TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
肺塞栓症	0	1 (1.9)	0	1 (1.5)	0
上気道の炎症	1 (2.9)	0	0	0	1 (1.6)
皮膚および皮下組織障害	10 (28.7)	12 (23.2)	17 (30.8)	15 (23.0)	18 (28.5)
ざ瘡	1 (2.9)	4 (7.7)	1 (1.8)	4 (6.1)	1 (1.6)
脱毛症	0	1 (1.9)	0	1 (1.5)	0
皮膚炎	0	0	2 (3.6)	0	2 (3.2)
アトピー性皮膚炎	0	0	1 (1.8)	0	1 (1.6)
皮膚乾燥	0	0	0	2 (3.1)	0
湿疹	0	0	1 (1.8)	0	1 (1.6)
皮脂欠乏性湿疹	0	0	1 (1.8)	0	1 (1.6)
紅斑	0	2 (3.9)	0	2 (3.1)	0
瘢痕そう痒感	0	0	0	0	1 (1.6)
神経皮膚炎	1 (2.9)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
寝汗	0	1 (1.9)	0	1 (1.5)	0
脂肪織炎	0	1 (1.9)	0	1 (1.5)	0
光線過敏性反応	0	0	1 (1.8)	0	1 (1.6)
そう痒症	1 (2.9)	1 (1.9)	0	1 (1.5)	0
発疹	4 (11.5)	1 (1.9)	4 (7.3)	1 (1.5)	4 (6.3)
斑状皮疹	0	0	1 (1.8)	0	1 (1.6)
斑状丘疹状皮疹	0	0	3 (5.4)	0	3 (4.8)
そう痒性皮疹	0	0	1 (1.8)	0	1 (1.6)
脂漏性皮膚炎	1 (2.9)	1 (1.9)	0	1 (1.5)	0
皮膚びらん	1 (2.9)	0	0	0	0
皮膚剥脱	0	0	0	1 (1.5)	0
皮膚色素過剰	1 (2.9)	0	0	0	0
蕁麻疹	0	0	1 (1.8)	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
血管障害	0	1 (1.9)	2 (3.6)	2 (3.1)	2 (3.2)
深部静脈血栓症	0	0	1 (1.8)	0	1 (1.6)
高血圧	0	1 (1.9)	1 (1.8)	1 (1.5)	1 (1.6)
静脈血栓症	0	0	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month					
Any adverse event	99 (417.6)	142 (345.6)	115 (247.5)	174 (328.5)	136 (256.2)
血液およびリンパ系障害	8 (33.7)	4 (9.7)	0	6 (11.3)	1 (1.9)
貧血	5 (21.1)	1 (2.4)	0	1 (1.9)	0
鉄欠乏性貧血	2 (8.4)	0	0	0	1 (1.9)
白血球減少症	0	1 (2.4)	0	1 (1.9)	0
小球性貧血	0	0	0	1 (1.9)	0
好中球減少症	1 (4.2)	1 (2.4)	0	1 (1.9)	0
汎血球減少症	0	0	0	1 (1.9)	0
脾腫	0	1 (2.4)	0	1 (1.9)	0
心臓障害	0	1 (2.4)	1 (2.2)	1 (1.9)	2 (3.8)
不整脈	0	1 (2.4)	0	1 (1.9)	0
僧帽弁閉鎖不全症	0	0	0	0	1 (1.9)
心膜炎	0	0	1 (2.2)	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
耳および迷路障害	0	2 (4.9)	1 (2.2)	2 (3.8)	1 (1.9)
感音性難聴	0	1 (2.4)	0	1 (1.9)	0
片耳難聴	0	0	1 (2.2)	0	1 (1.9)
耳痛	0	1 (2.4)	0	1 (1.9)	0
内分泌障害	0	0	0	0	1 (1.9)
甲状腺腫瘤	0	0	0	0	1 (1.9)
眼障害	1 (4.2)	1 (2.4)	0	1 (1.9)	0
角膜混濁	1 (4.2)	0	0	0	0
眼そう痒症	0	1 (2.4)	0	1 (1.9)	0
胃腸障害	28 (118.1)	18 (43.8)	16 (34.4)	23 (43.4)	19 (35.8)
腹部膨満	0	1 (2.4)	0	1 (1.9)	0
腹部腫瘤	1 (4.2)	0	0	0	0
腹痛	3 (12.7)	1 (2.4)	0	2 (3.8)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
胃腸障害 (Cont.)					
下腹部痛	1 (4.2)	0	0	0	0
上腹部痛	0	0	2 (4.3)	0	3 (5.7)
痔瘻	0	0	2 (4.3)	1 (1.9)	2 (3.8)
肛門の炎症	0	0	1 (2.2)	0	1 (1.9)
肛門そう痒症	1 (4.2)	0	0	0	0
アフタ性潰瘍	0	0	1 (2.2)	0	1 (1.9)
大腸炎	1 (4.2)	0	0	0	0
潰瘍性大腸炎	11 (46.4)	8 (19.5)	3 (6.5)	10 (18.9)	3 (5.7)
便秘	1 (4.2)	2 (4.9)	1 (2.2)	2 (3.8)	2 (3.8)
齲歯	0	1 (2.4)	0	1 (1.9)	1 (1.9)
下痢	1 (4.2)	0	0	0	0
消化不良	1 (4.2)	0	0	0	0
鼓腸	1 (4.2)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
胃腸障害 (Cont.)					
胃炎	0	0	1 (2.2)	0	1 (1.9)
胃食道逆流性疾患	1 (4.2)	0	0	0	0
痔核	1 (4.2)	2 (4.9)	1 (2.2)	3 (5.7)	1 (1.9)
鼠径ヘルニア	0	1 (2.4)	0	1 (1.9)	0
腸閉塞	0	1 (2.4)	0	1 (1.9)	0
過敏性腸症候群	0	0	1 (2.2)	0	1 (1.9)
大腸穿孔	1 (4.2)	0	0	0	0
悪心	1 (4.2)	0	1 (2.2)	0	1 (1.9)
嚥下痛	1 (4.2)	0	0	0	0
肛門周囲痛	0	1 (2.4)	0	1 (1.9)	0
歯の脱落	0	0	1 (2.2)	0	1 (1.9)
臍ヘルニア	1 (4.2)	0	0	0	0
嘔吐	0	0	1 (2.2)	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
一般・全身障害および投与部位の状態	4 (16.9)	3 (7.3)	2 (4.3)	5 (9.4)	4 (7.5)
胸部不快感	0	1 (2.4)	0	1 (1.9)	0
胸痛	1 (4.2)	1 (2.4)	0	1 (1.9)	1 (1.9)
疲労	0	0	0	1 (1.9)	1 (1.9)
インフルエンザ様疾患	0	0	0	1 (1.9)	0
末梢性浮腫	1 (4.2)	1 (2.4)	0	1 (1.9)	0
発熱	1 (4.2)	0	2 (4.3)	0	2 (3.8)
異物感	1 (4.2)	0	0	0	0
肝胆道系障害	0	1 (2.4)	2 (4.3)	3 (5.7)	2 (3.8)
硬化性胆管炎	0	0	0	1 (1.9)	0
薬物性肝障害	0	0	1 (2.2)	0	1 (1.9)
肝機能異常	0	1 (2.4)	0	1 (1.9)	0
脂肪肝	0	0	0	1 (1.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
肝胆道系障害 (Cont.)					
肝障害	0	0	1 (2.2)	0	1 (1.9)
免疫系障害	0	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
季節性アレルギー	0	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
感染症および寄生虫症	19 (80.1)	42 (102.2)	35 (75.3)	51 (96.3)	38 (71.6)
腹部膿瘍	1 (4.2)	0	0	0	0
ダニ皮膚炎	0	1 (2.4)	0	1 (1.9)	0
肛門膿瘍	0	1 (2.4)	0	1 (1.9)	0
気管支炎	1 (4.2)	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
COVID-19	2 (8.4)	0	4 (8.6)	2 (3.8)	5 (9.4)
COVID-19肺炎	0	0	0	1 (1.9)	0
蜂巣炎	0	1 (2.4)	0	1 (1.9)	0
クロストリジウム・ディフィシレ感染	0	1 (2.4)	0	1 (1.9)	0
結膜炎	0	1 (2.4)	0	1 (1.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
膀胱炎	0	2 (4.9)	1 (2.2)	2 (3.8)	1 (1.9)
毛嚢虫症	0	2 (4.9)	0	2 (3.8)	0
耳感染	0	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
眼感染	0	0	0	1 (1.9)	0
毛包炎	0	1 (2.4)	2 (4.3)	1 (1.9)	2 (3.8)
皮膚真菌感染	0	0	1 (2.2)	0	1 (1.9)
ウイルス性胃腸炎	0	0	1 (2.2)	0	1 (1.9)
陰部単純ヘルペス	0	0	0	0	1 (1.9)
ヘモフィルス感染	1 (4.2)	0	0	0	0
単純ヘルペス	0	1 (2.4)	0	1 (1.9)	0
帯状疱疹	0	2 (4.9)	3 (6.5)	2 (3.8)	4 (7.5)
麦粒腫	0	0	1 (2.2)	0	1 (1.9)
インフルエンザ	1 (4.2)	2 (4.9)	3 (6.5)	4 (7.6)	3 (5.7)

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
喉頭炎	0	0	1 (2.2)	0	1 (1.9)
下気道感染	0	1 (2.4)	0	1 (1.9)	0
伝染性軟属腫	1 (4.2)	0	0	0	0
上咽頭炎	4 (16.9)	9 (21.9)	6 (12.9)	10 (18.9)	6 (11.3)
口腔ヘルペス	0	2 (4.9)	3 (6.5)	2 (3.8)	3 (5.7)
咽頭炎	0	1 (2.4)	0	1 (1.9)	0
肺炎	1 (4.2)	0	0	0	0
腎盂腎炎	1 (4.2)	0	0	0	0
ウイルス性気道感染	0	1 (2.4)	0	1 (1.9)	0
鼻炎	0	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
セラチア感染	1 (4.2)	0	0	0	0
副鼻腔炎	0	2 (4.9)	1 (2.2)	2 (3.8)	1 (1.9)
ブドウ球菌感染	1 (4.2)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
足部白癬	0	1 (2.4)	0	1 (1.9)	0
扁桃炎	0	0	1 (2.2)	0	1 (1.9)
歯感染	0	0	0	1 (1.9)	0
上気道感染	1 (4.2)	4 (9.7)	4 (8.6)	4 (7.6)	4 (7.5)
尿路感染	1 (4.2)	2 (4.9)	0	2 (3.8)	0
ウイルス血症	1 (4.2)	0	0	0	0
ウイルス性咽頭炎	0	0	0	1 (1.9)	0
ウイルス性上気道感染	1 (4.2)	0	0	0	0
外陰腟真菌感染	0	1 (2.4)	0	1 (1.9)	0
傷害、中毒および処置合併症	2 (8.4)	1 (2.4)	3 (6.5)	1 (1.9)	5 (9.4)
挫傷	0	0	1 (2.2)	0	2 (3.8)
転倒	0	0	0	0	1 (1.9)
熱中症	1 (4.2)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
傷害、中毒および処置合併症 (Cont.)					
靭帯捻挫	1 (4.2)	0	1 (2.2)	0	1 (1.9)
皮膚裂傷	0	1 (2.4)	0	1 (1.9)	0
手首関節骨折	0	0	1 (2.2)	0	1 (1.9)
臨床検査	7 (29.5)	30 (73.0)	16 (34.4)	32 (60.4)	18 (33.9)
アラニンアミノトランスフェラーゼ増加	1 (4.2)	2 (4.9)	1 (2.2)	2 (3.8)	1 (1.9)
アスパラギン酸アミノトランスフェラーゼ増加	1 (4.2)	1 (2.4)	0	1 (1.9)	0
血中アルブミン減少	0	2 (4.9)	0	2 (3.8)	0
血中ビリルビン増加	0	2 (4.9)	0	2 (3.8)	0
血中コレステロール増加	0	0	1 (2.2)	0	1 (1.9)
血中クレアチンホスホキナーゼ増加	2 (8.4)	2 (4.9)	3 (6.5)	4 (7.6)	5 (9.4)
血中ブドウ糖増加	0	1 (2.4)	0	1 (1.9)	0
血中カリウム増加	0	1 (2.4)	0	1 (1.9)	0
血中ナトリウム増加	0	1 (2.4)	0	1 (1.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
臨床検査 (Cont.)					
尿中血陽性	0	0	1 (2.2)	0	1 (1.9)
γ-グルタミルトランスフェラーゼ増加	0	3 (7.3)	0	3 (5.7)	0
糸球体濾過率減少	0	1 (2.4)	0	1 (1.9)	0
ヘモグロビン減少	0	1 (2.4)	0	1 (1.9)	0
肝酵素上昇	0	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
リンパ球数減少	0	2 (4.9)	1 (2.2)	2 (3.8)	1 (1.9)
リンパ球数増加	0	0	1 (2.2)	0	1 (1.9)
リンパ球百分率減少	0	1 (2.4)	0	1 (1.9)	0
好中球数減少	1 (4.2)	1 (2.4)	2 (4.3)	1 (1.9)	2 (3.8)
好中球数増加	0	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
血小板数減少	1 (4.2)	0	0	0	0
プレアルブミン減少	0	1 (2.4)	0	1 (1.9)	0
総蛋白減少	0	1 (2.4)	0	1 (1.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
臨床検査 (Cont.)					
尿中蛋白陽性	0	1 (2.4)	0	1 (1.9)	0
血沈亢進	0	1 (2.4)	0	1 (1.9)	0
尿検査異常	0	1 (2.4)	0	1 (1.9)	0
体重増加	0	0	1 (2.2)	0	1 (1.9)
白血球数減少	1 (4.2)	1 (2.4)	2 (4.3)	1 (1.9)	2 (3.8)
白血球数増加	0	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
代謝および栄養障害	5 (21.1)	1 (2.4)	1 (2.2)	1 (1.9)	2 (3.8)
食欲減退	1 (4.2)	0	0	0	0
脂質異常症	0	0	1 (2.2)	0	2 (3.8)
高血糖	0	1 (2.4)	0	1 (1.9)	0
低カリウム血症	1 (4.2)	0	0	0	0
鉄欠乏	1 (4.2)	0	0	0	0
2型糖尿病	1 (4.2)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
代謝および栄養障害 (Cont.)					
ビタミンD欠乏	1 (4.2)	0	0	0	0
筋骨格系および結合組織障害	8 (33.7)	15 (36.5)	5 (10.8)	17 (32.1)	5 (9.4)
関節痛	3 (12.7)	4 (9.7)	2 (4.3)	5 (9.4)	2 (3.8)
腸炎性関節炎	1 (4.2)	0	0	0	0
関節障害	0	0	0	1 (1.9)	0
背部痛	2 (8.4)	5 (12.2)	0	5 (9.4)	0
腰部脊柱管狭窄症	0	0	1 (2.2)	0	1 (1.9)
筋骨格系胸痛	1 (4.2)	0	0	0	0
筋骨格痛	1 (4.2)	1 (2.4)	0	1 (1.9)	0
筋肉痛	0	1 (2.4)	0	1 (1.9)	0
筋炎	0	1 (2.4)	0	1 (1.9)	0
頚部痛	0	1 (2.4)	0	1 (1.9)	0
骨減少症	0	1 (2.4)	0	1 (1.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
四肢痛	0	1 (2.4)	1 (2.2)	1 (1.9)	1 (1.9)
関節周囲炎	0	0	1 (2.2)	0	1 (1.9)
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）	2 (8.4)	1 (2.4)	1 (2.2)	2 (3.8)	1 (1.9)
大腸腺腫	1 (4.2)	0	0	0	0
線維性組織球腫	0	0	1 (2.2)	0	1 (1.9)
皮膚血管腫	0	1 (2.4)	0	1 (1.9)	0
浸潤性乳癌	1 (4.2)	0	0	0	0
甲状腺腺腫	0	0	0	1 (1.9)	0
神経系障害	3 (12.7)	3 (7.3)	1 (2.2)	5 (9.4)	4 (7.5)
手根管症候群	1 (4.2)	0	0	0	0
浮動性めまい	0	0	0	0	1 (1.9)
本態性振戦	1 (4.2)	0	0	0	0
頭痛	1 (4.2)	1 (2.4)	1 (2.2)	3 (5.7)	3 (5.7)

