 (135.3)	924 (39.3)
アラニンアミノトランスフェラーゼ増加	8 (2.5)	3 (13.3)	27 (2.1)	14 (1.6)	41 (1.9)	10 (5.9)	54 (2.3)
αヒドロキシ酪酸脱水素酵素増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
アミラーゼ増加	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
抗好中球細胞質抗体陽性	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
抗核抗体増加	1 (0.3)	0	0	0	0	0	0
大動脈雑音	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
関節鏡検査	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
アスパラギン酸アミノトランスフェラーゼ増加	9 (2.8)	2 (8.9)	22 (1.7)	15 (1.7)	37 (1.7)	17 (10.0)	56 (2.4)
細菌検査陽性	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
好塩基球数増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血中アルブミン減少	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
血中アルブミン増加	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
血中アルカリホスファターゼ減少	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中アルカリホスファターゼ増加	1 (0.3)	0	2 (0.2)	1 (0.1)	3 (0.1)	1 (0.6)	4 (0.2)
血中重炭酸塩減少	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
血中ビリルビン増加	0	0	5 (0.4)	9 (1.0)	14 (0.6)	5 (3.0)	19 (0.8)
血中非抱合ビリルビン増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中カルシウム増加	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
血中クロール減少	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中コレステロール減少	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
血中コレステロール増加	0	0	9 (0.7)	10 (1.1)	19 (0.9)	4 (2.4)	23 (1.0)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
血中クレアチン増加	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
血中クレアチンホスホキナーゼＭＢ増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血中クレアチンホスホキナーゼ増加	14 (4.4)	0	74 (5.8)	78 (8.9)	152 (7.0)	61 (36.1)	213 (9.1)
血中クレアチニン増加	3 (0.9)	0	1 (<0.1)	5 (0.6)	6 (0.3)	5 (3.0)	11 (0.5)
血中葉酸減少	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
血中ブドウ糖	1 (0.3)	0	0	0	0	0	0
血中ブドウ糖減少	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
血中ブドウ糖増加	3 (0.9)	0	5 (0.4)	1 (0.1)	6 (0.3)	0	6 (0.3)
血中鉄減少	0	0	3 (0.2)	1 (0.1)	4 (0.2)	1 (0.6)	5 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
血中乳酸脱水素酵素増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中マグネシウム減少	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中リン減少	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	3 (1.8)	6 (0.3)
血中カリウム減少	0	0	4 (0.3)	0	4 (0.2)	0	4 (0.2)
血中カリウム増加	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
血圧上昇	0	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
血中ナトリウム増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血中トリグリセリド異常	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血中トリグリセリド減少	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
血中トリグリセリド増加	0	0	4 (0.3)	1 (0.1)	5 (0.2)	1 (0.6)	6 (0.3)
血中尿素増加	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
血中尿酸増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
尿中血陽性	0	0	1 (<0.1)	6 (0.7)	7 (0.3)	2 (1.2)	9 (0.4)
体温上昇	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
骨密度減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
炭水化物耐性低下	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
心雑音	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
クロストリジウム検査陽性	0	0	2 (0.2)	0	2 (<0.1)	3 (1.8)	5 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
凝固時間延長	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
尿中結晶陽性	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
心電図QT延長	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
心電図再分極異常	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
便中カルプロテクチン増加	0	0	4 (0.3)	0	4 (0.2)	0	4 (0.2)
γ-グルタミルトランスフェラーゼ増加	8 (2.5)	0	21 (1.6)	5 (0.6)	26 (1.2)	2 (1.2)	28 (1.2)
糸球体濾過率減少	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.1)
尿中ブドウ糖陽性	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
顆粒球数減少	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
握力低下	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ヘマトクリット減少	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
ヘモグロビン減少	5 (1.6)	2 (8.9)	7 (0.5)	7 (0.8)	14 (0.6)	5 (3.0)	21 (0.9)