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
神経系障害 (Cont.)					
感覚鈍麻	0	2 (4.9)	0	2 (3.8)	0
精神障害	1 (4.2)	2 (4.9)	6 (12.9)	2 (3.8)	6 (11.3)
不安	1 (4.2)	0	1 (2.2)	0	1 (1.9)
うつ病	0	0	2 (4.3)	0	2 (3.8)
不眠症	0	1 (2.4)	3 (6.5)	1 (1.9)	3 (5.7)
睡眠障害	0	1 (2.4)	0	1 (1.9)	0
腎および尿路障害	4 (16.9)	1 (2.4)	2 (4.3)	2 (3.8)	2 (3.8)
排尿困難	0	0	0	1 (1.9)	0
血尿	2 (8.4)	0	0	0	0
水腎症	1 (4.2)	0	0	0	0
腎結石症	1 (4.2)	1 (2.4)	0	1 (1.9)	0
腎仙痛	0	0	2 (4.3)	0	2 (3.8)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
生殖系および乳房障害	1 (4.2)	4 (9.7)	0	5 (9.4)	0
良性前立腺肥大症	0	1 (2.4)	0	1 (1.9)	0
乳房嚢胞	0	1 (2.4)	0	1 (1.9)	0
勃起不全	0	0	0	1 (1.9)	0
閉経期症状	1 (4.2)	0	0	0	0
前立腺炎	0	1 (2.4)	0	1 (1.9)	0
腟出血	0	1 (2.4)	0	1 (1.9)	0
呼吸器、胸郭および縦隔障害	2 (8.4)	3 (7.3)	11 (23.7)	3 (5.7)	11 (20.7)
気管支拡張症	1 (4.2)	0	0	0	0
咳嗽	0	1 (2.4)	2 (4.3)	1 (1.9)	2 (3.8)
労作性呼吸困難	0	0	1 (2.2)	0	1 (1.9)
肺気腫	0	0	1 (2.2)	0	1 (1.9)
肺過膨脹	0	0	1 (2.2)	0	1 (1.9)
鼻閉	1 (4.2)	0	1 (2.2)	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
非感染性気管支炎	0	0	1 (2.2)	0	1 (1.9)
口腔咽頭痛	0	1 (2.4)	2 (4.3)	1 (1.9)	2 (3.8)
湿性咳嗽	0	1 (2.4)	0	1 (1.9)	0
肺腫瘤	0	0	1 (2.2)	0	1 (1.9)
上気道咳症候群	0	0	1 (2.2)	0	1 (1.9)
皮膚および皮下組織障害	3 (12.7)	4 (9.7)	9 (19.4)	7 (13.2)	10 (18.8)
ざ瘡	1 (4.2)	1 (2.4)	2 (4.3)	2 (3.8)	2 (3.8)
皮膚炎	0	0	1 (2.2)	0	1 (1.9)
湿疹	0	0	1 (2.2)	0	2 (3.8)
結節性紅斑	0	0	1 (2.2)	0	1 (1.9)
爪甲剥離症	0	0	1 (2.2)	0	1 (1.9)
発疹	0	2 (4.9)	1 (2.2)	3 (5.7)	1 (1.9)
毛孔性皮疹	0	0	0	1 (1.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=116) (PYs=23.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=190) (PYs=41.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=208) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=242) (PYs=53.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=53.1) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
斑状皮疹	0	1 (2.4)	0	1 (1.9)	0
脂漏性皮膚炎	1 (4.2)	0	0	0	0
皮膚病変	0	0	2 (4.3)	0	2 (3.8)
蕁麻疹	1 (4.2)	0	0	0	0
外科および内科処置	0	2 (4.9)	0	2 (3.8)	0
人工流産	0	2 (4.9)	0	2 (3.8)	0
血管障害	1 (4.2)	2 (4.9)	2 (4.3)	2 (3.8)	3 (5.7)
深部静脈血栓症	0	0	1 (2.2)	0	1 (1.9)
高血圧	1 (4.2)	2 (4.9)	1 (2.2)	2 (3.8)	2 (3.8)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month					
Any adverse event	54 (344.1)	57 (190.6)	60 (169.3)	83 (199.2)	85 (210.1)
血液およびリンパ系障害	3 (19.1)	1 (3.3)	2 (5.6)	1 (2.4)	2 (4.9)
鉄欠乏性貧血	1 (6.4)	0	0	0	0
白血球増加症	1 (6.4)	0	0	0	0
白血球減少症	1 (6.4)	1 (3.3)	0	1 (2.4)	0
小球性貧血	0	0	1 (2.8)	0	1 (2.5)
好中球減少症	0	0	1 (2.8)	0	1 (2.5)
心臓障害	1 (6.4)	0	2 (5.6)	0	3 (7.4)
急性心筋梗塞	1 (6.4)	0	0	0	0
二束ブロック	0	0	1 (2.8)	0	1 (2.5)
上室性頻脈	0	0	1 (2.8)	0	1 (2.5)
心室性期外収縮	0	0	0	0	1 (2.5)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
先天性、家族性および遺伝性障害	0	1 (3.3)	0	1 (2.4)	0
ジルベール症候群	0	1 (3.3)	0	1 (2.4)	0
耳および迷路障害	1 (6.4)	2 (6.7)	0	3 (7.2)	0
耳痛	0	0	0	1 (2.4)	0
中耳滲出液	1 (6.4)	0	0	0	0
回転性めまい	0	2 (6.7)	0	2 (4.8)	0
眼障害	2 (12.7)	0	2 (5.6)	1 (2.4)	2 (4.9)
眼瞼炎	0	0	1 (2.8)	0	1 (2.5)
白内障	0	0	0	1 (2.4)	0
結膜充血	1 (6.4)	0	0	0	0
ドライアイ	0	0	1 (2.8)	0	1 (2.5)
眼瞼発疹	1 (6.4)	0	0	0	0
胃腸障害	14 (89.2)	9 (30.1)	9 (25.4)	15 (36.0)	12 (29.7)
腹部膨満	0	1 (3.3)	0	1 (2.4)	1 (2.5)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
胃腸障害 (Cont.)					
腹痛	0	1 (3.3)	1 (2.8)	1 (2.4)	1 (2.5)
下腹部痛	1 (6.4)	0	0	0	0
上腹部痛	0	1 (3.3)	0	2 (4.8)	0
腹部圧痛	0	0	1 (2.8)	0	1 (2.5)
異常便	1 (6.4)	0	0	0	0
潰瘍性大腸炎	6 (38.2)	1 (3.3)	2 (5.6)	5 (12.0)	2 (4.9)
結腸異形成	0	1 (3.3)	0	1 (2.4)	0
便秘	0	0	1 (2.8)	0	1 (2.5)
下痢	0	0	0	1 (2.4)	0
消化不良	2 (12.7)	1 (3.3)	0	1 (2.4)	0
嚥下障害	1 (6.4)	0	0	0	0
小腸炎	0	0	1 (2.8)	0	1 (2.5)
大腿ヘルニア	1 (6.4)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
胃腸障害 (Cont.)					
胃潰瘍	0	1 (3.3)	0	1 (2.4)	0
胃炎	0	1 (3.3)	0	1 (2.4)	0
胃食道逆流性疾患	0	0	1 (2.8)	0	1 (2.5)
舌痛	1 (6.4)	0	0	0	0
痔出血	1 (6.4)	0	0	0	0
痔核	0	1 (3.3)	0	1 (2.4)	0
悪心	0	0	1 (2.8)	0	2 (4.9)
口腔障害	0	0	1 (2.8)	0	1 (2.5)
歯痛	0	0	0	0	1 (2.5)
一般・全身障害および投与部位の状態	4 (25.5)	0	5 (14.1)	0	5 (12.4)
胸痛	0	0	1 (2.8)	0	1 (2.5)
医療機器に対する不耐性	1 (6.4)	0	0	0	0
疲労	1 (6.4)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
一般・全身障害および投与部位の状態 (Cont.)					
炎症	0	0	1 (2.8)	0	1 (2.5)
疼痛	1 (6.4)	0	0	0	0
末梢腫脹	1 (6.4)	0	0	0	0
発熱	0	0	3 (8.5)	0	3 (7.4)
肝胆道系障害	1 (6.4)	1 (3.3)	0	1 (2.4)	1 (2.5)
肝機能異常	1 (6.4)	1 (3.3)	0	1 (2.4)	1 (2.5)
免疫系障害	0	1 (3.3)	0	1 (2.4)	0
季節性アレルギー	0	1 (3.3)	0	1 (2.4)	0
感染症および寄生虫症	5 (31.9)	16 (53.5)	18 (50.8)	26 (62.4)	21 (51.9)
腹壁膿瘍	0	0	0	1 (2.4)	0
COVID-19	1 (6.4)	1 (3.3)	2 (5.6)	2 (4.8)	2 (4.9)
カンピロバクター感染	0	0	0	1 (2.4)	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	1 (2.4)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
感染性腸炎	0	0	1 (2.8)	0	1 (2.5)
毛包炎	0	0	1 (2.8)	0	1 (2.5)
せつ	0	1 (3.3)	0	1 (2.4)	0
胃腸炎	0	1 (3.3)	0	1 (2.4)	0
ウイルス性胃腸炎	0	0	0	1 (2.4)	0
歯肉炎	0	0	0	0	1 (2.5)
帯状疱疹	0	2 (6.7)	2 (5.6)	3 (7.2)	2 (4.9)
膿痂疹	0	1 (3.3)	0	1 (2.4)	0
インフルエンザ	0	1 (3.3)	1 (2.8)	1 (2.4)	1 (2.5)
潜伏結核	0	0	0	0	1 (2.5)
下気道感染	0	0	0	1 (2.4)	0
上咽頭炎	0	2 (6.7)	3 (8.5)	3 (7.2)	3 (7.4)
口腔ヘルペス	0	1 (3.3)	1 (2.8)	1 (2.4)	1 (2.5)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
咽頭炎	2 (12.7)	0	0	0	0
肺炎	0	0	1 (2.8)	0	1 (2.5)
膿皮症	0	0	1 (2.8)	0	1 (2.5)
ウイルス性気道感染	1 (6.4)	0	0	0	0
鼻炎	0	0	1 (2.8)	0	1 (2.5)
副鼻腔炎	0	0	1 (2.8)	0	1 (2.5)
歯感染	0	0	1 (2.8)	0	1 (2.5)
上気道感染	1 (6.4)	3 (10.0)	0	4 (9.6)	0
尿路感染	0	3 (10.0)	1 (2.8)	4 (9.6)	1 (2.5)
ウイルス性上気道感染	0	0	1 (2.8)	0	1 (2.5)
外陰部腟カンジダ症	0	0	0	0	1 (2.5)
傷害、中毒および処置合併症	0	4 (13.4)	0	5 (12.0)	0
足骨折	0	0	0	1 (2.4)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
傷害、中毒および処置合併症 (Cont.)					
四肢損傷	0	1 (3.3)	0	1 (2.4)	0
肉離れ	0	1 (3.3)	0	1 (2.4)	0
外傷後疼痛	0	1 (3.3)	0	1 (2.4)	0
皮膚裂傷	0	1 (3.3)	0	1 (2.4)	0
臨床検査	0	7 (23.4)	9 (25.4)	10 (24.0)	17 (42.0)
アラニンアミノトランスフェラーゼ増加	0	1 (3.3)	1 (2.8)	1 (2.4)	1 (2.5)
アミラーゼ増加	0	1 (3.3)	0	1 (2.4)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (6.7)	1 (2.8)	2 (4.8)	1 (2.5)
血中クレアチンホスホキナーゼ増加	0	1 (3.3)	2 (5.6)	2 (4.8)	3 (7.4)
血中ブドウ糖増加	0	0	1 (2.8)	0	1 (2.5)
血中トリグリセリド増加	0	0	0	0	1 (2.5)
リパーゼ増加	0	1 (3.3)	0	1 (2.4)	0
肝機能検査値上昇	0	0	1 (2.8)	0	1 (2.5)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
臨床検査 (Cont.)					
リンパ球数減少	0	0	1 (2.8)	0	2 (4.9)
好中球数減少	0	0	1 (2.8)	0	1 (2.5)
好中球数増加	0	0	0	0	1 (2.5)
血小板数増加	0	0	0	0	1 (2.5)
前立腺特異性抗原増加	0	0	0	1 (2.4)	0
網状赤血球数減少	0	0	0	1 (2.4)	0
ブドウ球菌検査陽性	0	1 (3.3)	0	1 (2.4)	0
尿中ケトン体陽性	0	0	0	0	1 (2.5)
白血球数減少	0	0	1 (2.8)	0	2 (4.9)
尿中白血球陽性	0	0	0	0	1 (2.5)
代謝および栄養障害	1 (6.4)	1 (3.3)	1 (2.8)	1 (2.4)	2 (4.9)
糖尿病	0	0	0	0	1 (2.5)
耐糖能障害	1 (6.4)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
代謝および栄養障害 (Cont.)					
痛風	0	1 (3.3)	0	1 (2.4)	0
高脂血症	0	0	1 (2.8)	0	1 (2.5)
筋骨格系および結合組織障害	10 (63.7)	6 (20.1)	2 (5.6)	6 (14.4)	2 (4.9)
関節痛	0	3 (10.0)	1 (2.8)	3 (7.2)	1 (2.5)
腸炎性関節炎	1 (6.4)	0	0	0	0
関節障害	1 (6.4)	0	0	0	0
背部痛	4 (25.5)	0	0	0	0
尾骨痛	1 (6.4)	0	0	0	0
外骨腫	0	1 (3.3)	0	1 (2.4)	0
側腹部痛	0	0	1 (2.8)	0	1 (2.5)
関節腫脹	0	1 (3.3)	0	1 (2.4)	0
筋力低下	1 (6.4)	0	0	0	0
筋骨格系胸痛	1 (6.4)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
四肢痛	1 (6.4)	0	0	0	0
肩回旋筋腱板症候群	0	1 (3.3)	0	1 (2.4)	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）	0	0	2 (5.6)	0	3 (7.4)
基底細胞癌	0	0	1 (2.8)	0	2 (4.9)
小細胞癌	0	0	1 (2.8)	0	1 (2.5)
神経系障害	3 (19.1)	1 (3.3)	2 (5.6)	2 (4.8)	5 (12.4)
灼熱感	0	0	0	1 (2.4)	0
頭痛	1 (6.4)	0	1 (2.8)	0	3 (7.4)
感覚鈍麻	0	1 (3.3)	0	1 (2.4)	0
片頭痛	2 (12.7)	0	1 (2.8)	0	1 (2.5)
ヘルペス後神経痛	0	0	0	0	1 (2.5)
精神障害	0	1 (3.3)	0	1 (2.4)	0
パニック発作	0	1 (3.3)	0	1 (2.4)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
腎および尿路障害	2 (12.7)	2 (6.7)	1 (2.8)	2 (4.8)	1 (2.5)
緊張性膀胱	0	0	1 (2.8)	0	1 (2.5)
腎石灰沈着症	1 (6.4)	0	0	0	0
腎結石症	1 (6.4)	1 (3.3)	0	1 (2.4)	0
腎機能障害	0	1 (3.3)	0	1 (2.4)	0
生殖系および乳房障害	2 (12.7)	0	0	0	0
不規則月経	1 (6.4)	0	0	0	0
前立腺炎	1 (6.4)	0	0	0	0
呼吸器、胸郭および縦隔障害	2 (12.7)	1 (3.3)	2 (5.6)	1 (2.4)	3 (7.4)
急性呼吸不全	0	0	1 (2.8)	0	1 (2.5)
咳嗽	1 (6.4)	0	0	0	0
鼻出血	0	0	0	0	1 (2.5)
鼻閉	0	0	1 (2.8)	0	1 (2.5)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
アレルギー性鼻炎	0	1 (3.3)	0	1 (2.4)	0
副鼻腔うっ血	1 (6.4)	0	0	0	0
皮膚および皮下組織障害	3 (19.1)	3 (10.0)	1 (2.8)	5 (12.0)	2 (4.9)
ざ瘡	0	0	0	0	1 (2.5)
皮膚炎	1 (6.4)	0	0	0	0
アトピー性皮膚炎	0	1 (3.3)	0	1 (2.4)	0
湿疹	0	1 (3.3)	0	1 (2.4)	0
光線性皮膚症	1 (6.4)	0	0	0	0
そう痒症	0	0	0	1 (2.4)	0
紅斑性皮疹	0	0	0	1 (2.4)	0
毛孔性皮疹	0	1 (3.3)	0	1 (2.4)	0
脂漏性皮膚炎	1 (6.4)	0	0	0	0
蕁麻疹	0	0	1 (2.8)	0	1 (2.5)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=75) (PYs=15.7) Events (E/100PYs)	 UPA 15 mg QD (N=143) (PYs=29.9) Events (E/100PYs)	 UPA 30 mg QD (N=166) (PYs=35.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=188) (PYs=41.7) Events (E/100PYs)	 UPA 30 mg QD (N=189) (PYs=40.5) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
血管障害	0	0	2 (5.6)	1 (2.4)	4 (9.9)
高血圧	0	0	2 (5.6)	1 (2.4)	2 (4.9)
低血圧	0	0	0	0	1 (2.5)
起立性低血圧	0	0	0	0	1 (2.5)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month					
Any adverse event	2 (487.0)	0	7 (680.0)	53 (220.0)	97 (327.0)
血液およびリンパ系障害	0	0	1 (97.1)	0	6 (20.2)
貧血	0	0	1 (97.1)	0	3 (10.1)
白血球減少症	0	0	0	0	1 (3.4)
リンパ球減少症	0	0	0	0	1 (3.4)
好中球減少症	0	0	0	0	1 (3.4)
心臓障害	0	0	1 (97.1)	0	4 (13.5)
不整脈	0	0	0	0	1 (3.4)
第一度房室ブロック	0	0	0	0	1 (3.4)
心不全	0	0	1 (97.1)	0	1 (3.4)
心室性期外収縮	0	0	0	0	1 (3.4)
耳および迷路障害	0	0	0	1 (4.2)	1 (3.4)
回転性めまい	0	0	0	1 (4.2)	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
胃腸障害	1 (243.5)	0	0	10 (41.5)	6 (20.2)
腹部圧痛	0	0	0	0	1 (3.4)
潰瘍性大腸炎	1 (243.5)	0	0	3 (12.5)	2 (6.7)
便秘	0	0	0	1 (4.2)	1 (3.4)
胃食道逆流性疾患	0	0	0	1 (4.2)	0
痔核	0	0	0	1 (4.2)	0
過敏性腸症候群	0	0	0	1 (4.2)	0
大腸ポリープ	0	0	0	0	1 (3.4)
口腔内潰瘍形成	0	0	0	1 (4.2)	0
直腸異形成	0	0	0	2 (8.3)	0
嘔吐	0	0	0	0	1 (3.4)
一般・全身障害および投与部位の状態	0	0	0	1 (4.2)	2 (6.7)
悪寒	0	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
一般・全身障害および投与部位の状態 (Cont.)					
異形成	0	0	0	1 (4.2)	0
末梢腫脹	0	0	0	0	1 (3.4)
感染症および寄生虫症	0	0	1 (97.1)	9 (37.4)	18 (60.7)
肛門膿瘍	0	0	0	1 (4.2)	0
COVID-19	0	0	0	0	1 (3.4)
カンピロバクター胃腸炎	0	0	0	0	1 (3.4)
結膜炎	0	0	0	0	1 (3.4)
膀胱炎	0	0	0	1 (4.2)	0
せつ	0	0	0	0	1 (3.4)
胃腸炎	0	0	0	0	1 (3.4)
帯状疱疹	0	0	0	3 (12.5)	1 (3.4)
耳帯状疱疹	0	0	0	1 (4.2)	0
麦粒腫	0	0	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
潜伏結核	0	0	0	0	1 (3.4)
上咽頭炎	0	0	0	0	3 (10.1)
爪真菌症	0	0	0	1 (4.2)	0
口腔ヘルペス	0	0	0	0	1 (3.4)
ウイルス性気道感染	0	0	0	0	1 (3.4)
扁桃炎	0	0	0	1 (4.2)	0
上気道感染	0	0	1 (97.1)	0	1 (3.4)
尿路感染	0	0	0	0	2 (6.7)
外陰部腟カンジダ症	0	0	0	0	3 (10.1)
傷害、中毒および処置合併症	0	0	0	2 (8.3)	0
仙骨骨折	0	0	0	1 (4.2)	0
過量投与	0	0	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	 UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	 UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	 UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
臨床検査	0	0	1 (97.1)	13 (54.0)	24 (80.9)
アラニンアミノトランスフェラーゼ増加	0	0	0	1 (4.2)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	0	1 (3.4)
血中アルカリホスファターゼ増加	0	0	0	0	1 (3.4)
血中重炭酸塩減少	0	0	0	1 (4.2)	0
血中ビリルビン増加	0	0	0	0	2 (6.7)
血中コレステロール増加	0	0	0	0	1 (3.4)
血中クレアチンホスホキナーゼ増加	0	0	0	2 (8.3)	6 (20.2)
血中ブドウ糖減少	0	0	0	0	1 (3.4)
血中リン減少	0	0	0	0	1 (3.4)
尿中血陽性	0	0	1 (97.1)	0	1 (3.4)
γ-グルタミルトランスフェラーゼ増加	0	0	0	3 (12.5)	1 (3.4)
ヘモグロビン減少	0	0	0	0	2 (6.7)
肝機能検査値上昇	0	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
臨床検査 (Cont.)					
リンパ球数減少	0	0	0	1 (4.2)	0
平均赤血球容積増加	0	0	0	0	1 (3.4)
好中球数減少	0	0	0	3 (12.5)	2 (6.7)
好中球数増加	0	0	0	1 (4.2)	0
赤血球数減少	0	0	0	0	2 (6.7)
白血球数減少	0	0	0	1 (4.2)	1 (3.4)
代謝および栄養障害	0	0	0	1 (4.2)	4 (13.5)
糖尿病	0	0	0	0	1 (3.4)
痛風	0	0	0	1 (4.2)	0
高コレステロール血症	0	0	0	0	1 (3.4)
肥満	0	0	0	0	1 (3.4)
ビタミンD欠乏	0	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
筋骨格系および結合組織障害	1 (243.5)	0	1 (97.1)	5 (20.8)	7 (23.6)
関節痛	1 (243.5)	0	1 (97.1)	0	2 (6.7)
関節障害	0	0	0	1 (4.2)	0
椎間板突出	0	0	0	1 (4.2)	0
筋肉痛	0	0	0	1 (4.2)	2 (6.7)
骨壊死	0	0	0	1 (4.2)	0
四肢痛	0	0	0	0	2 (6.7)
足底筋膜炎	0	0	0	1 (4.2)	0
腱炎	0	0	0	0	1 (3.4)
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）	0	0	0	0	4 (13.5)
ボーエン病	0	0	0	0	1 (3.4)
線維腫	0	0	0	0	1 (3.4)
脂漏性角化症	0	0	0	0	1 (3.4)
皮膚乳頭腫	0	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
神経系障害	0	0	0	1 (4.2)	3 (10.1)
浮動性めまい	0	0	0	1 (4.2)	0
頭痛	0	0	0	0	2 (6.7)
失神	0	0	0	0	1 (3.4)
精神障害	0	0	0	0	1 (3.4)
うつ病	0	0	0	0	1 (3.4)
腎および尿路障害	0	0	0	0	1 (3.4)
蛋白尿	0	0	0	0	1 (3.4)
生殖系および乳房障害	0	0	0	2 (8.3)	0
良性前立腺肥大症	0	0	0	1 (4.2)	0
不正子宮出血	0	0	0	1 (4.2)	0
呼吸器、胸郭および縦隔障害	0	0	0	5 (20.8)	2 (6.7)
咳嗽	0	0	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
鼻潰瘍	0	0	0	2 (8.3)	0
口腔咽頭痛	0	0	0	1 (4.2)	1 (3.4)
湿性咳嗽	0	0	0	0	1 (3.4)
睡眠時無呼吸症候群	0	0	0	1 (4.2)	0
皮膚および皮下組織障害	0	0	2 (194.3)	1 (4.2)	12 (40.5)
ざ瘡	0	0	0	0	1 (3.4)
脱毛症	0	0	0	0	1 (3.4)
ざ瘡様皮膚炎	0	0	0	1 (4.2)	0
アレルギー性皮膚炎	0	0	0	0	1 (3.4)
湿疹	0	0	0	0	1 (3.4)
皮脂欠乏性湿疹	0	0	0	0	1 (3.4)
紅斑	0	0	0	0	1 (3.4)
黒子	0	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=21) (PYs=0.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=0.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=51) (PYs=1.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=122) (PYs=24.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=137) (PYs=29.7) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
発疹	0	0	0	0	2 (6.7)
斑状皮疹	0	0	0	0	1 (3.4)
蕁麻疹	0	0	2 (194.3)	0	2 (6.7)
血管障害	0	0	0	2 (8.3)	2 (6.7)
高血圧	0	0	0	1 (4.2)	0
静脈炎	0	0	0	0	1 (3.4)
レイノー現象	0	0	0	1 (4.2)	0
白衣性高血圧	0	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	 UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	 UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=80) (PYs=17.3) Events (E/100PYs)	 UPA 30 mg QD (N=103) (PYs=21.4) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month					
Any adverse event	0	0	0	28 (162.2)	38 (177.4)
血液およびリンパ系障害	0	0	0	1 (5.8)	1 (4.7)
鉄欠乏性貧血	0	0	0	1 (5.8)	0
好中球減少症	0	0	0	0	1 (4.7)
耳および迷路障害	0	0	0	0	2 (9.3)
メニエール病	0	0	0	0	1 (4.7)
耳鳴	0	0	0	0	1 (4.7)
眼障害	0	0	0	0	1 (4.7)
白内障	0	0	0	0	1 (4.7)
胃腸障害	0	0	0	2 (11.6)	2 (9.3)
上腹部痛	0	0	0	1 (5.8)	0
腹部圧痛	0	0	0	1 (5.8)	0
潰瘍性大腸炎	0	0	0	0	2 (9.3)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=80) (PYs=17.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=103) (PYs=21.4) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
一般・全身障害および投与部位の状態	0	0	0	0	1 (4.7)
悪寒	0	0	0	0	1 (4.7)
肝胆道系障害	0	0	0	2 (11.6)	0
胆道ジスキネジア	0	0	0	1 (5.8)	0
脂肪肝	0	0	0	1 (5.8)	0
免疫系障害	0	0	0	0	1 (4.7)
アナフィラキシー反応	0	0	0	0	1 (4.7)
感染症および寄生虫症	0	0	0	8 (46.4)	12 (56.0)
COVID-19	0	0	0	1 (5.8)	2 (9.3)
COVID-19肺炎	0	0	0	0	1 (4.7)
カンピロバクター胃腸炎	0	0	0	1 (5.8)	0
蜂巣炎	0	0	0	3 (17.4)	1 (4.7)
クロストリジウム・ディフィシレ感染	0	0	0	0	1 (4.7)

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=80) (PYs=17.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=103) (PYs=21.4) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
耳感染	0	0	0	1 (5.8)	0
帯状疱疹	0	0	0	0	1 (4.7)
上咽頭炎	0	0	0	1 (5.8)	1 (4.7)
副鼻腔炎	0	0	0	0	2 (9.3)
歯膿瘍	0	0	0	0	1 (4.7)
上気道感染	0	0	0	1 (5.8)	0
尿路感染	0	0	0	0	1 (4.7)
ウイルス性上気道感染	0	0	0	0	1 (4.7)
傷害、中毒および処置合併症	0	0	0	1 (5.8)	2 (9.3)
挫傷	0	0	0	1 (5.8)	0
足骨折	0	0	0	0	1 (4.7)
四肢損傷	0	0	0	0	1 (4.7)

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=80) (PYs=17.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=103) (PYs=21.4) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
臨床検査	0	0	0	5 (29.0)	5 (23.3)
細菌検査陽性	0	0	0	1 (5.8)	0
血中コレステロール増加	0	0	0	0	1 (4.7)
血中クレアチンホスホキナーゼ増加	0	0	0	0	1 (4.7)
血中リン減少	0	0	0	0	1 (4.7)
γ-グルタミルトランスフェラーゼ増加	0	0	0	1 (5.8)	0
尿中ブドウ糖陽性	0	0	0	1 (5.8)	0
高比重リポ蛋白増加	0	0	0	1 (5.8)	0
好中球数減少	0	0	0	0	1 (4.7)
尿中蛋白陽性	0	0	0	1 (5.8)	0
白血球数減少	0	0	0	0	1 (4.7)
代謝および栄養障害	0	0	0	0	1 (4.7)
ビタミンD欠乏	0	0	0	0	1 (4.7)

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=80) (PYs=17.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=103) (PYs=21.4) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
筋骨格系および結合組織障害	0	0	0	3 (17.4)	3 (14.0)
関節痛	0	0	0	1 (5.8)	2 (9.3)
背部痛	0	0	0	1 (5.8)	1 (4.7)
筋骨格痛	0	0	0	1 (5.8)	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）	0	0	0	0	1 (4.7)
子宮頚部扁平上皮癌	0	0	0	0	1 (4.7)
神経系障害	0	0	0	3 (17.4)	2 (9.3)
頭痛	0	0	0	2 (11.6)	0
片頭痛	0	0	0	1 (5.8)	0
睡眠の質低下	0	0	0	0	1 (4.7)
視野欠損	0	0	0	0	1 (4.7)
精神障害	0	0	0	0	1 (4.7)
故意の自傷行為	0	0	0	0	1 (4.7)

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=80) (PYs=17.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=103) (PYs=21.4) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
生殖系および乳房障害	0	0	0	0	1 (4.7)
閉経後出血	0	0	0	0	1 (4.7)
皮膚および皮下組織障害	0	0	0	2 (11.6)	1 (4.7)
ざ瘡	0	0	0	0	1 (4.7)
接触皮膚炎	0	0	0	1 (5.8)	0
紅斑性皮疹	0	0	0	1 (5.8)	0
外科および内科処置	0	0	0	0	1 (4.7)
抜歯	0	0	0	0	1 (4.7)
血管障害	0	0	0	1 (5.8)	0
大動脈硬化症	0	0	0	1 (5.8)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	 UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	 UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=58) (PYs=12.6) Events (E/100PYs)	 UPA 30 mg QD (N=70) (PYs=13.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month					
Any adverse event	0	0	0	17 (135.1)	18 (131.9)
胃腸障害	0	0	0	1 (7.9)	3 (22.0)
潰瘍性大腸炎	0	0	0	0	1 (7.3)
腸炎	0	0	0	0	1 (7.3)
胃食道逆流性疾患	0	0	0	1 (7.9)	0
痔核	0	0	0	0	1 (7.3)
一般・全身障害および投与部位の状態	0	0	0	0	2 (14.7)
発熱	0	0	0	0	2 (14.7)
感染症および寄生虫症	0	0	0	5 (39.7)	12 (87.9)
肛門膿瘍	0	0	0	0	1 (7.3)
COVID-19	0	0	0	0	4 (29.3)
COVID-19肺炎	0	0	0	1 (7.9)	0
クロストリジウム・ディフィシレ感染	0	0	0	0	1 (7.3)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=58) (PYs=12.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=70) (PYs=13.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
膀胱炎	0	0	0	1 (7.9)	0
毛嚢虫症	0	0	0	0	1 (7.3)
胃腸炎	0	0	0	0	1 (7.3)
帯状疱疹	0	0	0	0	2 (14.7)
大腸感染	0	0	0	0	1 (7.3)
上咽頭炎	0	0	0	1 (7.9)	1 (7.3)
外耳炎	0	0	0	1 (7.9)	0
副鼻腔炎	0	0	0	1 (7.9)	0
傷害、中毒および処置合併症	0	0	0	1 (7.9)	0
足骨折	0	0	0	1 (7.9)	0
臨床検査	0	0	0	1 (7.9)	0
尿中白血球エステラーゼ陽性	0	0	0	1 (7.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=58) (PYs=12.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=70) (PYs=13.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month (Cont.)					
筋骨格系および結合組織障害	0	0	0	4 (31.8)	0
関節痛	0	0	0	3 (23.8)	0
弾発指	0	0	0	1 (7.9)	0
神経系障害	0	0	0	3 (23.8)	1 (7.3)
頭痛	0	0	0	1 (7.9)	0
片頭痛	0	0	0	1 (7.9)	0
後頭神経痛	0	0	0	1 (7.9)	0
失神寸前の状態	0	0	0	0	1 (7.3)
生殖系および乳房障害	0	0	0	1 (7.9)	0
不規則月経	0	0	0	1 (7.9)	0
皮膚および皮下組織障害	0	0	0	1 (7.9)	0
ざ瘡	0	0	0	1 (7.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=41) (PYs=7.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=40) (PYs=6.8) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month					
Any adverse event	0	0	0	14 (180.6)	7 (102.9)
胃腸障害	0	0	0	2 (25.8)	2 (29.4)
潰瘍性大腸炎	0	0	0	0	1 (14.7)
下痢	0	0	0	1 (12.9)	0
消化不良	0	0	0	1 (12.9)	0
大腸ポリープ	0	0	0	0	1 (14.7)
一般・全身障害および投与部位の状態	0	0	0	2 (25.8)	0
疲労	0	0	0	1 (12.9)	0
疼痛	0	0	0	1 (12.9)	0
肝胆道系障害	0	0	0	2 (25.8)	0
硬化性胆管炎	0	0	0	1 (12.9)	0
肝機能異常	0	0	0	1 (12.9)	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=41) (PYs=7.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=40) (PYs=6.8) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month (Cont.)					
感染症および寄生虫症	0	0	0	6 (77.4)	2 (29.4)
COVID-19	0	0	0	1 (12.9)	1 (14.7)
膀胱炎	0	0	0	1 (12.9)	0
鼠径部膿瘍	0	0	0	1 (12.9)	0
帯状疱疹	0	0	0	1 (12.9)	0
口腔カンジダ症	0	0	0	0	1 (14.7)
上気道感染	0	0	0	2 (25.8)	0
臨床検査	0	0	0	1 (12.9)	0
血中クレアチンホスホキナーゼ増加	0	0	0	1 (12.9)	0
筋骨格系および結合組織障害	0	0	0	1 (12.9)	1 (14.7)
関節痛	0	0	0	1 (12.9)	0
滑液包炎	0	0	0	0	1 (14.7)
生殖系および乳房障害	0	0	0	0	1 (14.7)
不正子宮出血	0	0	0	0	1 (14.7)

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=41) (PYs=7.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=40) (PYs=6.8) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month (Cont.)					
皮膚および皮下組織障害	0	0	0	0	1 (14.7)
寝汗	0	0	0	0	1 (14.7)

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=24) (PYs=24.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=16) (PYs=5.7) Events (E/100PYs)
Subgroup:>= 24 Month					
Any adverse event	0	0	0	51 (205.9)	12 (208.7)
血液およびリンパ系障害	0	0	0	4 (16.2)	1 (17.4)
貧血	0	0	0	1 (4.0)	0
内出血発生の増加傾向	0	0	0	0	1 (17.4)
白血球減少症	0	0	0	3 (12.1)	0
眼障害	0	0	0	1 (4.0)	0
硝子体浮遊物	0	0	0	1 (4.0)	0
胃腸障害	0	0	0	6 (24.2)	1 (17.4)
腹痛	0	0	0	1 (4.0)	0
下腹部痛	0	0	0	1 (4.0)	0
潰瘍性大腸炎	0	0	0	1 (4.0)	1 (17.4)
腸管ポリープ	0	0	0	1 (4.0)	0
過敏性腸症候群	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=24) (PYs=24.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=16) (PYs=5.7) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
胃腸障害 (Cont.)					
悪心	0	0	0	1 (4.0)	0
一般・全身障害および投与部位の状態	0	0	0	1 (4.0)	0
疲労	0	0	0	1 (4.0)	0
感染症および寄生虫症	0	0	0	9 (36.3)	5 (87.0)
COVID-19肺炎	0	0	0	1 (4.0)	0
カンピロバクター感染	0	0	0	1 (4.0)	0
結膜炎	0	0	0	1 (4.0)	0
膀胱炎	0	0	0	1 (4.0)	0
ヘリコバクター感染	0	0	0	1 (4.0)	0
潜伏結核	0	0	0	1 (4.0)	0
上咽頭炎	0	0	0	1 (4.0)	0
口腔ヘルペス	0	0	0	0	3 (52.2)
咽頭炎	0	0	0	0	1 (17.4)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=24) (PYs=24.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=16) (PYs=5.7) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
歯髄炎	0	0	0	1 (4.0)	0
白癬感染	0	0	0	0	1 (17.4)
尿路感染	0	0	0	1 (4.0)	0
傷害、中毒および処置合併症	0	0	0	3 (12.1)	0
関節損傷	0	0	0	1 (4.0)	0
靭帯断裂	0	0	0	1 (4.0)	0
過量投与	0	0	0	1 (4.0)	0
臨床検査	0	0	0	8 (32.3)	1 (17.4)
血圧上昇	0	0	0	1 (4.0)	0
ヘマトクリット減少	0	0	0	1 (4.0)	0
ヘモグロビン減少	0	0	0	1 (4.0)	0
リンパ球数減少	0	0	0	2 (8.1)	1 (17.4)
好中球数増加	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=24) (PYs=24.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=16) (PYs=5.7) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
臨床検査 (Cont.)					
赤血球数減少	0	0	0	1 (4.0)	0
尿中白血球エステラーゼ陽性	0	0	0	1 (4.0)	0
代謝および栄養障害	0	0	0	3 (12.1)	1 (17.4)
高コレステロール血症	0	0	0	0	1 (17.4)
高脂血症	0	0	0	1 (4.0)	0
鉄欠乏	0	0	0	1 (4.0)	0
過少体重	0	0	0	1 (4.0)	0
筋骨格系および結合組織障害	0	0	0	7 (28.3)	2 (34.8)
関節痛	0	0	0	1 (4.0)	1 (17.4)
背部痛	0	0	0	1 (4.0)	0
軟骨萎縮	0	0	0	1 (4.0)	0
椎間板突出	0	0	0	0	1 (17.4)
関節滲出液	0	0	0	1 (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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=24) (PYs=24.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=16) (PYs=5.7) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
筋痙縮	0	0	0	1 (4.0)	0
変形性関節症	0	0	0	1 (4.0)	0
軟骨下機能不全骨折	0	0	0	1 (4.0)	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）	0	0	0	2 (8.1)	0
肺の良性新生物	0	0	0	1 (4.0)	0
気管支の良性新生物	0	0	0	1 (4.0)	0
神経系障害	0	0	0	3 (12.1)	0
脳損傷	0	0	0	1 (4.0)	0
手根管症候群	0	0	0	1 (4.0)	0
頭痛	0	0	0	1 (4.0)	0
呼吸器、胸郭および縦隔障害	0	0	0	2 (8.1)	1 (17.4)
呼吸困難	0	0	0	1 (4.0)	0
鼻出血	0	0	0	0	1 (17.4)

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=0) (PYs=0.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=24) (PYs=24.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=16) (PYs=5.7) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
副鼻腔うっ血	0	0	0	1 (4.0)	0
皮膚および皮下組織障害	0	0	0	2 (8.1)	0
脱毛症	0	0	0	1 (4.0)	0
湿疹	0	0	0	1 (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.
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.

Program Source Code: [redacted]

表 2.7.4.7-38.

TABLE 14.3 2.5.2.1

Listing of Subjects with Treatment-Emergent Adverse Events Leading to Death
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD								
[redacted]# Age:7[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg								
	C2-3 0DB	1 to 434	403	403	N: [redacted] R: PANCREATIC ADENOCARCINOMA S: 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) P: 膵腺癌 L: Pancreatic adenocarcinoma	E: 434 L: 32 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (Concomitant medication or therapy started, DISCONTINUED STUDY, Other: HOSPITALIZED FOR FURTHER TESTING)	AE: No/No/No/No/No/No S: Yes, death of subject, hospitalization or prolonged hospitalization O: AGE RELATED CANCER A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1

Listing of Subjects with Treatment-Emergent Adverse Events Leading to Death
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
	C1-15OL	1 to 1187	1187	N: [redacted] R: ANOXIC BRAIN INJURY S: 神経系障害 P: 脳損傷 L: Anoxic brain damage	E: 1187 L: 1 Day	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, death of subject, hospitalization or prolonged hospitalization O: ACUTE RESPIRATORY FAILURE WITH HYPOXIA A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

表 2.7.4.7-39.

[redacted]20[redacted] 13:22 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 1
R&D/20/1294 - CLINICAL/STATISTICAL

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 30 mg [redacted]# Age: 6[redacted] Sex: Male Race: WHITE Weight: 7[redacted] kg								
	SUB1	1 to 8	6	6	R: EXACERBATION OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 154 L: 149 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: DISEASE UNDER STUDY A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch: Name	Epoch: Interval	Epoch: Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo [redacted] Age: 3[redacted] Sex: Female Race: ASIAN Weight: 3[redacted] kg								
[redacted]	POST	31 to 1	31	R: WORSENING OF UC S: 胃腸障害 P: 潰瘍性大腸炎 L: UC aggravated	E: 59 L: 29 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: INADEQUATE RESPONSE A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted]# Age: 4[redacted] Sex: Male Race: ASIAN Weight: 5[redacted].[redacted] kg							
[redacted]	SUB1	1 to 14 13	13	R: UC AGGRAVATED S: 胃腸障害 P: 潰瘍性大腸炎 L: UC aggravated	E: 26 L: 14 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY, CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: UC AGGRAVATED A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 30 mg [redacted]# Age: 3[redacted] Sex: Female Race: WHITE Weight: 7[redacted].[redacted] kg							
	SUB1	1 to 13 13	13	R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 16 L: 4 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY, CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: KNOWN HISTORY OF ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Name	Epoch	Interval	Rx Day	Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 30 mg [redacted]# Age: 3[redacted] Sex: Female Race: WHITE Weight: 7[redacted].[redacted] kg									
(Cont.)	POST	14 to	27	40	R: REFRACTORY ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Ulcerative colitis	E: 45 L: 6 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: LAPAROSCOPIC PROCTOCOLECTOMY	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: ONGOING KNOWN HISTORY OF ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: Placebo [redacted] Age: 4[redacted] Sex: Female Race: WHITE Weight: 11[redacted].[redacted] kg							
	SUB1	1 to 63 19	19	R: FACIAL CELLULITIS S: 感染症および寄生虫症 P: 蜂巣炎 L: Cellulitis of face	E: 28 L: 10 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention A: REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ABT494 15 mg [redacted]# Age: 6[redacted] Sex: Male Race: WHITE Weight: 7[redacted].[redacted] kg							
	SUB1	1 to 47 47	47	R: EXACERBATION OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 62 L: 16 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: WORSENNING OF DISEASE A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Name	Epoch Interval	Epoch Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted] Age: 2[redacted] Sex: Female Race: WHITE Weight: 5[redacted].[redacted] kg								
	SUB1	1 to 56	3	3	R: ABDOMINAL PAIN, FEVER S: 胃腸障害 P: 腹痛 L: Abdominal pain	E: 25 L: 23 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: HOSPITALIZATION [redacted], CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: FEVER ABOVE 39.0 CELSIUS AND ABDOMINAL PAIN SECONDARY TO ULERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted] Age: 2[redacted] Sex: Female Race: WHITE Weight: 5[redacted].[redacted] kg								
(Cont.)	SUB1	1 to 56	3	3	R: ABDOMINAL PAIN, FEVER S: 一般・全身障害および投与部位の状態 P: 発熱 L: Fever	E: 25 L: 23 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: HOSPITALIZATION [redacted], CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: FEVER ABOVE 39.0 CELSIUS AND ABDOMINAL PAIN SECONDARY TO ULERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo [redacted]# Age: 3[redacted] Sex: Female Race: WHITE Weight: 5[redacted].[redacted] kg								
		SUB1	1 to 17 15	15	R: WORSENING COLITIS ULCEROSA S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 26 L: 12 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (CONCOMITANT MEDICATION OR THERAPY STARTED, CONCOMITANT MEDICATION OR THERAPY DISCONTINUED, DISCONTINUED STUDY, HOSPITALISATION BECAUSE IS WORSENING ULCERATIVE COLITIS. COLONOSCOPY AN [redacted] IS SEVERE. GASTROSCOPY ON [redacted] IS MILD. [redacted] XRAY ABDOMEN. NO OUTCOME. [redacted] XRAY ABDOMEN. I.O.)	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: DETAILS SEE IN THE SAE SUPPLEMENTAL FORMS AND AE`S AN CONCOMITTANT MEDICATIONS. A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch: Name	Epoch: Interval	Epoch: Day	Rx Day of Onset	R: Reported Term / S: System Organ Class / P: MedDRA 23.0 Preferred Term / L: Lower Level Term	E: Rx Day Ended / O: Ongoing at the End of Study? / L: Length / I: Intermittent?	T: Rheumatology Toxicity / S: Severity / C: AE Related to COVID-19 Infection / R: Relationship to Study Drug / A: Actions Taken with Study Treatment / O: Other Actions Taken	AE1: Hepatic AE? / AE2: Cardiac AE? / AE3: Cerebral AE$? / AE4: Renal AE? / AE5: Herpes Zoster Infection AE? / AE6: Non-Cardiac AE*? / S: Serious AE? / O: Other Cause of Event / A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo [redacted]# Age: 3[redacted] Sex: Female Race: WHITE Weight: 5[redacted].[redacted] kg								
(Cont.)	POST	18 to	16	33	R: WORSENING COLITITS ULCEROSA S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 52 L: 20 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED, CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: WORSENING OF COLITIS ULCEROSA AGAIN. EVERY 2 TIMES TO GO ON TOILET FOR STOOL, DIARRHOE, BLOOD,PAIN ABDOMEN, CRP INCREASED. NO FEVER.HOSPITALISATION AGAIN. PANCOLITIS WITH CYTOMEGALOVIRUS INFECTION. A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted] Age: 4[redacted] Sex: Female Race: WHITE Weight: 8[redacted].[redacted] kg								
	SUB1	1 to 59	28	28	R: SEPSIS, RSV RESPIRATORY INFECTION S: 感染症および寄生虫症 P: RSウイルス感染 L: Respiratory syncytial virus infection	E: 31 L: 4 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted] Age: 4[redacted] Sex: Female Race: WHITE Weight: 8[redacted].[redacted] kg								
(Cont.)	SUB1	1 to 59	28	28	R: SEPSIS, RSV RESPIRATORY INFECTION S: 感染症および寄生虫症 P: 敗血症 L: Sepsis	E: 31 L: 4 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo [redacted]# Age: 2[redacted] Sex: Male Race: WHITE Weight: 7[redacted].[redacted] kg								
	SUB1	1 to 43	41	41	R: HYPOPHOSPHATEMIA S: 代謝および栄養障害 P: 低リン酸血症 L: Hypophosphatemia	O: Yes	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 30 mg [redacted]# Age: 5[redacted] Sex: Male Race: WHITE Weight: 6[redacted].[redacted] kg								
	POST	45 to	3	47	R: EXACERBATION UC S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 60 L: 14 Days	S: SEVERE R: NO REASONABLE POSSIBILITY O: COLECTOMY	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: EXACERBATION A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 30 mg [redacted]# Age: 5[redacted] Sex: Male Race: WHITE Weight: 6[redacted].[redacted] kg								
(Cont.)	POST	45 to 66	22	66	R: ILEUS S: 胃腸障害 P: イレウス L: Ileus	E: 81 L: 16 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: STOMA STENOSIS LEADING TO ILEUS A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 15 mg [redacted] Age: 5[redacted] Sex: Male Race: WHITE Weight: 9[redacted].[redacted] kg							
	SUB1	1 to 63 53	53	R: SEPTIC URINARY TRACT INFECTION S: 感染症および寄生虫症 P: 尿路性敗血症 L: Urosepsis	E: 62 L: 10 Days I: Yes	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: NONE	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch: Name	Epoch: Interval	Epoch: Day	Rx Day of Onset	R: Reported Term / S: System Organ Class / P: MedDRA 23.0 Preferred Term / L: Lower Level Term	E: Rx Day Ended / O: Ongoing at the End of Study? / L: Length / I: Intermittent?	T: Rheumatology Toxicity / S: Severity / C: AE Related to COVID-19 Infection / R: Relationship to Study Drug / A: Actions Taken with Study Treatment / O: Other Actions Taken	AE1: Hepatic AE? / AE2: Cardiac AE? / AE3: Cerebral AE$? / AE4: Renal AE? / AE5: Herpes Zoster Infection AE? / AE6: Non-Cardiac AE*? / S: Serious AE? / O: Other Cause of Event / A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 30 mg [redacted]# Age: 2[redacted] Sex: Male Race: WHITE Weight: 8[redacted].[redacted] kg								
	POST	44 to 5		48	R: ULCERATIVE COLITIS FLARE S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 54 L: 7 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: HISTORY OF ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted] Age: 5[redacted] Sex: Male Race: WHITE Weight: 8[redacted].[redacted] kg								
	SUB1	1 to 57	57	57	R: HIGH GRADE DYSPLASIA IN LEFT COLON S: 胃腸障害 P: 結腸異形成 L: Colon dysplasia	E: 93 L: 37 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 30 mg [redacted] Age: 5[redacted] Sex: Female Race: WHITE Weight: 6[redacted] kg								
	SUB1	1 to 56	12	12	R: HEMORAGIC CYSTITIS S: 腎および尿路障害 P: 出血性膀胱炎 L: Hemorrhagic cystitis	E: 14 L: 3 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted]# Age: 6[redacted] Sex: Male Race: WHITE Weight: 5[redacted] kg							
[redacted]	SUB1	1 to 45 35	35	R: PHARYNGITIS (VIRAL INFECTION) S: 感染症および寄生虫症 P: ウイルス性咽頭炎 L: Viral pharyngitis	E: 53 L: 19 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization, persistent or significant disability O: VIRAL INFECTION A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted]# Age: 6[redacted] Sex: Male Race: WHITE Weight: 5[redacted].[redacted] kg							
(Cont.)	SUB1	1 to 45 41	41	R: ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Ulcerative colitis	E: 53 L: 13 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY, CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: CONSTANT ACTIVITY OF ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch: Name	Epoch: Interval	Epoch: Day	Rx Day of Onset	R: Reported Term / S: System Organ Class / P: MedDRA 23.0 Preferred Term / L: Lower Level Term	E: Rx Day Ended / O: Ongoing at the End of Study? / L: Length / I: Intermittent?	T: Rheumatology Toxicity / S: Severity / C: AE Related to COVID-19 Infection / R: Relationship to Study Drug / A: Actions Taken with Study Treatment / O: Other Actions Taken	AE1: Hepatic AE? / AE2: Cardiac AE? / AE3: Cerebral AE$? / AE4: Renal AE? / AE5: Herpes Zoster Infection AE? / AE6: Non-Cardiac AE*? / S: Serious AE? / O: Other Cause of Event / A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted]# Age: 6[redacted] Sex: Male Race: WHITE Weight: 5[redacted].[redacted] kg								
(Cont.)	POST	46 to	25	70	R: DEEP VENOUS THROMBOSIS S: 血管障害 P: 深部静脈血栓症 L: Thrombosis venous deep	E: 74 L: 5 Days	S: MILD R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch: Name	Epoch: Interval	Epoch: Day	Rx Day of Onset	R: Reported Term / S: System Organ Class / P: MedDRA 23.0 Preferred Term / L: Lower Level Term	E: Rx Day Ended / O: Ongoing at the End of Study? / L: Length / I: Intermittent?	T: Rheumatology Toxicity / S: Severity / C: AE Related to COVID-19 Infection / R: Relationship to Study Drug / A: Actions Taken with Study Treatment / O: Other Actions Taken	AE1: Hepatic AE? / AE2: Cardiac AE? / AE3: Cerebral AE$? / AE4: Renal AE? / AE5: Herpes Zoster Infection AE? / AE6: Non-Cardiac AE*? / S: Serious AE? / O: Other Cause of Event / A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted]# Age: 6[redacted] Sex: Male Race: WHITE Weight: 5[redacted].[redacted] kg								
(Cont.)	POST	46 to	25	70	R: PULMONARY EMBOLISM S: 呼吸器、胸郭および縦隔障害 P: 肺塞栓症 L: Pulmonary embolism	E: 74 L: 5 Days	S: SEVERE R: REASONABLE POSSIBILITY O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention, life threatening A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted] Age: 2[redacted] Sex: Male Race: WHITE Weight: 7[redacted] kg								
	SUB1	1 to 56	30	30	R: AST INCREASED S: 臨床検査 P: アスパラギン酸アミノトランスフェラーゼ増加 L: AST increased	E: 34 L: 5 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: NONE	AE1: Yes AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: ONE TIME ALCHOHOL USE A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ABT494 45 mg [redacted] Age: 2[redacted] Sex: Male Race: WHITE Weight: 7[redacted] kg								
(Cont.)	SUB1	1 to 56	32	32	R: ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Ulcerative colitis	E: 38 L: 7 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: HOSPITALIZATION A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.2.1 A

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(Substudy 1 - SA1A and SA1B Population)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Drug A: Actions Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo [redacted] Age: 5[redacted] Sex: Male Race: WHITE Weight: 6[redacted].[redacted] kg								
	SUB1	1 to 53	41	41	R: WORSENING SINUSITIS S: 感染症および寄生虫症 P: 副鼻腔炎 L: Sinusitis	E: 48 L: 8 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: HOSPITALISATION, CONCOMITANT MEDICATION OR THERAPY STARTED	AE1: No AE2: No AE3: No AE4: No AE5: No S: Yes, hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY

SUB1 = Substudy 1 treatment; SUB3 = Substudy 3 treatment.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

表 2.7.4.7-40.

[redacted]20[redacted] 10:04 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 2
R&D/20/1294 - CLINICAL/STATISTICAL

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD								
[redacted]	Age:7[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg							
		SS2-DB	1 to 56	29	29	S1: [redacted] R: HYPOALBUMINEMIA S: 代謝および栄養障害 P: 低アルブミン血症 L: Hypoalbuminemia	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: DUE TO ULCERATIVE COLITIS

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset				
					S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45								
[redacted]#	Age:6[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	SS2-OL	57 to 70	1	57	S1: [redacted] R: SEVERE ANEMIC SYNDROME S: 血液およびリンパ系障害 P: 貧血 L: Anemic	E: 57 L: 1 Day I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: IRON DEFICIENCY ANEMIA DUE TO AKTIVE DISEASE MAYO 3 A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted] TRT: UPA 45 mg QD							
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	SS2-DB	1 to 57	49	49	S1: [redacted] R: ACUTE APPENDICITIS S: 感染症および寄生虫症 P: 虫垂炎 L: Acute appendicitis	E: 49 L: 1 Day	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: APPENDICECTOMY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: RARE COMPLICATION OF COLONOSCOPY A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Day	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD								
[redacted] Age:4[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg								
	SS2-DB	1 to 60	57	57	S1: [redacted] R: PULMONARY INFECTION S: 感染症および寄生虫症 P: 肺炎 L: Lung infection	E: 63 L: 7 Days	S: MILD C: No R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo							
[redacted]# Age:3[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
	FU	60 to 5	64	S1: [redacted] R: WORSERING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 87 L: 24 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: Other: PATIENT WAS NOT TAKING THE STUDY DRUG O: PATIENT IS DISCONTINUED IN THE MORNING	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: EXACERBATION OF THE DISEASE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo									
[redacted]# Age:3[redacted] Sex:Male Race:WHITE Weight:8[redacted]. [redacted] kg									
(Cont.)	FU	60 to	21	80		S1: [redacted] R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 87 L: 8 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: IP WAS ALREADY DISCONTINUED AT THE TIME OF AE	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: PROGRESSION OF DISEASE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo								
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
		SS2-DB	1 to 42	32	S1: [redacted] R: WORSENING OF UC S: 胃腸障害 P: 潰瘍性大腸炎 L: UC aggravated	O: Yes	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: LAST WEEK,NAUSEA, REDUCED APPETITE, WEIGHT LOSS. FROM [redacted] [redacted]VOMITING AND DIARRHEA CRP 80, LEUCOCYTES 12 A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo								
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
(Cont.)	FU	43 to	3	45	S1: [redacted] R: DIAPHRAGMATIC HERNIA WITHOUT OBSTRUCTION OR GANGRENE S: 胃腸障害 P: 横隔膜ヘルニア L: Diaphragmatic hernia	O: Yes	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 45 mg QD								
[redacted]# Age:6[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg								
	SS2-DB	1 to 51	51	51	S1: [redacted] R: VIRAL INFECTION S: 感染症および寄生虫症 P: ウイルス感染 L: Viral infection	E: 64 L: 14 Days I: Yes	S: MODERATE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo							
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
	SS2-DB	1 to 15	12	S1: [redacted] R: UC WORSENING S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, persistent or significant disability/incapacity A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD							
[redacted]# Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted] kg							
[redacted]	SS2-OL	57 to 70	1	57	S1: [redacted] R: WORSENING OF ANEMIA S: 血液およびリンパ系障害 P: 貧血 L: Anemia aggravated	E: 70 L: 14 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: HIGH ACTIVITY UC AND GIT BLEEDING. PATIENT WAS PLANNED ADMITTED TO HOSPITAL SCHEDULED FOR CORRECTION FOR LOW HEMOGLOBIN, HOSPITALIZATION WAS PROVIDED FOR THE PATIENT DUE TO DIFFICULTIES IN TRANSPORTI A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD								
[redacted]# Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted] kg								
(Cont.)	SS2-OL	57 to 70	1	57	S1: [redacted] R: RELAPS UC S: 胃腸障害 P: 潰瘍性大腸炎 L: Ulcerative colitis relapse	E: 90 L: 34 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: UC A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo							
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted] kg							
	SS2-DB	1 to 58 47	47	S1: [redacted] R: GLUTEAL ABSCESS S: 感染症および寄生虫症 P: 筋膿瘍 L: Muscle abscess	E: 91 L: 45 Days I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: DISEASE PROGRESSION

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo							
[redacted]# Age:3[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg							
	SS2-DB	1 to 15	7	S1: [redacted] R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 22 L: 16 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (DISCONTINUED STUDY, Other: SUBJECT WITHDRAWN DUE TO WORSENING OF ULCERATIVE COLITIS)	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Study Day	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD								
[redacted]# Age:7[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
	SS2-DB	1 to 22	3	3	S1: [redacted] R: FEVER S: 一般・全身障害および投与部位の状態 P: 発熱 L: Fever	E: 29 L: 27 Days I: Yes	S: MILD R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: ADMISSION	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD/UPA 45 mg QD								
[redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted] kg								
	SS2-OL	57 to 113	1	57	S1: [redacted] R: HYPOTENSION S: 血管障害 P: 低血圧 L: Hypotension	E: 58 L: 2 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: ANAMEIA AND COLONOSCOPY PREPARATION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset				
				S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD/UPA 45 mg QD							
[redacted]#	Age:2[redacted] Sex:Female Race:WHITE Weight:7[redacted] kg						
	SS2-OL	59 to 99	3	61	S1: [redacted] R: DISEASE WORSENING ULCERATIVE COLITIS DISEASE S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 70 L: 10 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: NONE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD/UPA 45 mg QD							
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:6[redacted] kg							
	SS2-DB	1 to 56	5	S1: [redacted] R: NOROVIRUS S: 感染症および寄生虫症 P: ノロウイルス性胃腸炎 L: Gastroenteritis norovirus	E: 9 L: 5 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: NONE	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: INTERCURRENT ILLNESS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset				
			Day	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 45 mg QD							
[redacted]# Age:3[redacted] Sex:Male Race:WHITE Weight:7[redacted] kg							
[redacted]	FU	9 to 7	15	S1: [redacted] R: SEVERE FLARE UP OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 146 L: 132 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted]([redacted] TRT: Placebo							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg							
	SS2-DB	1 to 3	3	3	S1: [redacted] R: UC FLARE DISEASE S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset				
					S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD								
[redacted]	Age:2[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted]kg							
	SS2-DB	1 to 56	56	56	S1: [redacted] R: APPENDICITIS S: 感染症および寄生虫症 P: 虫垂炎 L: Appendicitis	E: 63 L: 8 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted] TRT:								
[redacted]# Age:3[redacted] Sex:Male Race:BLACK OR AFRICAN AMERICAN Weight:12[redacted].[redacted] kg								
	SS2-DB	1	1	1	S1: [redacted] R: DIFFUSE COLITIS S: 胃腸障害 P: 大腸炎 L: Colitis	E: 5 L: 5 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: COMBINATION OF ULCERATIVE COLITIS DIAGNOSIS AND COLONOSCOPY. MAY HAVE INDUCED A FLARE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch Interval	Day	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted]([redacted] TRT: Placebo								
[redacted]# Age:3[redacted] Sex:Male Race:BLACK OR AFRICAN AMERICAN Weight:12[redacted].[redacted] kg								
(Cont.)	FU	2 to 6	7		S1: [redacted] R: DIFFUSE COLITIS S: 胃腸障害 P: 大腸炎 L: Colitis	E: 12 L: 6 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: IT IS LIKELY THAT THE COLONOSCOPY INDUCED A FLARE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch Interval	Day	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo								
[redacted]# Age:3[redacted] Sex:Male Race:BLACK OR AFRICAN AMERICAN Weight:12[redacted].[redacted] kg								
(Cont.)	FU	2 to	16	17	S1: [redacted] R: DIFFUSE COLITIS S: 胃腸障害 P: 大腸炎 L: Colitis	E: 20 L: 4 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: PATIENT WAS EXPERIENCING A FLARE DUE TO UC DIAGNOSIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo								
[redacted]# Age:3[redacted] Sex:Male Race:BLACK OR AFRICAN AMERICAN Weight:12[redacted].[redacted] kg								
(Cont.)	FU	2 to	23	24	S1: [redacted] R: DIFFUSE COLITIS S: 胃腸障害 P: 大腸炎 L: Colitis	E: 32 L: 9 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: DIFFUSE COLITIS FLARE FOLLOWING COLONOSCOPY SCREENING. POSSIBILITY A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Epoch Day	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted] TRT: Placebo								
[redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg								
	SS2-DB	1 to 57	13	13	S1: [redacted] R: RIGHT ANKLE CELLULITIS S: 感染症および寄生虫症 P: 蜂巣炎 L: Cellulitis of leg	E: 44 L: 32 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: RIGHT ANKLE TENDERNESS AND SWELLING AND REDNESS A: REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1 B

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S1: AE Serial Number S2: Previous Study AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Rheumatology Toxicity S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD								
[redacted]# Age:2[redacted] Sex:Male Race:ASIAN Weight:5[redacted].[redacted] kg								
	SS2-DB	1 to 5	1	1	S1: [redacted] R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: RELAPSE OF ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS2-DB = Substudy 2 Part 1 treatment; SS2-OL = Substudy 2 Part 2 treatment; SS3 = Substudy 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

表 2.7.4.7-41.