尿中ヘモグロビン陽性	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肝酵素上昇	0	0	11 (0.9)	11 (1.3)	22 (1.0)	5 (3.0)	27 (1.1)
B型肝炎DNA測定陽性	1 (0.3)	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
高比重リポ蛋白増加	0	0	6 (0.5)	2 (0.2)	8 (0.4)	1 (0.6)	9 (0.4)
ヒト乳頭腫ウイルス検査陽性	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
眼圧上昇	0	0	0	1 (0.1)	1 (<0.1)	2 (1.2)	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
臨床検査異常	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
リパーゼ増加	0	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
肝機能検査異常	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肝機能検査値上昇	1 (0.3)	0	3 (0.2)	2 (0.2)	5 (0.2)	0	5 (0.2)
低比重リポ蛋白減少	0	0	3 (0.2)	0	3 (0.1)	1 (0.6)	4 (0.2)
低比重リポ蛋白増加	0	0	2 (0.2)	6 (0.7)	8 (0.4)	1 (0.6)	9 (0.4)
リンパ球数減少	3 (0.9)	1 (4.4)	17 (1.3)	15 (1.7)	32 (1.5)	9 (5.3)	42 (1.8)
リンパ球数増加	1 (0.3)	1 (4.4)	1 (<0.1)	2 (0.2)	3 (0.1)	4 (2.4)	8 (0.3)
リンパ球百分率減少	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	4 (2.4)	8 (0.3)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
リンパ球百分率増加	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
平均赤血球容積異常	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
平均赤血球容積増加	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
単球数増加	0	0	5 (0.4)	0	5 (0.2)	0	5 (0.2)
結核菌群検査陽性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
好中球数減少	4 (1.2)	0	21 (1.6)	23 (2.6)	44 (2.0)	30 (17.7)	74 (3.1)
好中球数増加	3 (0.9)	0	12 (0.9)	3 (0.3)	15 (0.7)	2 (1.2)	17 (0.7)
好中球百分率増加	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
尿中亜硝酸塩陽性	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
血小板数減少	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
血小板数増加	0	0	2 (0.2)	3 (0.3)	5 (0.2)	1 (0.6)	6 (0.3)
プレアルブミン減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
前立腺特異性抗原増加	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
総蛋白減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
総蛋白増加	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
尿蛋白	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
尿中蛋白陽性	6 (1.9)	0	7 (0.5)	2 (0.2)	9 (0.4)	1 (0.6)	10 (0.4)
赤血球数減少	0	0	6 (0.5)	4 (0.5)	10 (0.5)	0	10 (0.4)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
赤血球数増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血沈亢進	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
網状赤血球数減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
網状赤血球数増加	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
血清フェリチン減少	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
尿比重増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ブドウ球菌検査陽性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
トランスアミナーゼ上昇	0	0	3 (0.2)	2 (0.2)	5 (0.2)	1 (0.6)	6 (0.3)
トランスフェリン増加	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
尿検査異常	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
尿中ケトン体陽性	1 (0.3)	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
尿中白血球エステラーゼ陽性	0	0	4 (0.3)	2 (0.2)	6 (0.3)	0	6 (0.3)
尿量減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ビタミンB12減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ビタミンD減少	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
ビタミンD増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
体重減少	2 (0.6)	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)
体重増加	2 (0.6)	0	7 (0.5)	4 (0.5)	11 (0.5)	2 (1.2)	13 (0.6)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)							
白血球数減少	7 (2.2)	0	20 (1.6)	15 (1.7)	35 (1.6)	20 (11.8)	55 (2.3)
白血球数増加	1 (0.3)	0	4 (0.3)	3 (0.3)	7 (0.3)	3 (1.8)	10 (0.4)
尿中白血球陽性	0	0	4 (0.3)	4 (0.5)	8 (0.4)	0	8 (0.3)
代謝および栄養障害	50 (15.6)	6 (26.6)	113 (8.8)	64 (7.3)	177 (8.2)	25 (14.8)	208 (8.9)
食欲障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乳製品不耐症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
食欲減退	5 (1.6)	1 (4.4)	6 (0.5)	1 (0.1)	7 (0.3)	1 (0.6)	9 (0.4)
脱水	2 (0.6)	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
糖尿病	2 (0.6)	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
糖尿病性代謝代償不全	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脂質異常症	0	0	8 (0.6)	2 (0.2)	10 (0.5)	0	10 (0.4)
体液貯留	0	1 (4.4)	0	0	0	0	1 (<0.1)
葉酸欠乏	0	0	2 (0.2)	2 (0.2)	4 (0.2)	1 (0.6)	5 (0.2)
耐糖能障害	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
痛風	0	0	3 (0.2)	2 (0.2)	5 (0.2)	1 (0.6)	6 (0.3)
ヒスタミン不耐性	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
高カルシウム血症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
高コレステロール血症	4 (1.2)	0	19 (1.5)	13 (1.5)	32 (1.5)	1 (0.6)	33 (1.4)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
高血糖	7 (2.2)	1 (4.4)	15 (1.2)	1 (0.1)	16 (0.7)	4 (2.4)	21 (0.9)
高ホモシステイン血症	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
高カリウム血症	0	0	0	0	0	1 (0.6)	1 (<0.1)
高リパーゼ血症	1 (0.3)	0	0	0	0	0	0
高脂血症	2 (0.6)	0	13 (1.0)	9 (1.0)	22 (1.0)	2 (1.2)	24 (1.0)
高ナトリウム血症	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
高トリグリセリド血症	2 (0.6)	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
高尿酸血症	1 (0.3)	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)
低アルブミン血症	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
低カリウム血症	5 (1.6)	2 (8.9)	7 (0.5)	1 (0.1)	8 (0.4)	1 (0.6)	11 (0.5)
低マグネシウム血症	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
低ナトリウム血症	3 (0.9)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
低リン酸血症	3 (0.9)	0	3 (0.2)	6 (0.7)	9 (0.4)	2 (1.2)	11 (0.5)
低蛋白血症	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
食欲亢進	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
鉄欠乏	5 (1.6)	1 (4.4)	4 (0.3)	3 (0.3)	7 (0.3)	1 (0.6)	9 (0.4)
ラクトース不耐性	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
栄養障害	0	0	0	0	0	1 (0.6)	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
代謝性アシドーシス	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
代謝症候群	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肥満	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
テタニー	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
2型糖尿病	2 (0.6)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
過少体重	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ビタミンB群欠乏	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ビタミンB1欠乏	1 (0.3)	0	0	0	0	0	0
ビタミンB12欠乏	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
ビタミンD欠乏	3 (0.9)	0	10 (0.8)	7 (0.8)	17 (0.8)	1 (0.6)	18 (0.8)
筋骨格系および結合組織障害	165 (51.5)	14 (62.2)	296 (23.1)	190 (21.7)	486 (22.5)	70 (41.4)	570 (24.3)
強直性脊椎炎	1 (0.3)	0	0	0	0	0	0
関節痛	42 (13.1)	7 (31.1)	66 (5.1)	50 (5.7)	116 (5.4)	18 (10.6)	141 (6.0)
関節炎	3 (0.9)	0	6 (0.5)	2 (0.2)	8 (0.4)	3 (1.8)	11 (0.5)
腸炎性関節炎	3 (0.9)	0	0	0	0	1 (0.6)	1 (<0.1)
関節障害	15 (4.7)	1 (4.4)	16 (1.2)	9 (1.0)	25 (1.2)	3 (1.8)	29 (1.2)
腋窩腫瘤	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
背部痛	21 (6.6)	1 (4.4)	36 (2.8)	19 (2.2)	55 (2.5)	7 (4.1)	63 (2.7)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
骨痛	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
滑液包炎	1 (0.3)	1 (4.4)	4 (0.3)	2 (0.2)	6 (0.3)	0	7 (0.3)
軟骨萎縮	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
頚部脊柱管狭窄症	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
軟骨軟化症	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
ばち状指	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
尾骨痛	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
コンパートメント症候群	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肋軟骨炎	2 (0.6)	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
指炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腱付着部症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
外骨腫	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
四肢拘縮	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
線維筋痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
側腹部痛	2 (0.6)	0	2 (0.2)	1 (0.1)	3 (0.1)	2 (1.2)	5 (0.2)
鼠径部痛	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
出血性関節症	1 (0.3)	0	0	0	0	0	0
椎間板変性症	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
椎間板障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