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA_UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day	Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg									
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg									
	SS3-DB	1 to	169	169		S: [redacted] R: HERPES ZOSTER MENINGITIS S1: 感染症および寄生虫症 P: 帯状疱疹性髄膜炎 L: Herpes zoster meningitis	E: 194 L: 26 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:6[redacted] Sex:Female Race:BLACK OR AFRICAN AMERICAN Weight:7[redacted].[redacted] kg								
		SS3-DB	1 to 159	159	S: [redacted] R: INVASIVE CARCINOMA OF THE RIGHT BREAST S1: 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) P: 浸潤性乳癌 L: Invasive breast carcinoma	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: IDIOPATHIC A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	FU	151 to 564 +	5	155	S: [redacted] R: COVID-19 PNEUMONIA INFECTION S1: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 185 L: 31 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: VIRAL INFECTION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] TRT: ABT494 15 mg								
[redacted] Age:3[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg								
	SS3-DB	1 to	51	51	S: [redacted] R: LACERATION OF SCALP (TRAUMA) S1: 傷害、中毒および処置合併症 P: 皮膚裂傷 L: Scalp laceration	E: 75 L: 25 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CRANIAL CT EXAMINATION AND INJECTION OF TETANUS NEEDLE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: WHEN RIDING AN ELECTRIC CAR, THE FRONT CAR STOPS AND OPENS THE DOOR.BLOCKED BY A CAR DOOR, CAUSING THE CAR TO ROLL OVER AND LACERATE ITS HEAD A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:5[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
		SS3-DB	1 to 363	193	S: [redacted] R: ANAL FISTULA S1: 胃腸障害 P: 痔瘻 L: Anal fistula	E: 194 L: 2 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ULCERATIVE PANCOLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg									
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg									
		SS3-DB	1 to 359 +	3	3	S: [redacted] R: MASTITIS LEFT BREAST S1: 感染症および寄生虫症 P: 乳腺炎 L: Mastitis	E: 70 L: 68 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: BACTERIAL INFECTION WITH DIABETES A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
(Cont.)	SS3-DB	1 to 359 +	14	14	S: [redacted] R: ABSCESS LEFT BREAST S1: 感染症および寄生虫症 P: 乳房膿瘍 L: Breast abscess	E: 70 L: 57 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: INCISION AND DRAINAGE OF ABSCESS O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: MASTITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
		SS3-DB	1 to 448	317	S: [redacted] R: ACUTE RESPIRATORY FAILURE S1: 呼吸器、胸郭および縦隔障害 P: 急性呼吸不全 L: Acute respiratory failure	E: 336 L: 20 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COVID-19 INFECTION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:5[redacted] Sex:Female Race:WHITE Weight:4[redacted].[redacted] kg								
		SS3-DB	1 to 283	283	S: [redacted] R: SEVERE INFECTION: PNEUMOCOCCAL PNEUMONIA S1: 感染症および寄生虫症 P: 肺炎球菌性肺炎 L: Pneumococcal pneumonia	O: Yes	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/ S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]#	Age:5[redacted]	Sex:Female	Race:WHITE	Weight:4[redacted].[redacted] kg				
(Cont.)	SS3-DB	1 to 283	283	283	S: [redacted] R: HEPATITIS INDETERMINATE ETIOLOGY S1: 肝胆道系障害 P: 肝炎 L: Hepatitis	E: 292 L: 10 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: Yes/No/No/No/No/ S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:7[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
		SS3-DB	1 to 364	55	S: [redacted] R: POSTERIOR CIRCULATION STROKE S1: 神経系障害 P: 脳血管発作 L: Stroke	E: 78 L: 24 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED O: Concomitant medication or therapy started	AE: No/No/Yes/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization O: HISTORY OF ATRIAL FIBRILATION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:7[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
(Cont.)	SS3-DB	1 to 364	106	106 &	S: [redacted] R: RIGHT TEMPLE SKIN LESIONS - BASAL CELL CARINOMA S1: 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) P: 基底細胞癌 L: Basal cell carcinoma	E: 183 L: 78 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: EXCISION OF LESION DAY PROCEDURE ON	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: ? SUN EXPOSURE- FARMER A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:7[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
	(Cont.)	SS3-DB	1 to 364	182	S: [redacted] R: SEBORRHEIC KERATOSIS- LEFT SIDE OF NECK S1: 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) P: 脂漏性角化症 L: Seborrheic keratosis	E: 182 L: 1 Day	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: EXCISION OF LESION	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: OCCUPATION- SKIN EXPOSURE - FARMING BACKGROUND A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:7[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
(Cont.)	SS3-DB	1 to 364	334	334	S: [redacted] R: BASAL CELL CARCINOMA WITH SUPERFICIAL AND NODULAR GROWING PATTERN - RIGHT TEMPLE-SKIN S1: 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) P: 基底細胞癌 L: Basal cell carcinoma	E: 334 L: 1 Day	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: EXCISION OF LESION	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: OCCUPATION- SUN EXPOSURE-FARMING BACKGROUND A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: ABT494 15 mg									
[redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg									
	FU	119 to 149	1	119		S: [redacted] R: RETROPERITONEAL PANNICULITIS S1: 皮膚および皮下組織障害 P: 脂肪織炎 L: Panniculitis	O: Yes	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
(Cont.)	FU	119 to 149	2	120	S: [redacted] R: PYOGENIC ARTHRITIS OF THE KNEE S1: 感染症および寄生虫症 P: 細菌性関節炎 L: Pyogenic arthritis	O: Yes	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (DISCONTINUED STUDY, Other: DRAINAGE[RIGHT KNEE])	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg								
		SS3-DB	1 to	185 185	S: [redacted] R: WORSENING ANXIETY, WORSENING DEPRESSION S1: 精神障害 P: 不安 L: Anxiety aggravated	E: 216 L: 32 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: MULTIPLE (Concomitant medication or therapy started, CONCOMITANT MEDICATION OR THERAPY DISCONTINUED, Other: INPATIENT TREATMENT)	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: IMPROVEMENT IN UC S/S LEADING TO ABILITY TO FOCUS ON TREATMENT FOR HIS ANXIETY/DEPRESSION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	SS3-DB	1 to	185	185	S: [redacted] R: WORSENING ANXIETY, WORSENING DEPRESSION S1: 精神障害 P: うつ病 L: Depression worsened	E: 216 L: 32 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: MULTIPLE (Concomitant medication or therapy started, CONCOMITANT MEDICATION OR THERAPY DISCONTINUED, Other: INPATIENT TREATMENT)	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: IMPROVEMENT IN UC S/S LEADING TO ABILITY TO FOCUS ON TREATMENT FOR HIS ANXIETY/DEPRESSION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted] Age:7[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
		SS3-DB	1 to	107 107	S: [redacted] R: CATARACT S1: 眼障害 P: 白内障 L: Cataract	E: 119 L: 13 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CATARACT SURGERY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: AGE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: ABT494 30 mg								
[redacted] Age:5[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
		SS3-DB	1 to	256	256	S: [redacted] R: RIGHT PULMONARY NODULE S1: 呼吸器、胸郭および縦隔障害 P: 肺腫瘤 L: Lung nodule		S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ASTHMA A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch Interval	Rx Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] [redacted] TRT: ABT494 30 mg								
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
	SS3-DB	1 to	155	155	S: [redacted] R: CRYPTOCOCCAL PNEUMONIA S1: 感染症および寄生虫症 P: クリプトコッカス性肺炎 L: Pneumonia cryptococcal		S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted]# Age:4[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg								
		SS3-DB	1 to 83	72	S: [redacted] R: PNEUMONIA S1: 感染症および寄生虫症 P: 肺炎 L: Pneumonia	O: Yes I: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:7[redacted] Sex:Male Race:WHITE Weight:15[redacted].[redacted] kg								
		SS3-DB	1 to 355	42	S: [redacted] R: EXACERBATION OF COPD S1: 呼吸器、胸郭および縦隔障害 P: 慢性閉塞性肺疾患 L: COPD exacerbation	E: 45 L: 4 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CXR O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PT HAS A H/O EX SMOKER 30 PACK YEARS, OBESITY, COPD, OSA, HF, A.FIB, ASTHMA THAT CAN CONTRIBUTE TO WORSENING COPD A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted]# Age:5[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg								
	SS3-DB	1 to 318	32	32	S: [redacted] R: SUBARACHNOID HAEMORRHAGE S1: 神経系障害 P: くも膜下出血 L: Subarachnoid haemorrhage	E: 48 L: 17 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/Yes/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: IT WAS CONSIDERED THAT THERE WAS NO CAUSAL RELATIONSHIP TO THE INVESTIGATIONAL DRUG, AS IT WAS CONSIDERED THAT THE INCREASE IN TEMPERATURE AND EXCESSIVE DRINKING WERE THE CAUSES. A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted]# Age:3[redacted] Sex:Male Race:ASIAN Weight:5[redacted].[redacted] kg								
	FU	9 to 78	15	23	S: [redacted] R: ADENOCARCINOMA(SIGMOID COLON)STAGE 0 S1: 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) P: 結腸腺癌 L: Adenocarcinoma of the colon stage 0	O: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: THIS MALIGNANT LESION DEVELOPED ON ASSOCIATION WITH ULCERATIVE COLITIS. MALIGNANT LESIONS ARE NOT DIRECTLY ASSOCIATION WITH DRUGS. A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg									
[redacted] Age:2[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg									
	SS3-DB	1 to 366	30	30		S: [redacted] R: INFECTIOUS COLITIS S1: 感染症および寄生虫症 P: 大腸感染 L: Infectious colitis	E: 41 L: 12 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: INFECTION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg								
		SS3-DB	1 to 259	104	S: [redacted] R: URINARY RETENTION S1: 腎および尿路障害 P: 尿閉 L: Urinary retention	E: 105 L: 2 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/ S: Yes, hospitalization or prolonged hospitalization O: PASIENT HAD A URINARY CATHETER DURING SURGERY. WHEN THEY REMOVED THE CATHETER THE SUBJECT WERE NOT ABLE TO URINATE, AND SUBJECT HAD TO STAY THE NIGHT OVER IN THE HOSPITAL TILL SUBJECT URINATED. A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg								
	SS3-DB	1 to 355	52	52	S: [redacted] R: RIGHT SEPTIC OLECRANON BURITIS S1: 感染症および寄生虫症 P: 感染性滑液包炎 L: Septic bursitis	E: 86 L: 35 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: 10ML OF FLUID ASPIRATED FROM RIGHT OLECRANON BURSA, AEROBIC AND ANAEROBIC CULTURE . PER PROGRESS NOTE, GREW OUT RARE STAPH. PT IS BEING SENT TO WOUND CARE FOR DEBRIDEMENT AND DRESSINGS O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: ABT494 15 mg								
[redacted]# Age:2[redacted] Sex:Female Race:WHITE Weight:4[redacted].[redacted] kg								
	FU	226 to 253	28	253	S: [redacted] R: ELECTIVE ABORTION S1: 外科および内科処置 P: 人工流産 L: Elective abortion	E: 253 L: 1 Day	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: PATIENT DECISION FOR PREGNANCY TERMINATION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
		SS3-DB	1 to 141	93	93	S: [redacted] R: MODERATE ULCERATIVE COLITIS FLARE S1: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/ S: Yes, hospitalization or prolonged hospitalization O: DISEASE WORSENING. ULCERATIVE COLITIS FLARE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 m								
[redacted] Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg								
		SS3-DB	1 to 312	166	S: [redacted] R: PULMONARY EMBOLISM S1: 呼吸器、胸郭および縦隔障害 P: 肺塞栓症 L: Pulmonary embolism	E: 168 L: 3 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/ S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: ABT494 15 mg								
[redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
		SS3-DB	1 to 307	247	247	S: [redacted] R: INFECTIOUS MONONUCLEOSIS S1: 感染症および寄生虫症 P: 伝染性単核症 L: Infectious mononucleosis	E: 264 L: 18 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/ S: Yes, hospitalization or prolonged hospitalization O: VIRAL INFECTION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg								
	SS3-DB	1 to 45	38	38	S: [redacted] R: WORSENING OF ULCERATIVE COLITIS S1: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED, DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ULCERATIVE COLITIS FLARE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	Day	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg									
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg									
		SS3-DB	1 to 364	231	231	S: [redacted] R: WORSENING OF COVID-19 INFECTION S1: 感染症および寄生虫症 P: COVID-19 L: COVID-19	E: 232 L: 2 Days	S: MODERATE C: Yes R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: SARS-COV-2 VIRUS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: ABT494 30 mg									
[redacted]#	Age:3[redacted]	Sex:Male	Race:WHITE	Weight:9[redacted].[redacted]	kg				
		SS3-DB	1 to 109	109	109	S: [redacted] R: COVID-19 PNEUMONIA INFECTION S1: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 118 L: 10 Days	S: SEVERE C: Yes R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
		SS3-DB	1 to	160 160	S: [redacted] R: CHONDROMALACIA LEFT KNEE S1: 筋骨格系および結合組織障害 P: 軟骨軟化症 L: Chondromalacia	E: 160 L: 1 Day	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: ARTHROSCOPY; MANUALLY LYMPHATIC DRAINAGE. PHYSIOTHERAPY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: AGE RETATED WEARING A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted]# Age:3[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
		SS3-DB	1 to 99	81	81	S: [redacted] R: RELAPS OF ULCERATIVE COLITIS S1: 胃腸障害 P: 潰瘍性大腸炎 L: Ulcerative colitis relapse	O: Yes	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: RELAPS OF ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: ABT494 15 mg								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
		SS3-DB	1 to	206 206	S: [redacted] R: COVID-19 PNEUMONIA S1: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 216 L: 11 Days	S: MODERATE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COVID-19 A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted] Age:6[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg								
		SS3-DB	1 to 314	162	S: [redacted] R: HERPES ZOSTER 5TH CRANIAL NERVE DERMATONE S1: 感染症および寄生虫症 P: 帯状疱疹 L: Herpes zoster	E: 183 L: 22 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/ S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: ABT494 15 mg								
[redacted] Age:3[redacted] Sex:Male Race:ASIAN Weight:9[redacted].[redacted] kg								
		SS3-DB	1 to 358	14	S: [redacted] R: PULMONARY CONTUSION S1: 傷害、中毒および処置合併症 P: 肺挫傷 L: Pulmonary contusion	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: FALL FROM HIGH PLACE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg									
[redacted] Age:3[redacted] Sex:Male Race:ASIAN Weight:9[redacted].[redacted] kg									
(Cont.)	SS3-DB	1 to 358	14	14		S: [redacted] R: THORACIC VERTEBRAL FRACTURE (TH2-6) S1: 傷害、中毒および処置合併症 P: 胸椎骨折 L: Thoracic vertebral fracture T6	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: SURGERY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: FALL FROM HIGH PLACE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
		SS3-DB	1 to	236	236	S: [redacted] R: INFLAMMATORY BRONCHOPATHY S1: 呼吸器、胸郭および縦隔障害 P: 非感染性気管支炎 L: Noninfective bronchitis	O: Yes	S: MODERATE C: No R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: REFERRED TO PULMONOLOGIST O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted]	Age:4[redacted] Sex:Female Race:WHITE Weight:10[redacted].[redacted] kg							
		SS3-DB	1 to	34	S: [redacted] R: FOCAL CIN I - II IN CERVIX S1: 生殖系および乳房障害 P: 子宮頚部上皮異形成 L: Cervical intraepithelial neoplasia	E: 35 L: 2 Days	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED A: Other: STOPPED FOR 2 DAY O: LLETZ PROCEDURE PERFORMED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: HUMAN PAPILOMAVIRUS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted] Age:2[redacted] Sex:Female Race:BLACK OR AFRICAN AMERICAN Weight:7[redacted].[redacted] kg								
	SS3-DB	1 to 364	131	131	S: [redacted] R: ACUTE BRONCHITIS S1: 感染症および寄生虫症 P: 気管支炎 L: Acute bronchitis	E: 134 L: 4 Days I: Yes	S: MODERATE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
		SS3-DB	1 to 319	198	S: [redacted] R: HEPATOPATHY S1: 肝胆道系障害 P: 肝障害 L: Hepatopathy	E: 212 L: 15 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED	AE: Yes/No/No/No/No/ S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: ALCOHOL, CONMEDS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
	FU	198 to 204	7	204	S: [redacted] R: ELECTIVE ABORTION S1: 外科および内科処置 P: 人工流産 L: Elective abortion	E: 204 L: 1 Day	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: PREGNANCY. A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]	Age:5[redacted] Sex:Male Race:BLACK OR AFRICAN AMERICAN Weight:10[redacted].[redacted] kg							
		SS3-DB	1 to 369	268	S: [redacted] R: CLOSTRIDIUM DIFFICILE INFECTION S1: 感染症および寄生虫症 P: クロストリジウム・ディフィシレ感染 L: Clostridium difficile infection	E: 295 L: 28 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: C-DIFF EXPOSURE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	FU	3 to 176	29	31	S: [redacted] R: PULMONARY EMBOLISM S1: 呼吸器、胸郭および縦隔障害 P: 肺塞栓症 L: Pulmonary embolism	O: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/Yes/No/No/No/ S: Yes, life threatening, important medical or surgical intervention O: SEVERE UC A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg								
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
		SS3-DB	1 to 364	257	257	S: [redacted] R: HERPES ZOSTER S1: 感染症および寄生虫症 P: 帯状疱疹 L: Herpes zoster	E: 281 L: 25 Days	S: MODERATE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
		SS3-DB	1 to 33	23	S: [redacted] R: ULCERATIVE COLITIS WORSENING S1: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: WORSENING OF ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
		SS3-DB	1 to 224	14	S: [redacted] R: ARTHRITIS OF THE KNEE S1: 筋骨格系および結合組織障害 P: 関節炎 L: Knee arthritis	O: Yes I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/ S: Yes, important medical or surgical intervention, persistent or significant disability/incapacity O: WORSENING OF PRE- EXISTING ARTHRITIS. A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted] Age:4[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
		SS3-DB	1 to 365	104	S: [redacted] R: INFLUENZA TYPE A INFECTION S1: 感染症および寄生虫症 P: インフルエンザ L: Influenza A virus infection	E: 109 L: 6 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: INFLUENZA TYPE A INFECTION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 30 mg									
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg									
		SS3-DB	1 to 308	180	180	S: [redacted] R: CIN-1 S1: 生殖系および乳房障害 P: 子宮頚部上皮異形成 L: Cervical intraepithelial neoplasia I	E: 182 L: 3 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: LLETZ PROCEDURE O: Concomitant medication or therapy started	AE: No/No/No/No/No/ S: Yes, hospitalization or prolonged hospitalization O: HPV POSITIVE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: ABT494 30 mg								
[redacted]# Age:5[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
	SS3-DB	1 to 356	333	333	S: [redacted] R: PROSTATE CANCER,SMALL CELL CARCINOMA S1: 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) P: 小細胞癌 L: Small cell carcinoma	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: UNKNOWN A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1.5

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA UPA Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S1: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/ Cardiovascular AE?/ Cerebral AE$?/Renal AE?/ Herpes Zoster Infection AE?/ Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: ABT494 15 mg								
[redacted]# Age:2[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg								
	FU	199 to 239	4	202	S: [redacted] R: CRISSUM ABSCESS(AROUND THE ANUS) S1: 感染症および寄生虫症 P: 肛門膿瘍 L: Perianal abscess	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: IT IS ASSOCIATED WITH UC DISEASE ACTIVITY A: NO REASONABLE POSSIBILITY

SCREEN = Screening; SS1-DB = Sub-study 1 treatment; SS2-DB = Sub-study 2 treatment; SS2-OL = Sub-study 2 part 2 treatment;
675-DB = Blinded treatment; 675-OL = Open label treatment; SS3-DB = Sub-study 3 treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.
+ Subject is ongoing.
& Date is estimated.

Program Source Code: [redacted]

表 2.7.4.7-42.

[redacted]20[redacted] 16:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-675
R&D/21/0078 - CLINICAL/STATISTICAL

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD								
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
[redacted]	DB	1 to 58	47	47	S: [redacted] R: WORSENING COLITIS S: 胃腸障害 P: 大腸炎 L: Colitis aggravated	E: 55 L: 9 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: UNDERLYING DISEASE - ULCERATIVE COLITIS - AND POSSIBLY COLONOSCOPY PROCEDURE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD/UPA [redacted] g QD								
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
	DB	1 to 58	9	9	S: [redacted] R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 16 L: 8 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: ULCERATIVE COLITIS(DISEASE UNDER STUDY) A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT:								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
	DB	1 to 4	4	4	S: [redacted] R: ULCERATIVE COLITIS WORSENING S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, life threatening, hospitalization or prolonged hospitalization O: EXACERBATION OF DISEASE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD									
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg									
		DB	1 to 34	33	33	S: [redacted] R: WORSENING OF ULCECERATE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED, DRUG WITHDRAWN O: ADMITTED TO HOSPITAL WARD, IV CORTICOSTERIODS AND ANTIBIOTICS O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: Placebo/UPA 45 mg QD								
[redacted] Age:7[redacted] Sex:Male Race:WHITE Weight:15[redacted].[redacted] kg								
[redacted]	OL	57 to 113	21	77	S: [redacted] R: WORSENING COPD S: 呼吸器、胸郭および縦隔障害 P: 慢性閉塞性肺疾患 L: COPD exacerbation	E: 79 L: 3 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: CHRONIC OBSTRUCTIVE PULMONARY DISEASE A: NO REASONABLE POSSIBILITY E: MORE LIKELY RELATED TO HISTORY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD									
[redacted]	Age:5[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg								
		DB	1 to 58	19	19	S: [redacted] R: MALNUTRITION S: 代謝および栄養障害 P: 栄養障害 L: Malnutrition	E: 32 L: 14 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: NUTRITIONAL THERAPY IN HOSPITAL BECAUSE OF HIS ILLNESS,INTAKE WAS DECVEASED. A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day	Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD									
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:6[redacted].[redacted] kg									
		DB	1 to 56	33	33	S: [redacted] R: PYODERMA GANGRENOSUM S: 皮膚および皮下組織障害 P: 壊疽性膿皮症 L: Pyoderma gangrenosum	O: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: PYODERMA GANGRENOSUM IS A COMPLICATION OF THE UNDERLYING DISEASE AND HAS NO CAUSAL RELATIONSHIP TO THE STUDY DRUG. A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD								
[redacted] Age:4[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg								
	DB	1 to 57	45	45	S: [redacted] R: CHEST PAIN S:一般・全身障害および投与部位の状態 P: 胸痛 L: Chest pain	O: Yes I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: Possibly AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: HE OCCASIONALLY HAD CHEST PAIN BEFORE THE STUDY DRUG ADMINISTRATION AND WAS ADMITTED FOR SCRUTINY. A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day	Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo									
[redacted]# Age:5[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg									
		DB	1 to 11	8	8	S: [redacted] R: VENOUS THROMBOSIS IN LEFT COMMUNIS ILLICA S: 血管障害 P: 骨盤静脈血栓症 L: Iliac vein thrombosis	O: Yes	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: Yes AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] [redacted] TRT: Placebo								
[redacted]# Age:5[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	DB	1 to 11	8	8	S: [redacted] R: PERIPHERAL PULMONARY EMBOLISME S: 呼吸器、胸郭および縦隔障害 P: 肺塞栓症 L: Pulmonary embolism	O: Yes	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: Yes AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD								
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:15[redacted].[redacted] kg								
	DB	1 to 9	5	5	S: [redacted] R: UC WORSENING S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity O: ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day	Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD									
[redacted]	Age:1[redacted] Sex:Female Race:WHITE Weight:4[redacted].[redacted] kg								
		FU	115 to	1	115	S: [redacted] R: UC FLARE S: 胃腸障害 P: 潰瘍性大腸炎 L: UC aggravated	E: 126 L: 12 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: NO OTHER CAUSES, ONLY UC A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD								
[redacted]	Age:1[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg							
	DB	1 to 58	17	17	S: [redacted] R: ANEMIA EXACERBATION S: 血液およびリンパ系障害 P: 貧血 L: Anemia aggravated	O: Yes	S: MODERATE C: No R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: UPA 45 mg QD/UPA 45 mg QD								
[redacted]# Age:1[redacted] Sex:Male Race:WHITE Weight:4[redacted].[redacted] kg								
	OL	59 to 93	35	93	S: [redacted] R: UC FLARE S: 胃腸障害 P: 潰瘍性大腸炎 L: UC aggravated	O: Yes	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: ONLY UC A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: Placebo								
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg								
	FU	29 to	1	29	S: [redacted] R: SIGMOID COLON PERFORATION S: 胃腸障害 P: 大腸穿孔 L: Colon perforation	E: 87 L: 59 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, life threatening, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity O: ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo									
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg									
(Cont.)	FU	29 to	6	34		S: [redacted] R: COLOSTOMY NECROSIS S: 傷害、中毒および処置合併症 P: 消化管ストーマ壊死 L: Gastrointestinal stoma necrosis	E: 34 L: 1 Day	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention, persistent or significant disability/incapacity O: ULCERATIVE COLOTIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo								
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg								
(Cont.)	FU	29 to	22	50	S: [redacted] R: COLOSTOMY INFECTION OF ENTEROCOCCUS FAECIUM VRE S: 感染症および寄生虫症 P: 腸球菌感染 L: Vancomycin-resistant enterococcal infection	E: 72 L: 23 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity O: ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo								
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg								
(Cont.)	FU	29 to	22	50	S: [redacted] R: COLOSTOMY INFECTION OF ESCHERICHA COLI S: 感染症および寄生虫症 P: 大腸菌感染 L: Escherichia coli infection	E: 72 L: 23 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity O: ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo								
[redacted]# Age:3[redacted] Sex:Male Race:ASIAN Weight:5[redacted].[redacted] kg								
	DB	1 to 12	10	10	S: [redacted] R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 17 L: 8 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: WORSENING OF ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD/UPA 45 mg QD								
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
	DB	1 to 68	1	1	S: [redacted] R: FRACTURA CAPITULI METACARPI V.L.DX S: 傷害、中毒および処置合併症 P: 手骨折 L: Fractured metacarpal	E: 49 L: 49 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: REPOSITIO OSTHEOSYTHESIS INTRAMEDULLARIS O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: THE PATIENT HIT THE WALL WITH HIS RIGHT HAND A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD									
[redacted]	Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted] kg								
		DB	1 to 61	19	19	S: [redacted] R: COVID-19 PNEUMONIA S: 感染症および寄生虫症 P: COVID－19肺炎 L: COVID-19 pneumonia	E: 29 L: 11 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: BC, BIOCHEMICAL BLOOD TEST. HAVE ALREADY DONE, BUT THE RESULTS ARE UNKNOWN, CAUSE THE PATIENT IS STILL IN THE HOSPITAL. O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, life threatening, hospitalization or prolonged hospitalization O: COVID 19 IS THE CAUSE OF FEVER AND COUGHT A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: UPA 45 mg QD/UPA 45 mg QD								
[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
	DB	1 to 62	1	1	S: [redacted] R: WORSENING ANEMIA S: 血液およびリンパ系障害 P: 貧血 L: Anemia aggravated	E: 28 L: 28 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: MORE LIKELY RELATED TO SCREENING COLONOSCOPY A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD								
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
	OL	57 to 118	23	79	S: [redacted] R: BURNING SENSATION IN THE ABDOMEN S: 胃腸障害 P: 腹部不快感 L: Burning sensation in abdomen	E: 91 L: 13 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: NO DATA AVAILABLE TO DETERMINE THE CAUSE OF SYMPTOMS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD								
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
(Cont.)	OL	57 to 118	53	109	S: [redacted] R: ABDOMINAL PAIN IN THE RIGHT ILIAC REGION S: 胃腸障害 P: 下腹部痛 L: Abdominal pain lower	E: 114 L: 6 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: NO DATA AVAILABLE TO DETERMINE THE CAUSE OF SYMPTOMS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: UPA 45 mg QD									
[redacted]	Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
		DB	1 to 58	28	28	S: [redacted] R: DENGUE VIRUS S: 感染症および寄生虫症 P: デング熱 L: Dengue	E: 46 L: 19 Days	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CHEST TC O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: DENGUE INFECTION A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Name	Epoch Interval	Rx Day Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted])								
TRT: UPA 45 mg QD								
[redacted]	Age:2[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg							
	DB	1 to 55	4	4	S: [redacted] R: ACUTE PSYCHOTIC EPISODE S: 精神障害 P: 急性精神病 L: Acute psychosis	O: Yes I: Yes	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: POTENTIALLY DUE TO HORMONAL CONTRACEPTIVE PATCH A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: Placebo/UPA 45 mg QD								
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:5[redacted].[redacted] kg								
[redacted]	OL	64 to 155	54	117	S: [redacted] R: COVID-19 PNEUMONIA S: 感染症および寄生虫症 P: COVID－19肺炎 L: COVID-19 pneumonia	E: 131 L: 15 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: COVID-19 A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] [redacted] TRT: Placebo								
[redacted]# Age:4[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg								
	DB	1 to 6	4	4	S: [redacted] R: EXACERBATION OF UC S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 31 L: 28 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: UNDERLYING DISEASE A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 Population and SA2 Population)

Subject Number	Epoch Name	Epoch Interval	Rx Day	Rx Day of Onset	S: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE1: Hepatic AE? AE2: Cardiac AE? AE3: Cerebral AE$? AE4: Renal AE? AE5: Herpes Zoster Infection AE? AE6: Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] [redacted] TRT:								
[redacted]# Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
	FU	13 to	1	13	S: [redacted] R: WORSENING OF COLITIS ULCEROSA S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE1: No AE2: No AE3: No AE4: No AE5: No AE6: No S: Yes, hospitalization or prolonged hospitalization O: THE PATIENT FIRST CAME AS A WORSENING OF THE UNDERLYING DISEASE, BUT AFTER 3 DAYS SHE GOT HOSPITALISED BECAUSE OF THIS A: NO REASONABLE POSSIBILITY

SCREEN = Screening; DB = Blinded treatment; OL = Open label treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued.