椎間板突出	2 (0.6)	0	11 (0.9)	4 (0.5)	15 (0.7)	0	15 (0.6)
関節滲出液	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
関節弛緩	0	0	0	0	0	1 (0.6)	1 (<0.1)
関節ロック	0	0	0	0	0	2 (1.2)	2 (<0.1)
関節雑音	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
関節硬直	1 (0.3)	0	3 (0.2)	0	3 (0.1)	0	3 (0.1)
関節腫脹	2 (0.6)	0	5 (0.4)	1 (0.1)	6 (0.3)	0	6 (0.3)
腰部脊柱管狭窄症	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
脛骨内側過労性症候群	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
筋拘縮	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
筋不快感	1 (0.3)	0	0	0	0	0	0
筋障害	0	0	0	0	0	1 (0.6)	1 (<0.1)
筋痙縮	6 (1.9)	1 (4.4)	10 (0.8)	6 (0.7)	16 (0.7)	6 (3.5)	23 (1.0)
筋緊張	0	0	0	0	0	1 (0.6)	1 (<0.1)
筋攣縮	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
筋力低下	1 (0.3)	0	0	0	0	0	0
筋骨格系胸痛	4 (1.2)	0	7 (0.5)	3 (0.3)	10 (0.5)	1 (0.6)	11 (0.5)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
筋骨格不快感	0	0	0	0	0	1 (0.6)	1 (<0.1)
筋骨格痛	4 (1.2)	1 (4.4)	7 (0.5)	6 (0.7)	13 (0.6)	1 (0.6)	15 (0.6)
筋骨格硬直	2 (0.6)	0	4 (0.3)	1 (0.1)	5 (0.2)	2 (1.2)	7 (0.3)
筋肉痛	7 (2.2)	0	30 (2.3)	18 (2.1)	48 (2.2)	4 (2.4)	52 (2.2)
筋膜疼痛症候群	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ミオパチー	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
筋炎	2 (0.6)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
頚部痛	4 (1.2)	0	5 (0.4)	8 (0.9)	13 (0.6)	0	13 (0.6)
骨炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
変形性関節症	3 (0.9)	0	6 (0.5)	1 (0.1)	7 (0.3)	0	7 (0.3)
骨端症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
骨壊死	0	0	4 (0.3)	1 (0.1)	5 (0.2)	0	5 (0.2)
骨減少症	1 (0.3)	1 (4.4)	3 (0.2)	2 (0.2)	5 (0.2)	0	6 (0.3)
骨粗鬆症	1 (0.3)	1 (4.4)	2 (0.2)	4 (0.5)	6 (0.3)	2 (1.2)	9 (0.4)
四肢痛	12 (3.7)	0	16 (1.2)	23 (2.6)	39 (1.8)	5 (3.0)	44 (1.9)
顎痛	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
膝蓋大腿関節痛症候群	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
病的骨折	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
関節周囲炎	0	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)
足底筋膜炎	0	0	6 (0.5)	4 (0.5)	10 (0.5)	0	10 (0.4)
多発性関節炎	1 (0.3)	0	0	0	0	0	0
姿勢異常	1 (0.3)	0	0	0	0	0	0
横紋筋融解症	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
関節リウマチ	1 (0.3)	0	0	0	0	0	0
肩回旋筋腱板症候群	2 (0.6)	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
仙腸骨炎	1 (0.3)	0	0	0	0	0	0
軟部組織腫瘤	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
脊柱変形	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
変形性脊椎症	1 (0.3)	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)
脊椎痛	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)
脊椎炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脊椎関節障害	5 (1.6)	0	4 (0.3)	1 (0.1)	5 (0.2)	1 (0.6)	6 (0.3)
軟骨下機能不全骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
滑液嚢腫	1 (0.3)	0	0	0	0	0	0
滑膜炎	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
顎関節症候群	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
腱痛	1 (0.3)	0	0	0	0	0	0
腱炎	2 (0.6)	0	4 (0.3)	1 (0.1)	5 (0.2)	1 (0.6)	6 (0.3)
腱鞘炎	1 (0.3)	0	0	0	0	0	0
狭窄性腱鞘炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
弾発指	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	1 (0.6)	4 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	9 (2.8)	4 (17.8)	39 (3.0)	45 (5.1)	84 (3.9)	5 (3.0)	93 (4.0)
アクロコルドン	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
結腸腺癌	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
膵腺癌	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)							
エナメル上皮腫	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血管肉腫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肛門性器疣贅	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
基底細胞癌	0	0	2 (0.2)	11 (1.3)	13 (0.6)	0	13 (0.6)
肺の良性新生物	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
精巣の良性新生物	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
良性脾腫瘍	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
ボーエン病	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)
乳癌	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）(Cont.)							