Program Source Code: [redacted]

表 2.7.4.7-43.

[redacted]20[redacted] 14:12 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/0544 - CLINICAL/STATISTICAL

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD								
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
	C2-1 5DB	1 to	97 97		N: [redacted] R: CELLULITIS 5TH FINGER RIGHT HAND S: 感染症および寄生虫症 P: 蜂巣炎 L: Cellulitis of finger	E: 131 L: 35 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
	C1-15OL	1 to 779	779	N: [redacted] R: ACUTE GANGRENOUS CHOLECYSTITIS S: 感染症および寄生虫症 P: 感染性胆嚢炎 L: Gangrenous cholecystitis	E: 866 L: 88 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD								
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg								
	C2-3 0DB	1 to	99 99		N: [redacted] R: COVID-19 INFECTION S: 感染症および寄生虫症 P: COVID-19 L: COVID-19	E: 113 L: 15 Days	S: MODERATE C: Yes R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: SARS-COV-2 INFECTION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted])								
TRT: COHORT 2 - UPA 30 MG QD								
[redacted] Age:4[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg								
[redacted]	C2-3 0DB	1 to	228	228	N: [redacted] R: WORSENING OF COVID 2019 INFECTION S: 感染症および寄生虫症 P: COVID-19 L: COVID-19	E: 239 L: 12 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: PNEUMONIA REQUIRING OXYGEN SUPPORT O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COVID 19 INFECTION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Male Race:ASIAN Weight:5[redacted].[redacted] kg								
	C1-3 0OL	61 to 296	188	248 /188	N: [redacted] R: HERPES ZOSTER S: 感染症および寄生虫症 P: 帯状疱疹 L: Herpes zoster	O: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

Subject Number	Epoch Name	Interval	Day	Rx Day of Onset /Dose Escal-ation			
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg							
	C1-3 0OL	43 to 85	1	43 /1	N: [redacted] R: HYPOPHOSPHOREMIA S: 代謝および栄養障害 P: 低リン酸血症 L: Hypophosphatemia	E: 50 L: 8 Days I: Yes	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: RISK FACTORS INCLUDE PRE-EXISTING ULCERATIVE COLITIS AND RECENT TREATMENT WITH FERINJECT.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	C1-3 0OL	43 to 85	9	51 /9	N: [redacted] R: RECIDIVISM HYPOPHOSPHOREMIA S: 代謝および栄養障害 P: 低リン酸血症 L: Hypophosphatemia	O: Yes	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization E: RISK FACTORS INCLUDE PRE-EXISTING ULCERATIVE COLITIS AND RECENT TREATMENT WITH FERINJECT.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg								
	C1-15OL	1 to 1073	1004	1004	N: [redacted] R: HIGH GRADE DYSPLASIA S: 一般・全身障害および投与部位の状態 P: 異形成 L: Dysplasia	E: 1033 L: 30 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (DISCONTINUED STUDY, Other: ENDOSCOPIC SUBMUCOSAL DISSECTION)	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg								
	C1-15OL	1 to	132	132	N: [redacted] R: LEFT DISTAL TIBIOFIBULA FRACTURE S: 傷害、中毒および処置合併症 P: 腓骨骨折 L: Fibula fracture	E: 147 L: 16 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SURGERY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: FELL DOWN THE STAIRS. A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO TRAUMA WHEN THE SUBJECT FELL DOWN THE STAIRS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 132	132		N: [redacted] R: LEFT DISTAL TIBIOFIBULA FRACTURE S: 傷害、中毒および処置合併症 P: 脛骨骨折 L: Tibia fracture	E: 147 L: 16 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SURGERY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: FELL DOWN THE STAIRS. A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO TRAUMA WHEN THE SUBJECT FELL DOWN THE STAIRS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:7[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C1-15OL	1 to 870	715	N: [redacted] R: DEEP VEIN THROMBOSIS - RIGHT LEG, PULMONARY EMBOLISM S: 血管障害 P: 深部静脈血栓症 L: Deep vein thrombosis leg	O: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE: No/Yes/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:7[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 870	715	N: [redacted] R: DEEP VEIN THROMBOSIS - RIGHT LEG, PULMONARY EMBOLISM S: 呼吸器、胸郭および縦隔障害 P: 肺塞栓症 L: Pulmonary embolism	O: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE: No/Yes/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 1 D								
[redacted] Age:5[redacted] Sex:Female Race:MULTIPLE Weight:8[redacted].[redacted] kg								
	C2-1 5DB	1 to	177 177		N: [redacted] R: COVID 19 PNEUMONIA S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 191 L: 15 Days	S: SEVERE C: Yes R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]) TRT: COHORT 2 - UPA 30 MG QD							
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
	C2-3 0DB	1 to	134 134	N: [redacted] R: FIRST EPISODE OF DEPRESSION S: 精神障害 P: うつ病 L: Depression		S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: THIS WAS THE FIRST ADMISSION FOR LOW MOOD. PATIENT APPARENTLY SUFFERED MULTIPLE HEAD INJURIES PREVIOUSLY, AND HAD ANGER MANAGEMENT ISSUES A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD							
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C2-30DB	1 to 134	134	N: [redacted] R: FIRST EPISODE OF ANXIETY S: 精神障害 P: 不安 L: Anxiety		S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: THIS WAS THE FIRST ADMISSION FOR LOW MOOD. PATIENT APPARENTLY SUFFERED MULTIPLE HEAD INJURIES PREVIOUSLY, AND HAD ANGER MANAGEMENT ISSUES A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg							
	C1-15OL	1 to 89	89	N: [redacted] R: RIGHT SIDED RENAL STONES S: 腎および尿路障害 P: 腎結石症 L: Renal stone	E: 90 L: 2 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NEPHROLITHOTRIPSY O: Concomitant medication or therapy started	AE: No/No/No/Yes/No/No S: Yes, hospitalization or prolonged hospitalization O: MEDICAL HISTORY OF KIDNEY STONES A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PAST HISTORY OF NEPHROLITHIASIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 164	134 134	N: [redacted] R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 163 L: 30 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (Concomitant medication or therapy started, CONCOMITANT MEDICATION OR THERAPY DISCONTINUED, DISCONTINUED STUDY, Other: LAPAROSCOPIC TOTAL PROCTOCOLECTOMY ILEOSTOMY)	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 164	152	152	N: [redacted] R: POST-PROCEDURAL ILEUS S: 傷害、中毒および処置合併症 P: 術後イレウス L: Postoperative ileus	E: 160 L: 9 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NG TUBE PLACED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: EVENT PART OF UNDERLYING DISEASE A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO RECENT LAPROSCOPIC TOTAL PROCTOCOLECTOMY AND ILEOSTOMY.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 1105	27 /-1079	N: [redacted] R: RENAL COLIC S: 腎および尿路障害 P: 腎仙痛 L: Renal colic	E: 29 L: 3 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization O: NO CLEAR CAUSE OF EVENT A: NO REASONABLE POSSIBILITY E: NO PLAUSIBLE MECHANISM TO IMPLICATE STUDY DRUG.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 1105	91	91 /-1015	N: [redacted] R: PERIANAL FISSURE S: 胃腸障害 P: 裂肛 L: Anal fissure	E: 92 L: 2 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: SURGERY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COLITIS ULCEROSA A: NO REASONABLE POSSIBILITY E: EVENT MORE LIKELY A COMPLICATION OF UNDERLYING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD [redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 1105	286	286 /-820	N: [redacted] R: GASTROENTERITIS S: 感染症および寄生虫症 P: 胃腸炎 L: Gastroenteritis	E: 288 L: 3 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: VIRAL INFECTION A: NO REASONABLE POSSIBILITY E: EVENT IS COMMON IN THE GENERAL POPULATION. ADDITIONAL RISK FACTOR INCLUDES PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD [redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
(Cont.)	C1-30OL	1106 to [redacted]	153 1258 /153	N: [redacted] R: INFECTIOUS MONONUCLEOSIS S: 感染症および寄生虫症 P: 伝染性単核症 L: Infectious mononucleosis		S: MODERATE C: No R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V/N/R/S/P/L	E/O/L/I	S/C/R/A/O	AE
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted] Age:4[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-3 0OL	41 to 449	489 /449	N: [redacted] R: GASTRITIS WITH POSITIVE HELICOBACTER PYLORI S: 感染症および寄生虫症 P: ヘリコバクター性胃炎 L: Helicobacter pylori gastritis	E: 505 L: 17 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: NONE A: NO REASONABLE POSSIBILITY E: EVENT MORE LIKELY RELATED TO HELICOBACTER PYLORI WHICH IS PREVALENT IN THE GENERAL POPULATION.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 617	617	N: [redacted] R: PNEUMONIA S: 感染症および寄生虫症 P: 肺炎 L: Pneumonia	E: 621 L: 5 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
	C1-3 0OL	44 to	19	62 /19	N: [redacted] R: GASTROENTERITIS S: 感染症および寄生虫症 P: 胃腸炎 L: Gastroenteritis	E: 66 L: 5 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: EVENT LIKELY DUE TO DISEASE FLARE AND/OR ACUTE INFECTIOUS ETIOLOGY.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-3 0OL	46 to 816	861 /816		N: [redacted] R: COVID-19 PNEUMONIA INFECTION S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 913 L: 53 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: COVID-19 A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] [redacted] TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
(Cont.)	C1-30OL	46 to	833	878 /833	N: [redacted] R: CATHETER RELATED SEPSIS S: 感染症および寄生虫症 P: 医療機器関連敗血症 L: Catheter sepsis	E: 886 L: 9 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: COVID-19 INFECTION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: 15 MG QD/UPA 30 MG QD								
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
	C1-3 0OL	43 to 1075	681	723 /681	N: [redacted] R: DEEP VEIN THROMBOSIS OF THE LOWER RIGHT LIMB S: 血管障害 P: 深部静脈血栓症 L: Deep vein thrombosis leg	O: Yes	S: MODERATE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/Yes S: Yes, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: A 15 MG QD/UPA 30 MG QD								
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
(Cont.)	C1-30OL	43 to 1075	833	875 /833 &	N: [redacted] R: BASAL CELL CARCINOMA ON TOP OF HEAD S: 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) P: 基底細胞癌 L: Basal cell carcinoma	E: 1018 L: 144 Days	S: MODERATE C: No R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: SURGICAL PROCEDURE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
(Cont.)	C1-30OL	43 to 1075	1012 1054 /1012	N: [redacted] R: ADENOMACARCINOMA SIGMOID COLON S: 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) P: 結腸腺癌 L: Adenocarcinoma of sigmoid colon	O: Yes	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN A: Other: PI WILL NOTIFY THE SUBJECT AND PATIENT WILL BE TOLD TO STOP STUDY TREATMENT O: MULTIPLE (DISCONTINUED STUDY, Other: WILL BE REFERRED TO SURGEON FOR COLECTOMY)	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:BLACK OR AFRICAN AMERICAN Weight:6[redacted].[redacted] kg							
	C2-1 5DB	1 to 336	10 10	N: [redacted] R: COVID-19 PNEUMONIA INFECTION S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 34 L: 25 Days	S: MODERATE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COVID 19 RELATED SYMPTOMS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD [redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
[redacted]	C1-3 0OL	103 to 90	192 /90	N: [redacted] R: FLARE OF UC S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 202 L: 11 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: EVENT MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

Subject Number	Epoch Name	Interval	Rx Day of Onset /Dose Escal-ation	V / N / R / S / P / L	E / O / L / I	S / C / R / A / O	AE / S / O / A / E
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
(Cont.)	C1-30OL	103 to 204	102 /102	N: [redacted] R: UROSEPSIS WITH E.COLI S: 感染症および寄生虫症 P: 大腸菌性敗血症 L: Escherichia sepsis	E: 225 L: 22 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: BENIGN PROSTATE HYPERPLASIA AND HOSPITAL STAY DUE TO SAE A FEW DAYS AGO A: NO REASONABLE POSSIBILITY E: EVENT MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF RECURRENT UROGENITAL INFECTIONS, BENIGN PROSTATIC HYPERPLASIA AND DIABETES MELLITUS. RECENT HOSPITALIZATION IS AN ADDITIONAL RISK FACTOR.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
(Cont.)	C1-30OL	103 to 388	490 /388	N: [redacted] R: ACUTE PROSTATITIS S: 生殖系および乳房障害 P: 前立腺炎 L: Acute prostatitis	E: 494 L: 5 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
(Cont.)	C1-30OL	103 to 637	739 /637	N: [redacted] R: POST OP BLEEDING S: 傷害、中毒および処置合併症 P: 処置後出血 L: Postoperative bleeding	E: 743 L: 5 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PREVIOUS PLANED TUR PROSTATA OPERATION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
(Cont.)	C1-30OL	103 to 652	754 /652		N: [redacted] R: VESICAL BLADDER TAMPONADE AFTER TUR OPERATION S: 腎および尿路障害 P: 膀胱タンポナーデ L: Bladder tamponade	E: 761 L: 8 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: BLADDER IRRIGATION AND BIPOLARE COAGULATION	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COMPLICATION AFTER AN ELECTIVE PROSTATA TUR OPERATION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-3 0OL	32 to 18	49 /18	N: [redacted] R: INGUINAL HERNIA BOTH SIDES S: 胃腸障害 P: 鼠径ヘルニア L: Bilateral inguinal hernia	O: Yes	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: REFER TO CHECK UP IN VISCERAL SURGERY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: PREFERED HERNIOTOMY TO AVOID INCARCERATION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD							
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C2-3 0DB	1 to	329 329	N: [redacted] R: BURSITIS RIGHT ELBOW S: 筋骨格系および結合組織障害 P: 滑液包炎 L: Elbow bursitis	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PT LIFTS WEIGHTS AND HAS HAD PREVIOUS TENNIS ELBOW A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 243	243	N: [redacted] R: WORSENING OF COLITIS ULCEROSA S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 246 L: 4 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: SUSPECTED FLARE OF STUDY DISEASE OR DUE TO INFECTION, FURTHER INVESTIGATIONS HAVE TO BE DONE A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO FLARE OF PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 864	864	N: [redacted] R: CHEST PAIN S: 一般・全身障害および投与部位の状態 P: 胸痛 L: Chest pain	E: 1211 & L: 348 Days I: Yes	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/Possibly S: Yes, hospitalization or prolonged hospitalization O: CHEST PAIN WITH MUSCULAR SKELETAL ORIGIN A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 1028	1028	N: [redacted] R: PARTIAL TENDON RUPTURE RIGHT SHOULDER S: 傷害、中毒および処置合併症 P: 腱断裂 L: Tendon rupture	O: Yes I: Yes	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: RUPTURE OF THE SHOULDER A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 877	610 610	N: [redacted] R: PNEUMONIA S: 感染症および寄生虫症 P: 肺炎 L: Pneumonia	E: 671 L: 62 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted] TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg							
[redacted]	C1-3 0OL	345 to 590	934 /590	N: [redacted] R: SINUS PILONIDALIS ABSCESS S: 感染症および寄生虫症 P: 毛巣嚢胞 L: Pilonidal abscess	E: 936 L: 3 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SURGICAL INTERVENTION	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: HOSPITALIZATION DUE TO SURGICAL INTERVENTION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-3 0OL	76 to 148	25	100 /25	N: [redacted] R: RHABDOMYOLYSIS S: 筋骨格系および結合組織障害 P: 横紋筋融解症 L: Rhabdomyolysis	E: 113 L: 14 Days I: Yes	S: MODERATE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ACUTE RHABDOMYOLYSIS NONTRAUMATIC A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

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INV: [redacted] TRT: COHORT 1 - UPA 15 PA 30 MG QD								
[redacted] Age:6[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg								
	C1-3 0OL	99 to #	73	171 /73	N: [redacted] R: WORSENING SYMPTOMS OF CARPAL TUNNEL SYNDROME S: 神経系障害 P: 手根管症候群 L: Carpal tunnel syndrome	E: 172 L: 2 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ENTEROPATHIC ARTHRITIS SECONDARY TO UC A: NO REASONABLE POSSIBILITY E: RISK FACTORS INCLUDE FEMALE GENDER AND PRE-EXISTING DIABETES MELLITUS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: MG QD/UPA 30 MG QD								
[redacted] Age:6[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg								
(Cont.)	C1-30OL	99 to 119	217 /119		N: [redacted] R: CERVICAL SPONDYLOSIS S: 筋骨格系および結合組織障害 P: 変形性脊椎症 L: Cervical spondylosis	E: 221 L: 5 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: OLD AGE, UNDERLYING RHEUMATOID ARTHRITIS A: NO REASONABLE POSSIBILITY E: RISK FACTOR INCLUDES SUBJECT'S AGE. ADDITIONALLY PER PI SUBJECT HAS UNDERLYING RHUEMATOID ARTHIRTIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:6[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg								
(Cont.)	C1-30OL	99 to	311	409 /311	N: [redacted] R: ACUTE GASTROENTERITIS S: 感染症および寄生虫症 P: 胃腸炎 L: Acute gastroenteritis	E: 418 L: 10 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: MOST PROBABLY CAUSED BY FOOD POISONING FOLLOWING A CHRISTMAS PARTY A: NO REASONABLE POSSIBILITY E: EVENT IS COMMON IN THE GENERAL POPULATION.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
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Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
	C1-15OL	1 to 226	226	N: [redacted] R: INTESTINAL INFECTION S: 感染症および寄生虫症 P: 消化管感染 L: GI infection	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: URGENT EVALUATION O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: FREE FLUID IN EDEMATOUS INTESTINAL WALL, WITHOUT EVIDENCE OF PERFORATION OR SIGNS OF INTESTINAL OBSTRUCTION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
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# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

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INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-15OL	1 to	264	264	N: [redacted] R: BRONCHITIS, SORE THROAT S: 感染症および寄生虫症 P: 気管支炎 L: Bronchitis	E: 277 L: 14 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: NONE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 264	264	N: [redacted] R: BRONCHITIS, SORE THROAT S: 呼吸器、胸郭および縦隔障害 P: 口腔咽頭痛 L: Sore throat	E: 277 L: 14 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: NONE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 439	439	N: [redacted] R: DYSARTRIA S: 神経系障害 P: 構語障害 L: Dysarthria	E: 449 L: 11 Days I: Yes	S: MILD R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 671	671	N: [redacted] R: OCCLUSIO INTESTINI S: 胃腸障害 P: 腸閉塞 L: Intestinal obstruction	E: 672 L: 2 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NASO-GASTRIC TUBE PLACEMENT	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
	C1-15OL	1 to 325	325	N: [redacted] R: ILEUS OF SMALL INTESTINE S: 胃腸障害 P: イレウス L: Ileus of intestine	E: 329 L: 5 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CONSERVATIVE NASOGASTRIC THERAPHY USING NASOGASTRIC TUBE FOR DECOMPRESION	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: CAUSE IS UNKNOWN AT THE MOMENT A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - PLACEBO								
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
	C2-PBO	1 to	138	138	N: [redacted] R: ACUTE GASTROENTERITIS S: 感染症および寄生虫症 P: 胃腸炎 L: Acute gastroenteritis	E: 144 L: 7 Days	S: MODERATE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA[redacted]G QD/UPA 30 MG QD [redacted]Age:3[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
	C1-15OL	1 to 324	320	320 /-5	N: [redacted] R: WORSENING OF LEFT SIDED ULCERATIVE COLITIS WITHOUT COMPLICATION S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated		S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: WORSENING OF DISEASE A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:6[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C1-15OL	1 to 466	423	423	N: [redacted] R: PROCEDURAL UTERINE PERFORATION S: 傷害、中毒および処置合併症 P: 子宮穿孔 L: Uterine perforation	E: 425 L: 3 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: PT HAD A SCHEDULED DILATION AND CURETTAGE PROCEDURE TO REMOVE AN ENDOMETRIAL POLYP ON [redacted]WHICH RESULTED IN AN UTERINE PERFORATION. A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY A COMPLICATION OF DILATION AND CURETTAGE PROCEDURE, AS REPORTED BY THE INVESTIGATOR.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] [redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:6[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 466	423 423	N: [redacted] R: PROCEDURAL SMALL BOWEL PERFORATION S: 傷害、中毒および処置合併症 P: 処置による腸管穿孔 L: Procedural intestinal perforation	E: 425 L: 3 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (Concomitant medication or therapy started, DISCONTINUED STUDY, Other: SURGERY)	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: PT HAD A SCHEDULED DILATION AND CURETTAGE PROCEDURE TO REMOVE AN ENDOMETRIAL POLYP ON [redacted] WHICH RESULTED IN A BOWEL PERFORATION A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY A COMPLICATION OF DILATION AND CURETTAGE PROCEDURE, AS REPORTED BY THE INVESTIGATOR.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] TRT: COHORT 2 - UPA 15							
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
	C2-1 5DB	1 to 120	120	N: [redacted] R: WORSENING OF UTERINE FIBROIDS S: 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) P: 子宮平滑筋腫 L: Uterine fibroids aggravated	E: 674 L: 555 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: UTERINE FIBROIDS ARE PART OF MEDICAL HISTORY FOR THIS SUBJECT A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD							
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:10[redacted].[redacted] kg							
	C2-3 0DB	1 to	406 406	N: [redacted] R: COVID 19 PNEUMONIA S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia		S: MODERATE C: Yes R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: NONE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-15OL	1 to 256	256	256	N: [redacted] R: UNSTABLE ANGINA S: 心臓障害 P: 不安定狭心症 L: Unstable angina	E: 261 L: 6 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: MULTIPLE (Concomitant medication or therapy started, CONCOMITANT MEDICATION OR THERAPY DISCONTINUED, Other: PERCUTANEOUS INTERVENTIONS)	AE: No/Yes/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization O: UNDERLYING CORONARY ARTERY DISEASE A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD								
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	C2-1 5DB	1 to 722	596	596	N: [redacted] R: PROSTATE CANCER S: 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) P: 前立腺癌 L: Prostate cancer	O: Yes I: Yes	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (DISCONTINUED STUDY, Other: ACTIVE SURVEILLANCE. NEXT PSA CHECK ON [redacted] 20[redacted])	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: FAMILY HISTORY – BROTHER ALSO HAD RADICAL PROSTATECTOMY A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 40	40	N: [redacted] R: CLOSED LEFT RIB FRACTURE S: 傷害、中毒および処置合併症 P: 肋骨骨折 L: Rib fracture		S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PATIENT FELL OFF OF A LADDER A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO ACCIDENTAL TRAUMA.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] [redacted] TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 428	428		N: [redacted] R: SUICIDAL ATTEMPT SECONDARY TO CHRONIC PAIN S: 一般・全身障害および投与部位の状態 P: 疼痛 L: Chronic pain	E: 434 L: 7 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: SUICIDAL ATTEMPT SECONDARY TO CHRONIC PAIN A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 428	428		N: [redacted] R: SUICIDAL ATTEMPT SECONDARY TO CHRONIC PAIN S: 精神障害 P: 自殺企図 L: Suicide attempt	E: 434 L: 7 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: SUICIDAL ATTEMPT SECONDARY TO CHRONIC PAIN A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:3[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted].[redacted] kg								
	C1-15OL	1 to 770	111	111 /-660	N: [redacted] R: EXACERBATION OF ASTHMA S: 呼吸器、胸郭および縦隔障害 P: 喘息 L: Exacerbation of asthma	E: 120 L: 10 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: BRONCHOSCOPY AND BRONCHIAL LAVAGE CT CHEST O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: PRE -EXISTING CONDITION A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF ASTHMA.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:3[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 770	371	371 /-400	N: [redacted] R: PNEUMONIA (VIRAL) S: 感染症および寄生虫症 P: ウイルス性肺炎 L: Viral pneumonia	E: 377 L: 7 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CXR AND LOCAL BLOOD TESTS O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: MEDICAL HISTORY A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UP MG QD [redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C1-15OL	1 to 341	341	N: [redacted] R: PNEUMONIA S: 感染症および寄生虫症 P: 肺炎 L: Pneumonia	E: 350 L: 10 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: INFLUENZA A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: PA 15 MG QD/UPA 30 MG QD							
[redacted] Age:3[redacted] Sex:Female Race:MULTIPLE Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 18	12 12 /-7	N: [redacted] R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: DISEASE UNDER STUDY A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted] Age:6[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
	C1-3 0OL	863 to 138	1000 /138	N: [redacted] R: COVID-19 PNEUMONIA S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 1006 L: 7 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COVID-19 A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-3 0OL	71 to 204	44 /114	N: [redacted] R: REFLEX SYNCOPE S: 神経系障害 P: 失神 L: Syncope vasovagal	E: 115 L: 2 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: SUBJECT HAS A SERIOUS UC AND WERE VERY DEHYDRATED AND THAT WAS THE REASON FOR THE PASIENT FAINTED.SUBJECT WAS IN HOSPITAL FOR OBSERVATION ONE DAY, AND HE GOT FLUID THERE. A: NO REASONABLE POSSIBILITY E: DEVELOPMENT OF THE EVENT IS NOT CONSISTENT WITH STUDY DRUG'S MECHANISM OF ACTION. ADDITIONAL RISK FACTORS INCLUDE SUBJECT'S AGE AND PRE-EXISTING UC.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-15OL	1 to [redacted]	467	467	N: [redacted] R: COVID 19 S: 感染症および寄生虫症 P: COVID-19 L: COVID-19	E: 551 & L: 85 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COV 19 A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD							
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
[redacted]	C2-3 0DB	1 to	518 518	N: [redacted] R: ACUTE APPENDICITIS S: 感染症および寄生虫症 P: 虫垂炎 L: Acute appendicitis	E: 521 L: 4 Days	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: APPENDECTOMY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: UNKNOWN AT THE MOMENT A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD								
[redacted] Age:1[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg								
	C2-3 0DB	1 to	205	205 &	N: [redacted] R: PERIANAL ABSCESS S: 感染症および寄生虫症 P: 肛門膿瘍 L: Perianal abscess		S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: CAUSE OF EVENT IS PATEINT ULCERATIVE COLITIES, AND THERE ARE NO KNOWN RISK FACTORS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD								
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg								
	C2-3 0DB	1 to 231	184	184	N: [redacted] R: SQUAMOUS CELL CARCINOMA OF CERVIX OF UTERI S: 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) P: 子宮頚部扁平上皮癌 L: Squamous cell carcinoma of the cervix	O: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (DISCONTINUED STUDY, Other: REFERRED TO SURGICAL THERAPY)	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: PROGRESSION FROM POSSIBLE DYSPLASIA A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
	C1-3 0OL	115 to 192	10	124 /10	N: [redacted] R: INFLAMMATION OF THE CERVIX DUE TO AN IUD S: 生殖系および乳房障害 P: 子宮頚部の炎症 L: Cervix inflammation	E: 151 L: 28 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: INFLAMMATION OF INTRAUTERINE DEVICE A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 2 - UPA 15 MG QD								
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	C2-1 5DB	1 to	24 24		N: [redacted] R: RAMSAY HUNT SYNDROME S: 感染症および寄生虫症 P: 耳帯状疱疹 L: Ramsay-Hunt syndrome		S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:6[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C1-15OL	1 to 30	18 18	N: [redacted] R: ACUTE VENOUS THROMBOSIS S: 血管障害 P: 静脈血栓症 L: Venous thrombosis	E: 21 L: 4 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/Yes S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]# Age:4[redacted] Sex:Male Race:ASIAN Weight:5[redacted].[redacted] kg							
	C1-3 0OL	46 to 977	476 521 /476	N: [redacted] R: DETERIORATION OF CALCULUS URETERIC S: 腎および尿路障害 P: 尿管結石症 L: Calculus ureteric	E: 536 L: 16 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: THE PATIENT WAS FOUND TO HAVE ASYMPTOMATIC CALCULUS BEFORE THE STUDY TREATMENT. A: NO REASONABLE POSSIBILITY E: THE INVESTIGATOR REPORTS ASYMPTOMATIC CALCULUS WAS PRESENT BEFORE THE STUDY TREATMENT. PRE-EXISTING ULCERATIVE COLITIS IS AN ADDITIONAL RISK FACTOR.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:4[redacted] Sex:Male Race:ASIAN Weight:5[redacted].[redacted] kg								
(Cont.)	C1-3 0OL	46 to 977	876	921 /876	N: [redacted] R: AVASCULAR NECROSIS FEMORAL HEAD S: 筋骨格系および結合組織障害 P: 骨壊死 L: Avascular necrosis femoral head	E: 977 L: 57 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: JOINT REPLACEMENT O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: DUE TO LONG TERM USE OF STEROIDS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]# Age:4[redacted] Sex:Male Race:ASIAN Weight:5[redacted].[redacted] kg							
(Cont.)	C1-3 0OL	46 to 977	876 /876	N: [redacted] R: WORSENING OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 967 L: 47 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED, DRUG WITHDRAWN O: MULTIPLE (DISCONTINUED STUDY, Other: TOTAL PROCTOCOLECTOMY)	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: DUE TO LONG-TERM USE OF STEROIDS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD							
[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C2-3 0DB	1 to	108 108	N: [redacted] R: PNEUMONIA BY COVID-19 INFECTION S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia		S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COVID-19 INFECTION (WORSENING OF SYMPTOMS) A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted])							
TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]#	Age:3[redacted]	Sex:Male	Race:WHITE	Weight:9[redacted].[redacted] kg			
	C1-3 0OL	169 to 243	34	202 /34	N: [redacted] R: WORSENING OF UC S: 胃腸障害 P: 潰瘍性大腸炎 L: UC aggravated	O: Yes	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: HOSPITALIZATION	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ULCERATIVE COLITIS WORSENING A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA QD								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
	C1-15OL	1 to	79	79	N: [redacted] R: ATRIAL FIBRILLATION S: 心臓障害 P: 心房細動 L: Atrial fibrillation		S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: STRESS AND EXERTION WAS MOVING INTO A NEW HOME A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 2 - PLACEBO							
[redacted] Age:5[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg							
	C2-PBO	1 to 97	97	N: [redacted] R: WORSENING OF HERPES ZOSTER S: 感染症および寄生虫症 P: 帯状疱疹 L: Herpes zoster	E: 169 L: 73 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V / N / R / S / P / L	E / L / I	S / C / R / A / O	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? / S: Serious AE? / O: Other Cause of Event / A: AbbVie Opinion of Causality / E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted] Age:4[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 1006	415 /-592	N: [redacted] R: REFLUX ESOPHAGITIS S: 胃腸障害 P: 胃食道逆流性疾患 L: Reflux esophagitis		S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: REFLUX ESOPHAGITIS WAS OCCUERED BY DIETARY DISORDER AND ESOPHAGEAL HERNIA.THUS,IT WAS CONSIDERED TO HAVE NO RELATIONSHIP WITH THE INVESTIGATIONAL AGENT. A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C1-15OL	1 to 78	30 30	N: [redacted] R: UC EXACBERATION S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 34 L: 5 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: HOSPITALIZATION O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: NO A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 1 QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 78	38	38	N: [redacted] R: UC EXACBERATION S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 63 L: 26 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: UC EXACBERATION A: NO REASONABLE POSSIBILITY E: RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

Subject Number	Epoch Name	Interval	Rx Day of Onset /Dose Escal-ation			
INV: [redacted] ([redacted])						
TRT: COHORT 2 - UPA 30 MG QD						
[redacted]# Age:7[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg						
	C2-3 0DB	1 to 434	403	403	N: [redacted] R: PANCREATIC ADENOCARCINOMA S: 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) P: 膵腺癌 L: Pancreatic adenocarcinoma	E: 434 L: 32 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (Concomitant medication or therapy started, DISCONTINUED STUDY, Other: HOSPITALIZED FOR FURTHER TESTING)	AE: No/No/No/No/No/No S: Yes, death of subject, hospitalization or prolonged hospitalization O: AGE RELATED CANCER A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD							
[redacted] Age:4[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C2-1 5DB	1 to 708	708	N: [redacted] R: COVID-19 PNEUMONIA S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 719 L: 12 Days	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: PT OBTAINING CHEST X-RAY AND APPT WITH INFECTIOUS DISEASE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: COVID-19 INFECTION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 2 - UPA 30 MG QD								
[redacted]# Age:4[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg								
	C2-3 0DB	1 to 335	154	154	N: [redacted] R: HERPES ZOSTER S: 感染症および寄生虫症 P: 帯状疱疹 L: Herpes zoster	E: 202 L: 49 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:3[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 160	83	83	N: [redacted] R: ORCHITIS S: 感染症および寄生虫症 P: 精巣炎 L: Orchitis	O: Yes	S: MILD R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: BACTERIAL INFECTION A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] [redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg							
	C1-15OL	1 to 474	474	N: [redacted] R: DEPRESSION S: 精神障害 P: うつ病 L: Depression		S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: MEDICAL HISTORY A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING DEPRESSION.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
	C1-15OL	1 to 323	323	N: [redacted] R: MYOCARDIAL INFARCTION S: 心臓障害 P: 心筋梗塞 L: Myocardial infarction	E: 326 L: 4 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CV STENT X 3 O: Concomitant medication or therapy started	AE: No/Yes/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PT HAS A H/O HTN, A. FIB, EX SMOKER X 30 YEARS, HIGH CHOLESTEROL A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD [redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
	C1-3 0OL	336 to 433	768 /433	N: [redacted] R: BACTERIAL PNEUMONIAE S: 感染症および寄生虫症 P: 細菌性肺炎 L: Pneumonia bacterial	E: 782 L: 15 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PI DETERMINED NOT DRUG RELATED. CAUSE IS BACTERIAL PER PI ASSESSMENT A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD [redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
(Cont.)	C1-30OL	336 to 550	885 /550	N: [redacted] R: SEVERE GASTROENTERITIS S: 感染症および寄生虫症 P: 胃腸炎 L: Gastroenteritis	E: 916 L: 32 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: ADMITTED TO HOSPITAL X2 DAYS NO MEDICATIONS GIVEN	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: SUBJECT WAS AROUND SICK FAMILY MEMBER A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

Subject Number	Epoch Name	Interval	Day	Rx Day of Onset /Dose Escal-ation			
INV: [redacted] ([redacted])							
TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:11[redacted].[redacted] kg							
	C1-3 0OL	70 to 387	273	342 /273	N: [redacted] R: SEPSIS, E. COLI S: 感染症および寄生虫症 P: 大腸菌感染 L: Escherichia coli infection	E: 350 L: 9 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: EXACT CAUSE OF INFECTION IS UNKNOWN. THERE ARE MULTIPLE WAYS THE SUBJECT COULD HAVE GOTTEN E. COLI A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:11[redacted].[redacted] kg								
(Cont.)	C1-30L	70 to 387	273	342 /273	N: [redacted] R: SEPSIS, E. COLI S: 感染症および寄生虫症 P: 敗血症 L: Sepsis	E: 350 L: 9 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY DISCONTINUED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: EXACT CAUSE OF INFECTION IS UNKNOWN. THERE ARE MULTIPLE WAYS THE SUBJECT COULD HAVE GOTTEN E. COLI A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA QD							
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:12[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 513	513	N: [redacted] R: RIGHT SHOULDER IMPINGEMENT SYNDROME DIAGNOSED ON [redacted]20[redacted] S: 筋骨格系および結合組織障害 P: 肩回旋筋腱板症候群 L: Impingement syndrome shoulder		S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SURGERY WITH FOLLOW UP PHYSICAL THERAPY X12 WEEKS O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: UNKNOWN A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-3 0OL	29 to 332	262	290 /262	N: [redacted] R: LEFT TESTICULAR SEMINOMA S: 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) P: 精巣（純粋）セミノーマ L: Testicular seminoma (pure)	E: 290 L: 1 Day	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: HISTORY OF BENIGN TESTICULAR LUMP A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
	C1-15OL	1 to 45	14	14 /-32	N: [redacted] R: GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE S: 胃腸障害 P: 下痢 L: Diarrhoea	E: 15 L: 2 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: MRI O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: EVENT LIKELY REPRESENTS WORSENING UC AND DISEASE FLARE

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 45	14	14 /-32	N: [redacted] R: GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE S: 一般・全身障害および投与部位の状態 P: 疲労 L: Fatigue	E: 15 L: 2 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: MRI O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: EVENT LIKELY REPRESENTS WORSENING UC AND DISEASE FLARE

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 45	14	14 /-32	N: [redacted] R: GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE S: 一般・全身障害および投与部位の状態 P: 倦怠感 L: Malaise	E: 15 L: 2 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: MRI O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: EVENT LIKELY REPRESENTS WORSENING UC AND DISEASE FLARE

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 45	14	14 /-32	N: [redacted] R: GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE S: 胃腸障害 P: 嘔吐 L: Vomiting	E: 15 L: 2 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: MRI O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: EVENT LIKELY REPRESENTS WORSENING UC AND DISEASE FLARE

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	C1-3 0OL	46 to 78	1	46 /1	N: [redacted] R: SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA S: 神経系障害 P: 健忘 L: Amnesia	E: 47 L: 2 Days I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PNES A: NO REASONABLE POSSIBILITY E: EVENT LIKELY RELATED TO SLEEP DEPRIVATION; SUBJECT HAS PRIOR HISTORY OF SEIZURE DUE TO SLEEP DEPRIVATION.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	C1-3 0OL	46 to 78	1	46 /1	N: [redacted] R: SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA S: 神経系障害 P: 頭痛 L: Headache	E: 47 L: 2 Days I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PNES A: NO REASONABLE POSSIBILITY E: EVENT LIKELY RELATED TO SLEEP DEPRIVATION; SUBJECT HAS PRIOR HISTORY OF SEIZURE DUE TO SLEEP DEPRIVATION.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg								
(Cont.)	C1-30L	46 to 78	1	46 /1	N: [redacted] R: SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA S: 胃腸障害 P: 悪心 L: Nausea	E: 47 L: 2 Days I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PNES A: NO REASONABLE POSSIBILITY E: EVENT LIKELY RELATED TO SLEEP DEPRIVATION; SUBJECT HAS PRIOR HISTORY OF SEIZURE DUE TO SLEEP DEPRIVATION.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
E: Rx Day Ended
S: Severity
AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	O: Ongoing at the End of Study? L: Length I: Interm-ittent?	C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg							
(Cont.)	C1-30OL	46 to 78	1	46 /1	N: [redacted] R: SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA S: 神経系障害 P: 発作様現象 L: Seizure like phenomena	E: 47 L: 2 Days I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PNES A: NO REASONABLE POSSIBILITY E: EVENT LIKELY RELATED TO SLEEP DEPRIVATION; SUBJECT HAS PRIOR HISTORY OF SEIZURE DUE TO SLEEP DEPRIVATION.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg							
(Cont.)	C1-3 0OL	46 to 78	11 56 /11	N: [redacted] R: ONGOING UC, NO IMPROVEMENT FROM TREATMENT S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 70 L: 15 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: Other: THIS WAS DURING 30-DAY FU O: SURGERY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: ONGOING UC A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted])								
TRT: [redacted] M UPA 30 MG QD								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg								
	C1-3 0OL	106 to 264	27	132 /27	N: [redacted] R: C-DIFFICILE INFECTION S: 感染症および寄生虫症 P: クロストリジウム・ディフィシレ感染 L: Clostridium difficile infection	E: 142 L: 11 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: NONE	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO RECURRENCE OF PRE-EXISTING CLOSTRIDIUM DIFFICILE INFECTION. ULCERATIVE COLITIS IS AN ADDITIONAL RISK FACTOR.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset /Dose Escal-ation	
INV: [redacted] ([redacted])						
TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD						
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg						
(Cont.)	C1-3 0OL	106 to 264	36	141	/36	N: [redacted] R: L FOOT PAIN S: 筋骨格系および結合組織障害 P: 四肢痛 L: Foot pain E: 145 L: 5 Days I: Yes S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PARTICIPANT HOSPITALIZED ON [redacted] FOR SEVERE FOOT PAIN RELATING TO ARTHRALGIA FROM ULCERATIVE COLITIS A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING OSTEOARTHRITIS AND ANKLE PAIN.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-15OL	1 to 216	104	104 /-113	N: [redacted] R: COVID-19 PNEUMONIA INFECTION S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 140 L: 37 Days I: Yes	S: MODERATE C: Yes R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: PATIENT WAS HOSPITALIZED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg								
	C1-15OL	1 to	337 337		N: [redacted] R: COLONIC POLYP S: 胃腸障害 P: 大腸ポリープ L: Colonic polyp	E: 450 L: 114 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: COLONIC POLYPECTOMY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: SPORADIC LESION A: NO REASONABLE POSSIBILITY E: RISK FACTORS INCLUDE MALE GENDER, AGE AND PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Name	Epoch	Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD									
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg									
(Cont.)	C1-15OL	1 to	589	589		N: [redacted] R: CALCULOUS PYELONEPHRITIS S: 腎および尿路障害 P: 腎結石症 L: Nephrolithiasis	E: 596 L: 8 Days I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/Yes/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: NEPHROLITHIASIS A: NO REASONABLE POSSIBILITY E: EVENT MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF NEPHROLITHIASIS. ADDITIONAL RISK FACTOR IS PRE-EXISTING HYPERURICEMIA.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	589	589	N: [redacted] R: CALCULOUS PYELONEPHRITIS S: 感染症および寄生虫症 P: 腎盂腎炎 L: Pyelonephritis	E: 596 L: 8 Days I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/Yes/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: NEPHROLITHIASIS A: NO REASONABLE POSSIBILITY E: EVENT MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF NEPHROLITHIASIS. ADDITIONAL RISK FACTOR IS PRE-EXISTING HYPERURICEMIA.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	631	631	N: [redacted] R: WORSENING OF NEPHROLITHIASIS(RIGHT) S: 腎および尿路障害 P: 腎結石症 L: Nephrolithiasis	E: 633 L: 3 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/Yes/No/No S: Yes, hospitalization or prolonged hospitalization O: TREATMENT FOR ADVERSE EVENT "WORSENING OF NEPHROLITHIASIS(RIGHT)". A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF NEPHROLITHIASIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	1199 1199		N: [redacted] R: COLON POLYP S: 胃腸障害 P: 大腸ポリープ L: Colonic polyp	E: 1199 L: 1 Day	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: ENDOSCOPIC MUCOUSAL RESECTION	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: NONE A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:4[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 1346	1346	N: [redacted] R: COLON POLYP S: 胃腸障害 P: 大腸ポリープ L: Colonic polyp	E: 1346 L: 1 Day	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: ENDOSCOPIC MUCOUSAL RESECTION	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: NONE A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:5[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg							
	C1-1 5OL	1 to 43	38 38	N: [redacted] R: WORSENING UC S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: HOSPITALISATION + ON [redacted]20[redacted] TOTAL COLECTOMY WITH ILEOSTOMY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: UNDERLYING DISEASE A: NO REASONABLE POSSIBILITY E: EVENT IS CLEARLY CONSISTENT WITH PROGRESSION OR WORSENING OF THE UNDERLYING DISEASE AND IS CONSIDERED EXPECTED FOR THIS STUDY.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]#	Age:5[redacted]	Sex:Male	Race:WHITE	Weight:6[redacted].[redacted] kg				
	C1-3 0OL	71 to 409	329	399 /329	N: [redacted] R: WORSENING UC S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: Other: NOT APPLICABLE O: HOSPITALISATION WITH SURGERY ON [redacted]20[redacted]	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: UNDERLYING DISEASE A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:9[redacted].[redacted] kg							
	C1-15OL	1 to 58	31 31	N: [redacted] R: WORSENING ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 34 L: 4 Days	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: LACK OF RESPONSE TO STUDY DRUG A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg								
	C1-3 0OL	49 to 176	224 /176		N: [redacted] R: UROLITHIASIS S: 腎および尿路障害 P: 尿路結石 L: Urolithiasis	E: 231 L: 8 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/Yes/No/No S: Yes, hospitalization or prolonged hospitalization O: INSUFFICIENT FLUID INTAKE A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
	C1-3 0OL	85 to	55	139 /55	N: [redacted] R: KIDNEY STONES S: 腎および尿路障害 P: 腎結石症 L: Kidney stones	E: 148 L: 10 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/Yes/No/No S: Yes, hospitalization or prolonged hospitalization O: SAE DUE TO KIDNEY STONES SURGERY A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
(Cont.)	C1-30OL	85 to 128	212 /128	N: [redacted] R: KIDNEY STONE SURGERY S: 腎および尿路障害 P: 腎結石症 L: Kidney stone	E: 215 L: 4 Days	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/Yes/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: KIDNEY STONES (COMORBIDITY) A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-15OL	1 to 8	8	8	N: [redacted] R: PERSISTENT ULCERATIVE COLITIS ACTIVITY S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: DEHYDRATION WEIGHT LOSS 20X BM/D A: NO REASONABLE POSSIBILITY E: EVENT MORE LIKELY DUE TO PROGRESSION OF PRE-EXISTING ULCERATIVE COLITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:11[redacted].[redacted] kg							
	C1-15OL	1 to 688	688	N: [redacted] R: PERFORATION OF SIGMOID COLON S: 胃腸障害 P: 大腸穿孔 L: Perforated colon	E: 688 L: 1 Day	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SURGICAL INTERVENTION	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: ACUTE ANGLE OF SIGMOID COLON A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
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# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:11[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	783	783	N: [redacted] R: VENTRICULAR TACHYCARDIA S: 心臓障害 P: 心室性頻脈 L: Ventricular tachycardia	E: 785 L: 3 Days I: Yes	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/Yes/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: ANGINA AND PREMATURE VENTRICULAR CONTRACTIONS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:11[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	985	985	N: [redacted] R: VENTRICULAR TACHYCARDIA S: 心臓障害 P: 心室性頻脈 L: Ventricular tachycardia	E: 989 L: 5 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/Yes/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: ANGINA AND PREMATURE VENTRICULAR CONTRACTIONS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:2[redacted] Sex:Female Race:BLACK OR AFRICAN AMERICAN Weight:4[redacted].[redacted] kg								
	C1-15OL	1 to 77	1	1 /-77	V: [redacted] N: 17093002002 R: PULMONARY EMBOLUS S: 呼吸器、胸郭および縦隔障害 P: 肺塞栓症 L: Pulmonary embolus	E: 7 L: 7 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/Possibly/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: WORSENING OF ULCERATIVE COLITIS

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
	C1-15OL	1 to 57	29 29	N: [redacted] R: ACUTE LACUNAR INFARCT RIGHT THALAMUS S: 神経系障害 P: ラクナ梗塞 L: Lacunar infarction	E: 31 L: 3 Days I: Yes	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: Concomitant medication or therapy started	AE: No/No/Yes/No/No/No S: Yes, hospitalization or prolonged hospitalization O: INVESTIGATIONS ONGOING A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:2[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C1-1 5OL	1 to	1026 1026	N: [redacted] R: LOWER LIMBS VARICOSE VEINS S: 血管障害 P: 静脈瘤 L: Varicose veins of lower extremities	E: 1120 L: 95 Days	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SURGERY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: LOWER LIMBS INSUFFICIENCY A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

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INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg								
	C1-15OL	1 to 1187	310	310	N: [redacted] R: WORSENING OF MIGRAINE HEADACHES S: 神経系障害 P: 片頭痛 L: Migraine aggravated	E: 311 L: 2 Days	S: SEVERE R: REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY E: RISK FACTORS INCLUDE PRE-EXISTING MIGRAINE HEADACHE, FIBROMYALGIA AND OBESITY.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
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Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

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INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 1187	1181	1181	N: [redacted] R: OPIOD OVERDOSE S: 傷害、中毒および処置合併症 P: 過量投与 L: Drug overdose	E: 1181 L: 1 Day	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, important medical or surgical intervention O: DRUG OVERDOSE A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
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# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 1187	1187	N: [redacted] R: ANOXIC BRAIN INJURY S: 神経系障害 P: 脳損傷 L: Anoxic brain damage	E: 1187 L: 1 Day	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY	AE: No/No/No/No/No/No S: Yes, death of subject, hospitalization or prolonged hospitalization O: ACUTE RESPIRATORY FAILURE WITH HYPOXIA A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg								
	C1-15OL	1 to 828	25	25 /-804	N: [redacted] R: OBSTRUCTIVE DISTAL LEFT URETER STONE, URETERIC OBSTRUCTION, URETEROLITHIASIS S: 腎および尿路障害 P: 尿管閉塞 L: Ureteric obstruction	E: 36 L: 12 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SUBJECT HAD STENT PLACED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: UNRELATED DISORDER A: NO REASONABLE POSSIBILITY E: WEAK TEMPORAL ASSOCIATION. KIDNEY STONE FORMATION IS UNLIKELY WITH LESS THAN 3 MONTHS OF STUDY DRUG EXPOSURE (INCLUDING PRIOR CLINICAL TRIAL). ADDITIONALLY, RENAL STONE DISEASE IS A RELATIVELY COMMON, PROBLEM WITH AN ESTIMATED 19 PERCENT OF MEN AND 9 PERCENT OF WOMEN WILL BE DIAGNOSED WITH A KIDNEY STONE BY THE AGE OF 70 YEARS. (CURHAN G. RISK FACTORS FOR CALCIUM STONES IN ADULTS. IN: UPTODATE, POS, T TW(ED), UPTODATE, WALTHAM, MA. (ACCESSED ON [redacted] 20[redacted].))

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
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Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 828	25	25 /-804	N: [redacted] R: OBSTRUCTIVE DISTAL LEFT URETER STONE, URETERIC OBSTRUCTION, URETEROLITHIASIS S: 腎および尿路障害 P: 尿管結石症 L: Ureterolithiasis	E: 36 L: 12 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SUBJECT HAD STENT PLACED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization, important medical or surgical intervention O: UNRELATED DISORDER A: NO REASONABLE POSSIBILITY E: WEAK TEMPORAL ASSOCIATION. KIDNEY STONE FORMATION IS UNLIKELY WITH LESS THAN 3 MONTHS OF STUDY DRUG EXPOSURE (INCLUDING PRIOR CLINICAL TRIAL). ADDITIONALLY, RENAL STONE DISEASE IS A RELATIVELY COMMON, PROBLEM WITH AN ESTIMATED 19 PERCENT OF MEN AND 9 PERCENT OF WOMEN WILL BE DIAGNOSED WITH A KIDNEY STONE BY THE AGE OF 70 YEARS. (CURHAN G. RISK FACTORS FOR CALCIUM STONES IN ADULTS. IN: UPTODATE, POS, T TW(ED), UPTODATE, WALTHAM, MA. (ACCESSED ON [redacted]20[redacted].))