気管支の良性新生物	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
大腸腺腫	3 (0.9)	0	4 (0.3)	1 (0.1)	5 (0.2)	0	5 (0.2)
線維腫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
線維性組織球腫	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
神経節腫	0	0	0	0	0	1 (0.6)	1 (<0.1)
血管腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮膚血管腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
浸潤性乳癌	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
喉頭扁平上皮癌	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）(Cont.)							
脂肪腫	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
悪性黒色腫	0	1 (4.4)	0	0	0	0	1 (<0.1)
メラノサイト性母斑	0	2 (8.9)	2 (0.2)	1 (0.1)	3 (0.1)	0	5 (0.2)
髄膜腫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
口腔線維腫	1 (0.3)	0	0	0	0	0	0
皮膚骨腫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
卵巣胚細胞良性奇形腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
前立腺癌	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
直腸腺腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）(Cont.)							
脂漏性角化症	3 (0.9)	0	2 (0.2)	3 (0.3)	5 (0.2)	0	5 (0.2)
皮膚乳頭腫	0	1 (4.4)	6 (0.5)	8 (0.9)	14 (0.6)	2 (1.2)	17 (0.7)
小細胞癌	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
扁平上皮癌	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮膚有棘細胞癌	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	0	4 (0.2)
子宮頚部扁平上皮癌	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
舌扁平上皮癌	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
精巣（純粋）セミノーマ	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
精巣癌	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)							
甲状腺腺腫	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
子宮平滑筋腫	0	0	4 (0.3)	0	4 (0.2)	1 (0.6)	5 (0.2)
神経系障害	72 (22.5)	7 (31.1)	141 (11.0)	118 (13.5)	259 (12.0)	77 (45.5)	343 (14.6)
健忘	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
脳損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
灼熱感	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
頚動脈硬化症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
手根管症候群	3 (0.9)	0	3 (0.2)	5 (0.6)	8 (0.4)	0	8 (0.3)
大脳障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)							
脳虚血	0	0	0	0	0	2 (1.2)	2 (<0.1)
脳血管発作	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
頚髄圧迫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
頚髄神経根障害	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
注意力障害	0	1 (4.4)	2 (0.2)	0	2 (<0.1)	0	3 (0.1)
浮動性めまい	5 (1.6)	1 (4.4)	16 (1.2)	13 (1.5)	29 (1.3)	10 (5.9)	40 (1.7)
異常感覚	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
構語障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
味覚不全	1 (0.3)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)							
てんかん	1 (0.3)	0	0	0	0	0	0
本態性振戦	1 (0.3)	0	0	0	0	0	0
頭痛	38 (11.9)	4 (17.8)	64 (5.0)	48 (5.5)	112 (5.2)	46 (27.2)	162 (6.9)
知覚過敏	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
感覚鈍麻	1 (0.3)	0	7 (0.5)	5 (0.6)	12 (0.6)	1 (0.6)	13 (0.6)
頭蓋内動脈瘤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ラクナ梗塞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腰仙部神経根障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
記憶障害	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)							
片頭痛	7 (2.2)	0	13 (1.0)	7 (0.8)	20 (0.9)	3 (1.8)	23 (1.0)
前兆を伴う片頭痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脊髄症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
神経圧迫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
神経痛	0	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.1)
神経炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
末梢性ニューロパチー	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
後頭神経痛	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
起立不耐性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)							
錯感覚	4 (1.2)	0	5 (0.4)	5 (0.6)	10 (0.5)	1 (0.6)	11 (0.5)
末梢性感覚ニューロパチー	1 (0.3)	0	0	0	0	0	0
睡眠の質低下	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
ヘルペス後神経痛	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