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:WHITE Weight:7[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 828	803	803 /-26	N: [redacted] R: BACK PAIN S: 筋骨格系および結合組織障害 P: 背部痛 L: Back pain		S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: COEXISTENT MEDICAL PROBLEM: KIDNEY STONES, BACK PAIN A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg							
	C1-15OL	1 to 225	225	N: [redacted] R: CERVIX CONISATION AFTER PREBIOPSIAN SUSPECT S: 生殖系および乳房障害 P: 子宮頚部障害 L: Cervix disorder	E: 227 L: 3 Days	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: CERVIX CONISATION PERFORMED.	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: DUE TO SCREENING PROCEDURE, NO SYMPTOMS, PAITIENT INDICATED TO CONISATION OF CERVIX OF UTERUS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
N: AE Serial Number
R: Reported Term
S: System Organ Class
P: MedDRA 23.0 Preferred Term
L: Lower Level Term

E: Rx Day Ended
O: Ongoing at the End of Study?
L: Length
I: Interm-ittent?

S: Severity
C: AE Related to COVID-19 Infection
R: Relationship to Study Treatment
A: Action Taken with Study Treatment
O: Other Actions Taken

AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?
S: Serious AE?
O: Other Cause of Event
A: AbbVie Opinion of Causality
E: Sponsor Alternate Etiology

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V/N/R/S/P/L	E/O/L/I	S/C/R/A/O	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$? /Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 167	167	N: [redacted] R: HEADACHE S: 神経系障害 P: 頭痛 L: Headache	E: 169 L: 3 Days I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: SHE HAS A HISTORY OF SEVERE HEADACHE WITH VOMITING. IN ADDITION, TIME HAS PASSED SINCE THE START OF THE INVESTIGATIONAL AGENT. SO I THINK THAT THE SYMPTOMS ARE NOT DUE TO INVESTIGATIONAL AGENT. A: NO REASONABLE POSSIBILITY E: EVENT MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF MIGRAINE HEADACHE.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted] TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:4[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	838	838	N: [redacted] R: HERPES ZOSTER S: 感染症および寄生虫症 P: 帯状疱疹 L: Herpes zoster	E: 851 L: 14 Days I: Yes	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

V: AE Serial Number in Previous Study
E: Rx Day Ended
S: Severity
AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*?

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	O: Ongoing at the End of Study? L: Length I: Interm-ittent?	C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:2[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg							
	C1-15OL	1 to 357	321	N: [redacted] R: ABDOMINAL PAIN S: 胃腸障害 P: 腹痛 L: Abdominal pain	E: 334 L: 14 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: MEDICAL HISTORY OF PRIMARY SCLEROSING CHDANGITIS AND GALLBLADDER ENLARGEMENT WAS FOUND. A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS AND PRIMARY SCLEROSING CHOLANGITIS.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code:[redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
	C1-3 0OL	160 to	50	209 /50	N: [redacted] R: EXACERBATION OF ULCERATIVE COLITIS S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 211 L: 3 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: LACK OF EFFECTIVENESS OF THE STUDY DRUG A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:3[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg							
	C1-15OL	1 to 104	104	N: [redacted] R: FOLLICULAR ADENOMA OF THE LEFT LOBE OF THE THYROID GLAND S: 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) P: 甲状腺腺腫 L: Thyroid adenoma	E: 106 L: 3 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: LEFT HEMITHYROIDECTOMY PERFORMED [redacted]20[redacted]	AE: Yes/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: DIFFUSE NODULAR GOITER A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 39	39	N: [redacted] R: PNEUMONIA S: 感染症および寄生虫症 P: 肺炎 L: Pneumonia	E: 48 L: 10 Days	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: PNEUMONIA A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 76	76	N: [redacted] R: ENLARGEMENT OF PULMONARY NODULE IN RIGHT LUNG FROM 3 TO 4 MM S: 呼吸器、胸郭および縦隔障害 P: 肺腫瘤 L: Lung nodule	O: Yes	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: BRONCHOSCOPY WITH BIOPSY	AE: No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY E: EVENT IS MORE LIKELY RELATED TO PRIOR PNEUMONIA.

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted]# Age:4[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 704	658	658	N: [redacted] R: MALIGNANT TESTICULAR TUMOR (LEFT SIDED) S: 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) P: 精巣癌 L: Malignant neoplasm of testis	O: Yes	S: SEVERE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: DISCONTINUED STUDY O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: UNKNOWN A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 483	483	N: [redacted] R: LUMBAGO S: 筋骨格系および結合組織障害 P: 背部痛 L: Lumbago	I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: EXERCISE O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity O: MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 671	671	N: [redacted] R: LUMBAR SPINAL CANAL STENOSIS S: 筋骨格系および結合組織障害 P: 腰部脊柱管狭窄症 L: Lumbar spinal stenosis	I: Yes	S: MILD R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SURGICAL OPERATION	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION. A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted] TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:ASIAN Weight:5[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	788	788	N: [redacted] R: EXACERBATION OF LUMBAR DISC HERNIATION S: 筋骨格系および結合組織障害 P: 椎間板突出 L: Lumbar disc herniation	I: Yes	S: MODERATE R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SURGICAL OPERATION	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION. A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:6[redacted].[redacted] kg							
	C1-15OL	1 to 647	647	N: [redacted] R: DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA S: 傷害、中毒および処置合併症 P: 挫傷 L: Contusion	E: 649 L: 3 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: TRAFFIC ACCIDENT A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted] TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:6[redacted].[redacted] kg							
(Cont.)	C1-15OL	1 to 647	647	N: [redacted] R: DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA S: 傷害、中毒および処置合併症 P: 挫傷 L: Contusion of knee	E: 649 L: 3 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: TRAFFIC ACCIDENT A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:6[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	647	647	N: [redacted] R: DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA S: 筋骨格系および結合組織障害 P: 椎間板障害 L: Intervertebral disc disorder	E: 649 L: 3 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: TRAFFIC ACCIDENT A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD								
[redacted] Age:4[redacted] Sex:Female Race:ASIAN Weight:6[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to	647	647	N: [redacted] R: DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA S: 筋骨格系および結合組織障害 P: 脊柱変形 L: Spinal deformity	E: 649 L: 3 Days	S: MILD R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: TRAFFIC ACCIDENT

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escal-ation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD							
[redacted] Age:6[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 871	871	N: [redacted] R: HERPES ZOSTER S: 感染症および寄生虫症 P: 帯状疱疹 L: Herpes zoster	O: Yes I: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: OCULAR SURGERY O: Concomitant medication or therapy started	AE: No/No/No/No/Yes/No S: Yes, hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted]([redacted]) TRT: COHORT 2 - UPA 15 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
	C2-15DB	1 to 591	66 66	N: [redacted] R: INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION S: 精神障害 P: 不安 L: Anxiety aggravated	E: 73 L: 8 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization O: SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C2-15DB	1 to 591	66 66	N: [redacted] R: INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION S: 精神障害 P: うつ病 L: Depression aggravated	E: 73 L: 8 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization O: SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C2-1 5DB	1 to 591	66 66	N: [redacted] R: INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION S: 傷害、中毒および処置合併症 P: 企図的過量投与 L: Intentional overdose	E: 73 L: 8 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization O: SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD							
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
(Cont.)	C2-15DB	1 to 591	66 66	N: [redacted] R: INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION S: 精神障害 P: 自殺念慮 L: Active suicidal ideation	E: 73 L: 8 Days I: Yes	S: SEVERE R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: NONE	AE: No/No/No/No/No/No S: Yes, life threatening, hospitalization or prolonged hospitalization O: SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

TABLE 14.3 2.5.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Event
(SA1 and SA2 Populations)

Subject Number	Epoch Name	Epoch Interval	Day	Rx Day of Onset /Dose Escalation	V: AE Serial Number in Previous Study N: AE Serial Number R: Reported Term S: System Organ Class P: MedDRA 23.0 Preferred Term L: Lower Level Term	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Interm-ittent?	S: Severity C: AE Related to COVID-19 Infection R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	AE: Hepatic AE?/Cardiac AE?/Cerebral AE$?/Renal AE?/Herpes Zoster Infection AE?/Non-Cardiac AE*? S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality E: Sponsor Alternate Etiology
INV: [redacted] ([redacted]) TRT: COHORT 1 - UPA 15 MG QD/UPA 30 MG QD								
[redacted]# Age:2[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted].[redacted] kg								
	C1-3 0OL	770 to 919	47	816 /47	N: [redacted] R: SEPSIS DUE TO UNSPECIFIED ORGANISM S: 感染症および寄生虫症 P: 敗血症 L: Sepsis	E: 820 L: 5 Days	S: MODERATE R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

C1-15OL = Cohort 1 - UPA 15 mg QD open label treatment; C1-30OL = Cohort 1 - UPA 30 mg QD open label treatment; C2-7.5DB = Cohort 2 - UPA 7.5 mg QD blinded treatment; C2-15DB = Cohort 2 - UPA 15 mg QD blinded treatment; C2-30DB = Cohort 2 - UPA 30 mg QD blinded treatment; C2-PBO = Cohort 2 - placebo blinded treatment; FU = Follow-up.
$ Cerebral vascular accident or transient ischemic attack AE.
* Non-cardiac, non-CNS embolic or thrombotic event (i.e., deep vein thrombosis or pulmonary embolism) AE.
# Subject prematurely discontinued. & Date is estimated.

Program Source Code: [redacted]

表 2.7.4.7-44.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 10

TABLE 2.4 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=56) (PYs=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
Any adverse event	5 (29.9)	7 (90.0)	6 (9.1)
胃腸障害	2 (11.9)	3 (38.6)	2 (3.0)
腹痛	0	0	1 (1.5)
潰瘍性大腸炎	2 (11.9)	0	1 (1.5)
胃食道逆流性疾患	0	0	0
大腸ポリープ	0	3 (38.6)	0
膵炎	0	0	0
一般・全身障害および投与部位の状態	0	0	0
胸痛	0	0	0
発熱	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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
Any adverse event	4 (163.2)	9 (14.7)	6 (7.2)	9 (12.0)	35 (12.9)
胃腸障害	2 (81.6)	3 (4.9)	0	1 (1.3)	8 (2.9)
腹痛	0	0	0	0	1 (0.4)
潰瘍性大腸炎	2 (81.6)	2 (3.3)	0	0	3 (1.1)
胃食道逆流性疾患	0	0	0	1 (1.3)	1 (0.4)
大腸ポリープ	0	0	0	0	3 (1.1)
膵炎	0	1 (1.6)	0	0	0
一般・全身障害および投与部位の状態	1 (40.8)	0	0	1 (1.3)	2 (0.7)
胸痛	0	0	0	1 (1.3)	1 (0.4)
発熱	1 (40.8)	0	0	0	1 (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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=56) (PYs=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
感染症および寄生虫症	0	2 (25.7)	1 (1.5)
虫垂炎	0	0	0
細菌性関節炎	0	0	0
帯状疱疹	0	1 (12.9)	1 (1.5)
帯状疱疹性髄膜炎	0	0	0
大腸感染	0	0	0
ニューモシスチス・イロベチイ肺炎	0	0	0
肺炎	0	0	0
腎盂腎炎	0	1 (12.9)	0
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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
感染症および寄生虫症	1 (40.8)	3 (4.9)	3 (3.6)	4 (5.3)	11 (4.0)
虫垂炎	0	0	1 (1.2)	0	1 (0.4)
細菌性関節炎	0	0	1 (1.2)	0	1 (0.4)
帯状疱疹	0	1 (1.6)	0	2 (2.7)	4 (1.5)
帯状疱疹性髄膜炎	0	0	0	1 (1.3)	1 (0.4)
大腸感染	0	0	1 (1.2)	0	1 (0.4)
ニューモシスチス・イロベチイ肺炎	0	1 (1.6)	0	0	0
肺炎	0	1 (1.6)	0	1 (1.3)	1 (0.4)
腎盂腎炎	0	0	0	0	1 (0.4)
ウイルス感染	1 (40.8)	0	0	0	1 (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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=56) (PYs=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
傷害、中毒および処置合併症	0	0	0
肺挫傷	0	0	0
胸椎骨折	0	0	0
代謝および栄養障害	1 (6.0)	0	0
低アルブミン血症	1 (6.0)	0	0
栄養障害	0	0	0
筋骨格系および結合組織障害	0	0	1 (1.5)
背部痛	0	0	0
椎間板突出	0	0	0
腰部脊柱管狭窄症	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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
傷害、中毒および処置合併症	0	0	2 (2.4)	0	2 (0.7)
肺挫傷	0	0	1 (1.2)	0	1 (0.4)
胸椎骨折	0	0	1 (1.2)	0	1 (0.4)
代謝および栄養障害	0	0	0	1 (1.3)	1 (0.4)
低アルブミン血症	0	0	0	0	0
栄養障害	0	0	0	1 (1.3)	1 (0.4)
筋骨格系および結合組織障害	0	3 (4.9)	0	0	4 (1.5)
背部痛	0	1 (1.6)	0	0	1 (0.4)
椎間板突出	0	1 (1.6)	0	0	1 (0.4)
腰部脊柱管狭窄症	0	1 (1.6)	0	0	1 (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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=56) (PYs=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
骨壊死	0	0	1 (1.5)
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）	0	0	0
結腸腺癌	0	0	0
神経系障害	1 (6.0)	0	1 (1.5)
手根管症候群	1 (6.0)	0	0
頭痛	0	0	1 (1.5)
くも膜下出血	0	0	0
腎および尿路障害	0	2 (25.7)	1 (1.5)
腎結石症	0	2 (25.7)	0
尿管結石症	0	0	1 (1.5)

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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
骨壊死	0	0	0	0	1 (0.4)
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)	0	0	0	1 (1.3)	1 (0.4)
結腸腺癌	0	0	0	1 (1.3)	1 (0.4)
神経系障害	0	0	0	1 (1.3)	2 (0.7)
手根管症候群	0	0	0	0	0
頭痛	0	0	0	0	1 (0.4)
くも膜下出血	0	0	0	1 (1.3)	1 (0.4)
腎および尿路障害	0	0	0	0	3 (1.1)
腎結石症	0	0	0	0	2 (0.7)
尿管結石症	0	0	0	0	1 (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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=56) (PYs=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
皮膚および皮下組織障害	1 (6.0)	0	0
脂肪織炎	0	0	0
壊疽性膿皮症	1 (6.0)	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 4.3.3 J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
皮膚および皮下組織障害	0	0	1 (1.2)	0	1 (0.4)
脂肪織炎	0	0	1 (1.2)	0	1 (0.4)
壊疽性膿皮症	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]

表 2.7.4.7-45.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	44 (36.5)	4 (3.7)	53 (9.0)
血液およびリンパ系障害	0	0	0
リンパ球減少症	0	0	0
心臓障害	0	0	0
急性心筋梗塞	0	0	0
耳および迷路障害	0	0	0
耳鳴	0	0	0
眼障害	0	0	1 (0.2)
霧視	0	0	0
視力障害	0	0	1 (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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	34 (141.2)	23 (6.4)	24 (5.1)	21 (4.7)	140 (7.7)
血液およびリンパ系障害	1 (4.2)	0	1 (0.2)	0	2 (0.1)
リンパ球減少症	1 (4.2)	0	1 (0.2)	0	2 (0.1)
心臓障害	0	1 (0.3)	0	0	0
急性心筋梗塞	0	1 (0.3)	0	0	0
耳および迷路障害	1 (4.2)	0	0	0	1 (<0.1)
耳鳴	1 (4.2)	0	0	0	1 (<0.1)
眼障害	1 (4.2)	0	0	0	2 (0.1)
霧視	1 (4.2)	0	0	0	1 (<0.1)
視力障害	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害	30 (24.9)	1 (0.9)	27 (4.6)
腹部膨満	1 (0.8)	0	0
腹痛	0	0	1 (0.2)
上腹部痛	0	0	1 (0.2)
肛門潰瘍	0	0	0
大腸炎	2 (1.7)	0	0
潰瘍性大腸炎	26 (21.6)	1 (0.9)	18 (3.1)
結腸異形成	0	0	2 (0.3)
クローン病	0	0	1 (0.2)
腸閉塞	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害	14 (58.1)	9 (2.5)	11 (2.4)	3 (0.7)	58 (3.2)
腹部膨満	0	0	0	0	0
腹痛	0	0	0	0	1 (<0.1)
上腹部痛	0	0	0	0	1 (<0.1)
肛門潰瘍	1 (4.2)	0	0	0	1 (<0.1)
大腸炎	0	0	0	0	0
潰瘍性大腸炎	12 (49.8)	7 (2.0)	8 (1.7)	2 (0.5)	43 (2.4)
結腸異形成	0	0	1 (0.2)	0	3 (0.2)
クローン病	0	0	0	0	1 (<0.1)
腸閉塞	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
大腸穿孔	1 (0.8)	0	0
大腸ポリープ	0	0	1 (0.2)
悪心	0	0	2 (0.3)
膵炎	0	0	0
直腸異形成	0	0	0
直腸出血	0	0	1 (0.2)
一般・全身障害および投与部位の状態	2 (1.7)	0	3 (0.5)
無力症	1 (0.8)	0	0
悪寒	0	0	1 (0.2)
異形成	0	0	1 (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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
大腸穿孔	0	1 (0.3)	0	0	0
大腸ポリープ	0	0	0	0	1 (<0.1)
悪心	0	0	0	0	2 (0.1)
膵炎	0	1 (0.3)	0	1 (0.2)	1 (<0.1)
直腸異形成	1 (4.2)	0	1 (0.2)	0	2 (0.1)
直腸出血	0	0	0	0	1 (<0.1)
一般・全身障害および投与部位の状態	2 (8.3)	1 (0.3)	1 (0.2)	0	6 (0.3)
無力症	0	0	0	0	0
悪寒	0	0	0	0	1 (<0.1)
異形成	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
疲労	1 (0.8)	0	0
発熱	0	0	1 (0.2)
肝胆道系障害	0	0	2 (0.3)
硬化性胆管炎	0	0	0
薬物性肝障害	0	0	0
肝機能異常	0	0	1 (0.2)
肝炎	0	0	1 (0.2)
感染症および寄生虫症	3 (2.5)	0	2 (0.3)
腹部膿瘍	0	0	0
急性心内膜炎	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
疲労	0	0	0	0	0
発熱	2 (8.3)	1 (0.3)	0	0	3 (0.2)
肝胆道系障害	0	0	0	3 (0.7)	5 (0.3)
硬化性胆管炎	0	0	0	1 (0.2)	1 (<0.1)
薬物性肝障害	0	0	0	1 (0.2)	1 (<0.1)
肝機能異常	0	0	0	1 (0.2)	2 (0.1)
肝炎	0	0	0	0	1 (<0.1)
感染症および寄生虫症	5 (20.8)	3 (0.8)	2 (0.4)	4 (0.9)	13 (0.7)
腹部膿瘍	0	1 (0.3)	0	0	0
急性心内膜炎	0	1 (0.3)	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
細菌性関節炎	0	0	0
COVID-19肺炎	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0
腸球菌感染	1 (0.8)	0	0
大腸菌感染	1 (0.8)	0	0
帯状疱疹	0	0	0
筋膿瘍	1 (0.8)	0	0
肺炎	0	0	1 (0.2)
結核	0	0	1 (0.2)
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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
細菌性関節炎	0	0	1 (0.2)	0	1 (<0.1)
COVID-19肺炎	0	0	0	1 (0.2)	1 (<0.1)
クロストリジウム・ディフィシレ感染	0	0	0	1 (0.2)	1 (<0.1)
腸球菌感染	0	0	0	0	0
大腸菌感染	0	0	0	0	0
帯状疱疹	3 (12.5)	0	1 (0.2)	1 (0.2)	5 (0.3)
筋膿瘍	0	0	0	0	0
肺炎	0	1 (0.3)	0	1 (0.2)	2 (0.1)
結核	0	0	0	0	1 (<0.1)
ウイルス感染	1 (4.2)	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) 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
傷害、中毒および処置合併症	1 (0.8)	0	2 (0.3)
消化管ストーマ壊死	1 (0.8)	0	0
過量投与	0	0	0
処置による腸管穿孔	0	0	1 (0.2)
子宮穿孔	0	0	1 (0.2)
臨床検査	2 (1.7)	0	6 (1.0)
アラニンアミノトランスフェラーゼ増加	0	0	2 (0.3)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	2 (0.3)
血中クレアチンホスホキナーゼ増加	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) 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	0	0	1 (<0.1)
傷害、中毒および処置合併症	1 (4.2)	0	0	0	3 (0.2)
消化管ストーマ壊死	0	0	0	0	0
過量投与	1 (4.2)	0	0	0	1 (<0.1)
処置による腸管穿孔	0	0	0	0	1 (<0.1)
子宮穿孔	0	0	0	0	1 (<0.1)
臨床検査	2 (8.3)	0	1 (0.2)	4 (0.9)	13 (0.7)
アラニンアミノトランスフェラーゼ増加	0	0	0	1 (0.2)	3 (0.2)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	0	2 (0.1)
血中クレアチンホスホキナーゼ増加	1 (4.2)	0	1 (0.2)	1 (0.2)	3 (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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
ヘモグロビン減少	1 (0.8)	0	0
肝酵素上昇	0	0	1 (0.2)
B型肝炎DNA測定陽性	1 (0.8)	0	1 (0.2)
好中球数減少	0	0	0
代謝および栄養障害	1 (0.8)	0	0
低リン酸血症	1 (0.8)	0	0
筋骨格系および結合組織障害	0	0	0
関節痛	0	0	0
関節炎	0	0	0
横紋筋融解症	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
ヘモグロビン減少	0	0	0	1 (0.2)	1 (<0.1)
肝酵素上昇	0	0	0	0	1 (<0.1)
B型肝炎DNA測定陽性	0	0	0	1 (0.2)	2 (0.1)
好中球数減少	1 (4.2)	0	0	0	1 (<0.1)
代謝および栄養障害	0	0	0	1 (0.2)	1 (<0.1)
低リン酸血症	0	0	0	1 (0.2)	1 (<0.1)
筋骨格系および結合組織障害	3 (12.5)	0	1 (0.2)	0	4 (0.2)
関節痛	1 (4.2)	0	0	0	1 (<0.1)
関節炎	1 (4.2)	0	0	0	1 (<0.1)
横紋筋融解症	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
弾発指	0	0	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）	0	2 (1.8)	2 (0.3)
結腸腺癌	0	1 (0.9)	0
膵腺癌	0	0	1 (0.2)
浸潤性乳癌	0	0	0
喉頭扁平上皮癌	0	1 (0.9)	0
悪性黒色腫	0	0	1 (0.2)
前立腺癌	0	0	0
小細胞癌	0	0	0
子宮頚部扁平上皮癌	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
弾発指	1 (4.2)	0	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)	0	2 (0.6)	2 (0.4)	3 (0.7)	10 (0.5)
結腸腺癌	0	0	0	0	1 (<0.1)
膵腺癌	0	0	0	0	1 (<0.1)
浸潤性乳癌	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
喉頭扁平上皮癌	0	0	0	0	1 (<0.1)
悪性黒色腫	0	0	0	0	1 (<0.1)
前立腺癌	0	1 (0.3)	0	0	1 (<0.1)
小細胞癌	0	0	0	1 (0.2)	1 (<0.1)
子宮頚部扁平上皮癌	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) 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.)			
精巣（純粋）セミノーマ	0	0	0
精巣癌	0	0	0
神経系障害	2 (1.7)	0	4 (0.7)
健忘	0	0	1 (0.2)
脳損傷	0	0	0
灼熱感	0	0	0
頭痛	1 (0.8)	0	2 (0.3)
ラクナ梗塞	0	0	0
片頭痛	1 (0.8)	0	0
発作様現象	0	0	1 (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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) 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.)					
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)
神経系障害	1 (4.2)	0	1 (0.2)	1 (0.2)	7 (0.4)
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	0	0	1 (<0.1)
頭痛	0	0	0	0	2 (0.1)
ラクナ梗塞	0	0	0	1 (0.2)	1 (<0.1)
片頭痛	0	0	0	0	0
発作様現象	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
精神障害	0	0	2 (0.3)
抑うつ気分	0	0	1 (0.2)
易刺激性	0	0	1 (0.2)
腎および尿路障害	0	0	0
慢性腎臓病	0	0	0
腎機能障害	0	0	0
呼吸器、胸郭および縦隔障害	1 (0.8)	0	1 (0.2)
胞隔炎	0	0	0
間質性肺疾患	0	0	0
肺塞栓症	1 (0.8)	0	1 (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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害	0	0	0	0	2 (0.1)
抑うつ気分	0	0	0	0	1 (<0.1)
易刺激性	0	0	0	0	1 (<0.1)
腎および尿路障害	1 (4.2)	0	1 (0.2)	0	2 (0.1)
慢性腎臓病	1 (4.2)	0	0	0	1 (<0.1)
腎機能障害	0	0	1 (0.2)	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	1 (4.2)	1 (0.3)	0	0	2 (0.1)
胞隔炎	1 (4.2)	0	0	0	1 (<0.1)
間質性肺疾患	0	1 (0.3)	0	0	0
肺塞栓症	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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害	1 (0.8)	1 (0.9)	0
ざ瘡	0	0	0
紅斑	0	0	0
結節性紅斑	0	0	0
脂肪織炎	0	0	0
そう痒症	1 (0.8)	0	0
発疹	0	0	0
斑状丘疹状皮疹	0	1 (0.9)	0
脂漏性皮膚炎	0	0	0
血管障害	1 (0.8)	0	1 (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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害	1 (4.2)	4 (1.1)	2 (0.4)	1 (0.2)	6 (0.3)
ざ瘡	0	1 (0.3)	0	0	1 (<0.1)
紅斑	0	0	1 (0.2)	0	1 (<0.1)
結節性紅斑	0	1 (0.3)	0	0	0
脂肪織炎	0	0	1 (0.2)	0	1 (<0.1)
そう痒症	0	1 (0.3)	0	0	0
発疹	1 (4.2)	1 (0.3)	0	0	2 (0.1)
斑状丘疹状皮疹	0	0	0	0	0
脂漏性皮膚炎	0	0	0	1 (0.2)	1 (<0.1)
血管障害	0	2 (0.6)	1 (0.2)	1 (0.2)	3 (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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
血管障害 (Cont.)			
深部静脈血栓症	0	0	1 (0.2)
高血圧	0	0	0
骨盤静脈血栓症	1 (0.8)	0	0
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 4.3.6

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血管障害 (Cont.)					
深部静脈血栓症	0	0	0	1 (0.2)	2 (0.1)
高血圧	0	1 (0.3)	0	0	0
骨盤静脈血栓症	0	0	0	0	0
静脈血栓症	0	1 (0.3)	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]

表 2.7.4.7-46.