失神寸前の状態	1 (0.3)	0	0	3 (0.3)	3 (0.1)	1 (0.6)	4 (0.2)
回内筋症候群	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
橈骨神経麻痺	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
神経根痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
下肢静止不能症候群	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)							
坐骨神経痛	2 (0.6)	0	6 (0.5)	4 (0.5)	10 (0.5)	1 (0.6)	11 (0.5)
発作様現象	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
副鼻腔炎に伴う頭痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
傾眠	0	0	0	2 (0.2)	2 (<0.1)	1 (0.6)	3 (0.1)
会話障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脊椎炎性脊髄症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
くも膜下出血	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
硬膜下滲出液	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
失神	2 (0.6)	0	3 (0.2)	4 (0.5)	7 (0.3)	1 (0.6)	8 (0.3)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)							
味覚障害	0	0	0	0	0	1 (0.6)	1 (<0.1)
緊張性頭痛	2 (0.6)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
振戦	0	1 (4.4)	1 (<0.1)	0	1 (<0.1)	3 (1.8)	5 (0.2)
視野欠損	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
妊娠、産褥および周産期の状態	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
自然流産	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
精神障害	41 (12.8)	5 (22.2)	74 (5.8)	47 (5.4)	121 (5.6)	19 (11.2)	145 (6.2)
異常な夢	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
急性精神病	0	0	0	0	0	1 (0.6)	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)							
急性ストレス反応	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
感情障害	0	0	0	0	0	1 (0.6)	1 (<0.1)
激越	0	1 (4.4)	0	0	0	0	1 (<0.1)
不安	16 (5.0)	0	18 (1.4)	8 (0.9)	26 (1.2)	4 (2.4)	30 (1.3)
不安障害	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
注意欠如・多動性障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
自閉症スペクトラム障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
双極1型障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
双極性障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)							
抑うつ気分	0	1 (4.4)	0	2 (0.2)	2 (<0.1)	0	3 (0.1)
うつ病	5 (1.6)	1 (4.4)	22 (1.7)	8 (0.9)	30 (1.4)	2 (1.2)	33 (1.4)
薬物依存	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
全般性不安障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
初期不眠症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
不眠症	13 (4.1)	1 (4.4)	18 (1.4)	20 (2.3)	38 (1.8)	6 (3.5)	45 (1.9)
故意の自傷行為	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
易刺激性	2 (0.6)	1 (4.4)	1 (<0.1)	0	1 (<0.1)	0	2 (<0.1)
リビドー減退	0	0	0	0	0	1 (0.6)	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)							
精神障害	1 (0.3)	0	0	0	0	0	0
気分変化	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
悪夢	0	0	0	0	0	1 (0.6)	1 (<0.1)
パニック発作	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
心的外傷後ストレス障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
落ち着きのなさ	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
睡眠障害	2 (0.6)	0	4 (0.3)	0	4 (0.2)	2 (1.2)	6 (0.3)
社交不安障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ストレス	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)							
自殺念慮	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
自殺企図	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
腎および尿路障害	26 (8.1)	2 (8.9)	48 (3.7)	50 (5.7)	98 (4.5)	15 (8.9)	115 (4.9)
急性腎障害	1 (0.3)	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)
膀胱痛	1 (0.3)	0	0	0	0	0	0
膀胱タンポナーデ	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
膀胱結石	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
尿路結石	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
着色尿	1 (0.3)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)							
慢性腎臓病	0	0	0	0	0	2 (1.2)	2 (<0.1)
肋骨脊柱角圧痛	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
出血性膀胱炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
非感染性膀胱炎	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
排尿困難	3 (0.9)	0	10 (0.8)	7 (0.8)	17 (0.8)	3 (1.8)	20 (0.9)
糖尿	1 (0.3)	0	0	0	0	0	0
血尿	3 (0.9)	0	3 (0.2)	7 (0.8)	10 (0.5)	1 (0.6)	11 (0.5)
水腎症	1 (0.3)	0	0	0	0	0	0
緊張性膀胱	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)							
ケトン尿	1 (0.3)	0	0	0	0	0	0
白血球尿	1 (0.3)	0	0	0	0	1 (0.6)	1 (<0.1)
排尿異常	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
尿意切迫	0	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)
腎炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腎石灰沈着症	1 (0.3)	0	0	0	0	0	0
腎結石症	3 (0.9)	0	8 (0.6)	9 (1.0)	17 (0.8)	2 (1.2)	19 (0.8)
夜間頻尿	0	0	3 (0.2)	0	3 (0.1)	0	3 (0.1)
頻尿	3 (0.9)	1 (4.4)	0	1 (0.1)	1 (<0.1)	1 (0.6)	3 (0.1)

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TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
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(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)							
多尿	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
蛋白尿	6 (1.9)	0	8 (0.6)	5 (0.6)	13 (0.6)	1 (0.6)	14 (0.6)
腎萎縮	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腎仙痛	0	0	1 (<0.1)	5 (0.6)	6 (0.3)	2 (1.2)	8 (0.3)
腎嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腎機能障害	0	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
腎臓痛	0	1 (4.4)	0	0	0	1 (0.6)	2 (<0.1)
腎尿細管機能障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
尿管閉塞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

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TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
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腎および尿路障害 (Cont.)							
尿管結石症	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	1 (0.6)	5 (0.2)
尿閉	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
生殖系および乳房障害	9 (2.8)	1 (4.4)	44 (3.4)	27 (3.1)	71 (3.3)	10 (5.9)	82 (3.5)
無月経	0	0	2 (0.2)	1 (0.1)	3 (0.1)	1 (0.6)	4 (0.2)
萎縮性外陰腟炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
バルトリン嚢腫	1 (0.3)	0	0	0	0	0	0
良性前立腺肥大症	0	0	5 (0.4)	3 (0.3)	8 (0.4)	1 (0.6)	9 (0.4)
乳房嚢胞	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乳房障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
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TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
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生殖系および乳房障害 (Cont.)							
乳房腫大	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乳房腫瘤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乳房痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
子宮頚部上皮異形成	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	0	4 (0.2)
子宮頚管ポリープ	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
子宮頚部障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
子宮頚部の炎症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
性交出血	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
機能不全性子宮出血	1 (0.3)	0	0	0	0	0	0

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生殖系および乳房障害 (Cont.)							
月経困難症	0	0	2 (0.2)	1 (0.1)	3 (0.1)	1 (0.6)	4 (0.2)
性交困難	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
子宮内膜症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
勃起不全	0	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
性器びらん	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
閉経期症状	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
月経過多	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
不規則月経	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	2 (1.2)	4 (0.2)
不正子宮出血	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)

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生殖系および乳房障害 (Cont.)							
卵巣嚢胞	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
卵巣静脈血栓症	1 (0.3)	0	0	0	0	0	0
多嚢胞性卵巣	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
閉経後出血	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
月経前頭痛	0	0	0	0	0	1 (0.6)	1 (<0.1)
月経前症候群	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
前立腺腫瘤	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
前立腺炎	1 (0.3)	0	2 (0.2)	7 (0.8)	9 (0.4)	0	9 (0.4)
精液変色	0	0	0	2 (0.2)	2 (<0.1)	1 (0.6)	3 (0.1)

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