[redacted]20[redacted] 16:56 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=56) (PYs=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
Any adverse event	5 (29.9)	0	5 (7.6)
胃腸障害	5 (29.9)	0	2 (3.0)
潰瘍性大腸炎	5 (29.9)	0	2 (3.0)
膵炎	0	0	0
一般・全身障害および投与部位の状態	0	0	0
発熱	0	0	0
肝胆道系障害	0	0	1 (1.5)
肝機能異常	0	0	1 (1.5)
感染症および寄生虫症	0	0	1 (1.5)
細菌性関節炎	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 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
Any adverse event	10 (408.1)	5 (8.1)	2 (2.4)	4 (5.3)	22 (8.1)
胃腸障害	3 (122.4)	3 (4.9)	0	0	5 (1.8)
潰瘍性大腸炎	3 (122.4)	2 (3.3)	0	0	5 (1.8)
膵炎	0	1 (1.6)	0	0	0
一般・全身障害および投与部位の状態	1 (40.8)	0	0	0	1 (0.4)
発熱	1 (40.8)	0	0	0	1 (0.4)
肝胆道系障害	0	0	0	1 (1.3)	2 (0.7)
肝機能異常	0	0	0	1 (1.3)	2 (0.7)
感染症および寄生虫症	3 (122.4)	0	1 (1.2)	2 (2.7)	7 (2.6)
細菌性関節炎	0	0	1 (1.2)	0	1 (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 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=56) (PYs=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
帯状疱疹	0	0	0
肺炎	0	0	1 (1.5)
ウイルス感染	0	0	0
臨床検査	0	0	0
血中クレアチンホスホキナーゼ増加	0	0	0
筋骨格系および結合組織障害	0	0	0
関節炎	0	0	0
弾発指	0	0	0
神経系障害	0	0	1 (1.5)
頭痛	0	0	1 (1.5)

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 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
帯状疱疹	2 (81.6)	0	0	1 (1.3)	3 (1.1)
肺炎	0	0	0	1 (1.3)	2 (0.7)
ウイルス感染	1 (40.8)	0	0	0	1 (0.4)
臨床検査	0	0	0	1 (1.3)	1 (0.4)
血中クレアチンホスホキナーゼ増加	0	0	0	1 (1.3)	1 (0.4)
筋骨格系および結合組織障害	2 (81.6)	0	0	0	2 (0.7)
関節炎	1 (40.8)	0	0	0	1 (0.4)
弾発指	1 (40.8)	0	0	0	1 (0.4)
神経系障害	0	0	0	0	1 (0.4)
頭痛	0	0	0	0	1 (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 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=56) (PYs=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
腎および尿路障害	0	0	0
慢性腎臓病	0	0	0
皮膚および皮下組織障害	0	0	0
ざ瘡	0	0	0
脂肪織炎	0	0	0
血管障害	0	0	0
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 4.3.6 J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
腎および尿路障害	1 (40.8)	0	0	0	1 (0.4)
慢性腎臓病	1 (40.8)	0	0	0	1 (0.4)
皮膚および皮下組織障害	0	1 (1.6)	1 (1.2)	0	2 (0.7)
ざ瘡	0	1 (1.6)	0	0	1 (0.4)
脂肪織炎	0	0	1 (1.2)	0	1 (0.4)
血管障害	0	1 (1.6)	0	0	0
静脈血栓症	0	1 (1.6)	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]

表 2.7.4.7-47.

[redacted]20[redacted] 11:04 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 1.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Placebo-Controlled Induction Analysis Set)

	Placebo (N=378) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 45 mg QD (N=719) n/PYs (n/100 PYs) [SSA n/100 PYs]	- Treatment Comparison (95% CI) [A] - UPA 45 mg QD - PBO
Any serious infections	5/55.4 (9.0) [8.4]	9/109.4 (8.2) [8.4]	0.1 (-9.2, 9.3)
Any opportunistic infection excluding tuberculosis and herpes zoster	1/55.7 (1.8) [1.3]	3/109.8 (2.7) [2.7]	1.4 (-2.7, 5.4)
Any active tuberculosis	0/55.7	0/109.9	0.0
Any herpes zoster	0/55.7	4/109.6 (3.6) [3.8]	3.8 (0.1, 7.5)
Any adjudicated gastrointestinal perforations	1/55.7 (1.8) [1.8]	0/109.9	-1.8 (-5.4, 1.7)
Any anemia	21/54.2 (38.7) [39.4]	25/107.6 (23.2) [22.9]	-16.5 (-35.6, 2.7)
Any neutropenia	1/55.6 (1.8) [1.9]	33/107.4 (30.7) [30.6]	28.7 (17.6, 39.8)
Any lymphopenia	2/55.5 (3.6) [3.7]	18/108.4 (16.6) [16.7]	12.9 (3.6, 22.3)
Any creatine phosphokinase (CPK) elevation	5/55.2 (9.1) [9.5]	37/106.8 (34.6) [35.1]	25.7 (11.6, 39.7)
Any hepatic disorder	9/54.8 (16.4) [17.0]	25/108.0 (23.1) [24.1]	7.1 (-7.6, 21.8)
Any renal dysfunction	0/55.7	0/109.9	0.0
Any malignancy	0/55.7	0/109.9	0.0
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/55.7	0/109.9	0.0
Any NMSC	0/55.7	0/109.9	0.0
Any lymphoma	0/55.7	0/109.9	0.0
Any adjudicated MACE *	0/55.7	0/109.9	0.0
Any adjudicated VTE **	1/55.6 (1.8) [1.8]	1/110.0 (0.9) [1.1]	-0.7 (-4.9, 3.4)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
n/100PYs = Number of subjects per 100 patient-years.
SSA = Study-size adjusted.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-48.

[redacted]20[redacted] 16:56 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
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TABLE 2.4 1.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Placebo-Controlled Induction Analysis Set - Japan Analysis Set)

	Placebo (N=56) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 45 mg QD (N=117) n/PYs (n/100 PYs) [SSA n/100 PYs]	- Treatment Comparison (95% CI) [A] - UPA 45 mg QD - PBO
Any serious infections	0/8.0	2/17.4 (11.5) [11.0]	11.0 (-4.3, 26.4)
Any opportunistic infection excluding tuberculosis and herpes zoster	0/8.0	1/17.3 (5.8) [6.1]	6.1 (-5.8, 18.0)
Any active tuberculosis	0/8.0	0/17.4	0.0
Any herpes zoster	0/8.0	1/17.4 (5.8) [5.5]	5.5 (-5.3, 16.3)
Any adjudicated gastrointestinal perforations	0/8.0	0/17.4	0.0
Any anemia	4/7.8 (51.1) [60.5]	4/17.2 (23.3) [22.3]	-38.2 (-101.5, 25.2)
Any neutropenia	0/8.0	14/16.2 (86.4) [87.6]	87.6 (41.7, 133.6)
Any lymphopenia	0/8.0	5/17.0 (29.4) [28.7]	28.7 (3.5, 54.0)
Any creatine phosphokinase (CPK) elevation	0/8.0	5/17.0 (29.5) [30.6]	30.6 (3.8, 57.4)
Any hepatic disorder	1/8.0 (12.5) [14.5]	6/16.8 (35.7) [35.8]	21.2 (-19.2, 61.7)
Any renal dysfunction	0/8.0	0/17.4	0.0
Any malignancy	0/8.0	0/17.4	0.0
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/8.0	0/17.4	0.0
Any NMSC	0/8.0	0/17.4	0.0
Any lymphoma	0/8.0	0/17.4	0.0
Any adjudicated MACE *	0/8.0	0/17.4	0.0
Any adjudicated VTE **	0/8.0	0/17.4	0.0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
n/100PYs = Number of subjects per 100 patient-years.
SSA = Study-size adjusted.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-49.

[redacted]20[redacted] 10:52 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 2.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Extended Induction Analysis Set)

	UPA 45 mg QD (N=127)	
	End of DB Induction[1] (Week 8) n/PYs (n/100 PYs)	End of OL Extended Induction[2] (Week 16) n/PYs (n/100 PYs)
Any serious infections	1/19.9 (5.0)	1/38.8 (2.6)
Any opportunistic infection excluding tuberculosis and herpes zoster	2/20.0 (10.0)	2/38.7 (5.2)
Any active tuberculosis	0/20.0	0/39.1
Any herpes zoster	1/19.9 (5.0)	5/38.7 (12.9)
Any adjudicated gastrointestinal perforations	0/20.0	0/39.1
Any anemia	10/19.2 (52.0)	13/36.7 (35.4)
Any neutropenia	3/19.7 (15.2)	4/38.2 (10.5)
Any lymphopenia	2/19.9 (10.1)	4/38.6 (10.4)
Any creatine phosphokinase (CPK) elevation	8/19.3 (41.4)	13/37.1 (35.1)
Any hepatic disorder	3/19.8 (15.2)	5/38.2 (13.1)
Any renal dysfunction	0/20.0	0/39.1
Any malignancy	0/20.0	0/39.1
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/20.0	0/39.1
Any NMSC	0/20.0	0/39.1
Any lymphoma	0/20.0	0/39.1
Any adjudicated MACE *	0/20.0	0/39.1
Any adjudicated VTE **	0/20.0	0/39.1

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the induction period (Part 2) or until one day prior to the first dose of study drug in any subsequent maintenance or long-term extension period.
n/100PYs = Number of subjects per 100 patient-years.
[1] All events and exposure time from Part 1 induction studies (for the extended induction analysis set).
[2] All events and exposure time from Parts 1 and 2 induction studies (for the extended induction analysis set).
DB = double blind. OL = open label.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-50.

[redacted]20[redacted] 16:56 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
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TABLE 2.4 2.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Extended Induction Analysis Set - Japan Analysis Set)

	UPA 45 mg QD (N=14)	
	End of DB Induction[1] (Week 8) n/PYs (n/100 PYs)	End of OL Extended Induction[2] (Week 16) n/PYs (n/100 PYs)
Any serious infections	0/2.1	0/4.3
Any opportunistic infection excluding tuberculosis and herpes zoster	1/2.1 (47.6)	1/4.1 (24.3)
Any active tuberculosis	0/2.1	0/4.3
Any herpes zoster	0/2.1	1/4.3 (23.0)
Any adjudicated gastrointestinal perforations	0/2.1	0/4.3
Any anemia	0/2.1	0/4.3
Any neutropenia	3/1.8 (162.6)	3/3.6 (84.5)
Any lymphopenia	1/2.1 (47.7)	1/4.1 (24.3)
Any creatine phosphokinase (CPK) elevation	1/2.1 (47.6)	3/3.9 (76.3)
Any hepatic disorder	0/2.1	0/4.3
Any renal dysfunction	0/2.1	0/4.3
Any malignancy	0/2.1	0/4.3
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/2.1	0/4.3
Any NMSC	0/2.1	0/4.3
Any lymphoma	0/2.1	0/4.3
Any adjudicated MACE *	0/2.1	0/4.3
Any adjudicated VTE **	0/2.1	0/4.3

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the induction period (Part 2) or until one day prior to the first dose of study drug in any subsequent maintenance or long-term extension period.
n/100PYs = Number of subjects per 100 patient-years.
[1] All events and exposure time from Part 1 induction studies (for the extended induction analysis set).
[2] All events and exposure time from Parts 1 and 2 induction studies (for the extended induction analysis set).
DB = double blind. OL = open label.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-51.

[redacted]20[redacted] 16:56 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245)	UPA 15 mg QD (N=250)	UPA 30 mg QD (N=251)	UPA 15 mg QD (N=285)	UPA 30 mg QD (N=291)
Subgroup: 0 - < 3 Month					
Exposure-adjusted event rate:	(PYs=53.5) Events (E/100PYs) [95% CI]	(PYs=59.1) Events (E/100PYs) [95% CI]	(PYs=60.7) Events (E/100PYs) [95% CI]	(PYs=70.6) Events (E/100PYs) [95% CI]	(PYs=70.1) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	3 (5.6) [1.2, 16.4]	3 (5.1) [1.0, 14.8]	1 (1.6) [0.0, 9.2]	3 (4.3) [0.9, 12.4]	2 (2.9) [0.3, 10.3]
Any opportunistic infection excluding tuberculosis and herpes zoster	2 (3.7) [0.5, 13.5]	2 (3.4) [0.4, 12.2]	0	2 (2.8) [0.3, 10.2]	0
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	2 (3.4) [0.4, 12.2]	4 (6.6) [1.8, 16.9]	2 (2.8) [0.3, 10.2]	4 (5.7) [1.6, 14.6]
Any adjudicated gastrointestinal perforations	1 (1.9) [0.0, 10.4]	1 (1.7) [0.0, 9.4]	0	1 (1.4) [0.0, 7.9]	0
Any anemia	10 (18.7) [9.0, 34.4]	8 (13.5) [5.8, 26.7]	6 (9.9) [3.6, 21.5]	11 (15.6) [7.8, 27.9]	9 (12.8) [5.9, 24.4]
Any neutropenia	4 (7.5) [2.0, 19.2]	6 (10.1) [3.7, 22.1]	12 (19.8) [10.2, 34.5]	6 (8.5) [3.1, 18.5]	14 (20.0) [10.9, 33.5]

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=245)	UPA 15 mg QD (N=250)	UPA 30 mg QD (N=251)	UPA 15 mg QD (N=285)	UPA 30 mg QD (N=291)
Subgroup: 0 - < 3 Month (Cont.)					
Any lymphopenia	5 (9.4) [3.0, 21.8]	5 (8.5) [2.7, 19.7]	3 (4.9) [1.0, 14.4]	5 (7.1) [2.3, 16.5]	3 (4.3) [0.9, 12.5]
Any creatine phosphokinase (CPK) elevation	2 (3.7) [0.5, 13.5]	10 (16.9) [8.1, 31.1]	10 (16.5) [7.9, 30.3]	11 (15.6) [7.8, 27.9]	11 (15.7) [7.8, 28.1]
Any hepatic disorder	4 (7.5) [2.0, 19.2]	13 (22.0) [11.7, 37.6]	9 (14.8) [6.8, 28.2]	14 (19.8) [10.8, 33.3]	14 (20.0) [10.9, 33.5]
Any renal dysfunction	1 (1.9) [0.0, 10.4]	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=168)	UPA 15 mg QD (N=221)	UPA 30 mg QD (N=232)	UPA 15 mg QD (N=279)	UPA 30 mg QD (N=267)
Subgroup: >= 3 - < 6 Month					
Exposure-adjusted event rate:	(PYs=34.8) Events (E/100PYs) [95% CI]	(PYs=51.7) Events (E/100PYs) [95% CI]	(PYs=55.1) Events (E/100PYs) [95% CI]	(PYs=65.2) Events (E/100PYs) [95% CI]	(PYs=63.1) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	3 (8.6) [1.8, 25.2]	4 (7.7) [2.1, 19.8]	4 (7.3) [2.0, 18.6]	4 (6.1) [1.7, 15.7]	4 (6.3) [1.7, 16.2]
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	1 (1.8) [0.0, 10.1]	0	1 (1.6) [0.0, 8.8]
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	5 (9.7) [3.1, 22.6]	3 (5.4) [1.1, 15.9]	6 (9.2) [3.4, 20.0]	4 (6.3) [1.7, 16.2]
Any adjudicated gastrointestinal perforations	0	1 (1.9) [0.0, 10.8]	1 (1.8) [0.0, 10.1]	2 (3.1) [0.4, 11.1]	1 (1.6) [0.0, 8.8]
Any anemia	1 (2.9) [0.1, 16.0]	1 (1.9) [0.0, 10.8]	0	1 (1.5) [0.0, 8.5]	1 (1.6) [0.0, 8.8]
Any neutropenia	1 (2.9) [0.1, 16.0]	3 (5.8) [1.2, 17.0]	2 (3.6) [0.4, 13.1]	4 (6.1) [1.7, 15.7]	2 (3.2) [0.4, 11.5]

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=168)	UPA 15 mg QD (N=221)	UPA 30 mg QD (N=232)	UPA 15 mg QD (N=279)	UPA 30 mg QD (N=267)
Subgroup: >= 3 - < 6 Month (Cont.)					
Any lymphopenia	0	1 (1.9) [0.0, 10.8]	2 (3.6) [0.4, 13.1]	2 (3.1) [0.4, 11.1]	2 (3.2) [0.4, 11.5]
Any creatine phosphokinase (CPK) elevation	1 (2.9) [0.1, 16.0]	1 (1.9) [0.0, 10.8]	7 (12.7) [5.1, 26.2]	1 (1.5) [0.0, 8.5]	7 (11.1) [4.5, 22.9]
Any hepatic disorder	0	5 (9.7) [3.1, 22.6]	2 (3.6) [0.4, 13.1]	5 (7.7) [2.5, 17.9]	2 (3.2) [0.4, 11.5]
Any renal dysfunction	0	0	1 (1.8) [0.0, 10.1]	0	1 (1.6) [0.0, 8.8]

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=116)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=208)	UPA 15 mg QD (N=242)	UPA 30 mg QD (N=237)
Subgroup: >= 6 - < 9 Month					
Exposure-adjusted event rate:	(PYs=23.7) Events (E/100PYs) [95% CI]	(PYs=41.1) Events (E/100PYs) [95% CI]	(PYs=46.5) Events (E/100PYs) [95% CI]	(PYs=53.0) Events (E/100PYs) [95% CI]	(PYs=53.1) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	2 (8.4) [1.0, 30.5]	2 (4.9) [0.6, 17.6]	1 (2.2) [0.1, 12.0]	3 (5.7) [1.2, 16.6]	2 (3.8) [0.5, 13.6]
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	0	0
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	2 (4.9) [0.6, 17.6]	3 (6.5) [1.3, 18.9]	2 (3.8) [0.5, 13.6]	4 (7.5) [2.1, 19.3]
Any adjudicated gastrointestinal perforations	0	0	1 (2.2) [0.1, 12.0]	0	1 (1.9) [0.0, 10.5]
Any anemia	7 (29.5) [11.9, 60.8]	2 (4.9) [0.6, 17.6]	0	3 (5.7) [1.2, 16.6]	1 (1.9) [0.0, 10.5]
Any neutropenia	2 (8.4) [1.0, 30.5]	2 (4.9) [0.6, 17.6]	2 (4.3) [0.5, 15.5]	2 (3.8) [0.5, 13.6]	2 (3.8) [0.5, 13.6]

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=116)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=208)	UPA 15 mg QD (N=242)	UPA 30 mg QD (N=237)
Subgroup: >= 6 - < 9 Month (Cont.)					
Any lymphopenia	0	3 (7.3) [1.5, 21.3]	1 (2.2) [0.1, 12.0]	3 (5.7) [1.2, 16.6]	1 (1.9) [0.0, 10.5]
Any creatine phosphokinase (CPK) elevation	2 (8.4) [1.0, 30.5]	2 (4.9) [0.6, 17.6]	3 (6.5) [1.3, 18.9]	4 (7.6) [2.1, 19.3]	5 (9.4) [3.1, 22.0]
Any hepatic disorder	2 (8.4) [1.0, 30.5]	10 (24.3) [11.7, 44.8]	4 (8.6) [2.3, 22.0]	11 (20.8) [10.4, 37.2]	4 (7.5) [2.1, 19.3]
Any renal dysfunction	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=75)	UPA 15 mg QD (N=143)	UPA 30 mg QD (N=166)	UPA 15 mg QD (N=188)	UPA 30 mg QD (N=189)
Subgroup: >= 9 - < 12 Month					
Exposure-adjusted event rate:	(PYs=15.7) Events (E/100PYs) [95% CI]	(PYs=29.9) Events (E/100PYs) [95% CI]	(PYs=35.4) Events (E/100PYs) [95% CI]	(PYs=41.7) Events (E/100PYs) [95% CI]	(PYs=40.5) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	0	0	0	0	0
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	0	0
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	2 (6.7) [0.8, 24.2]	2 (5.6) [0.7, 20.4]	3 (7.2) [1.5, 21.0]	3 (7.4) [1.5, 21.7]
Any adjudicated gastrointestinal perforations	0	0	0	0	0
Any anemia	1 (6.4) [0.2, 35.5]	0	1 (2.8) [0.1, 15.7]	0	1 (2.5) [0.1, 13.8]
Any neutropenia	0	0	2 (5.6) [0.7, 20.4]	0	2 (4.9) [0.6, 17.9]

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=75)	UPA 15 mg QD (N=143)	UPA 30 mg QD (N=166)	UPA 15 mg QD (N=188)	UPA 30 mg QD (N=189)
Subgroup: >= 9 - < 12 Month (Cont.)					
Any lymphopenia	0	0	1 (2.8) [0.1, 15.7]	0	2 (4.9) [0.6, 17.9]
Any creatine phosphokinase (CPK) elevation	0	1 (3.3) [0.1, 18.6]	2 (5.6) [0.7, 20.4]	2 (4.8) [0.6, 17.3]	3 (7.4) [1.5, 21.7]
Any hepatic disorder	1 (6.4) [0.2, 35.5]	4 (13.4) [3.6, 34.2]	3 (8.5) [1.7, 24.7]	4 (9.6) [2.6, 24.6]	4 (9.9) [2.7, 25.3]
Any renal dysfunction	0	1 (3.3) [0.1, 18.6]	0	1 (2.4) [0.1, 13.4]	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=21)	UPA 15 mg QD (N=45)	UPA 30 mg QD (N=51)	UPA 15 mg QD (N=122)	UPA 30 mg QD (N=137)
Subgroup: >= 12 - < 15 Month					
Exposure-adjusted event rate:	(PYs=0.4)	(PYs=0.6)	(PYs=1.0)	(PYs=24.1)	(PYs=29.7)
	Events (E/100PYs) [95% CI]	Events (E/100PYs) [95% CI]	Events (E/100PYs) [95% CI]	Events (E/100PYs) [95% CI]	Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	0	0	0	1 (4.2) [0.1, 23.1]	0
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	0	0
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	0	0	4 (16.6) [4.5, 42.5]	1 (3.4) [0.1, 18.8]
Any adjudicated gastrointestinal perforations	0	0	0	0	0
Any anemia	0	0	1 (97.1) [2.5, 541.2]	0	6 (20.2) [7.4, 44.0]
Any neutropenia	0	0	0	3 (12.5) [2.6, 36.4]	3 (10.1) [2.1, 29.6]

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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=21)	UPA 15 mg QD (N=45)	UPA 30 mg QD (N=51)	UPA 15 mg QD (N=122)	UPA 30 mg QD (N=137)
Subgroup: >= 12 - < 15 Month (Cont.)					
Any lymphopenia	0	0	0	1 (4.2) [0.1, 23.1]	1 (3.4) [0.1, 18.8]
Any creatine phosphokinase (CPK) elevation	0	0	0	2 (8.3) [1.0, 30.0]	6 (20.2) [7.4, 44.0]
Any hepatic disorder	0	0	0	4 (16.6) [4.5, 42.5]	5 (16.9) [5.5, 39.3]
Any renal dysfunction	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=0)	UPA 15 mg QD (N=0)	UPA 30 mg QD (N=0)	UPA 15 mg QD (N=80)	UPA 30 mg QD (N=103)
Subgroup: >= 15 - < 18 Month					
Exposure-adjusted event rate:	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=17.3) Events (E/100PYs) [95% CI]	(PYs=21.4) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	0	0	0	1 (5.8) [0.1, 32.3]	2 (9.3) [1.1, 33.7]
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	0	0
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	0	0	0	1 (4.7) [0.1, 26.0]
Any adjudicated gastrointestinal perforations	0	0	0	0	0
Any anemia	0	0	0	1 (5.8) [0.1, 32.3]	0
Any neutropenia	0	0	0	0	2 (9.3) [1.1, 33.7]

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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=0)	UPA 15 mg QD (N=0)	UPA 30 mg QD (N=0)	UPA 15 mg QD (N=80)	UPA 30 mg QD (N=103)
Subgroup: >= 15 - < 18 Month (Cont.)					
Any lymphopenia	0	0	0	0	0
Any creatine phosphokinase (CPK) elevation	0	0	0	0	1 (4.7) [0.1, 26.0]
Any hepatic disorder	0	0	0	2 (11.6) [1.4, 41.9]	0
Any renal dysfunction	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=0)	UPA 15 mg QD (N=0)	UPA 30 mg QD (N=0)	UPA 15 mg QD (N=58)	UPA 30 mg QD (N=70)
Subgroup: >= 18 - < 21 Month					
Exposure-adjusted event rate:	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=12.6) Events (E/100PYs) [95% CI]	(PYs=13.6) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	0	0	0	0	2 (14.7) [1.8, 52.9]
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	0	0
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	0	0	0	2 (14.7) [1.8, 52.9]
Any adjudicated gastrointestinal perforations	0	0	0	0	0
Any anemia	0	0	0	0	0
Any neutropenia	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=0)	UPA 15 mg QD (N=0)	UPA 30 mg QD (N=0)	UPA 15 mg QD (N=58)	UPA 30 mg QD (N=70)
Subgroup: >= 18 - < 21 Month (Cont.)					
Any lymphopenia	0	0	0	0	0
Any creatine phosphokinase (CPK) elevation	0	0	0	0	0
Any hepatic disorder	0	0	0	0	0
Any renal dysfunction	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=0)	UPA 15 mg QD (N=0)	UPA 30 mg QD (N=0)	UPA 15 mg QD (N=41)	UPA 30 mg QD (N=40)
Subgroup: >= 21 - < 24 Month					
Exposure-adjusted event rate:	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=7.8) Events (E/100PYs) [95% CI]	(PYs=6.8) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	0	0	0	1 (12.9) [0.3, 71.9]	0
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	0	0
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	0	0	1 (12.9) [0.3, 71.9]	0
Any adjudicated gastrointestinal perforations	0	0	0	0	0
Any anemia	0	0	0	0	0
Any neutropenia	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=0)	UPA 15 mg QD (N=0)	UPA 30 mg QD (N=0)	UPA 15 mg QD (N=41)	UPA 30 mg QD (N=40)
Subgroup: >= 21 - < 24 Month (Cont.)					
Any lymphopenia	0	0	0	0	0
Any creatine phosphokinase (CPK) elevation	0	0	0	1 (12.9) [0.3, 71.9]	0
Any hepatic disorder	0	0	0	1 (12.9) [0.3, 71.9]	0
Any renal dysfunction	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=0)	UPA 15 mg QD (N=0)	UPA 30 mg QD (N=0)	UPA 15 mg QD (N=24)	UPA 30 mg QD (N=16)
Subgroup: >= 24 Month					
Exposure-adjusted event rate:	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=24.8) Events (E/100PYs) [95% CI]	(PYs=5.7) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any serious infections	0	0	0	0	0
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	0	0
Any active tuberculosis	0	0	0	0	0
Any herpes zoster	0	0	0	0	0
Any adjudicated gastrointestinal perforations	0	0	0	0	0
Any anemia	0	0	0	3 (12.1) [2.5, 35.4]	0
Any neutropenia	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.
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.

Program Source Code: [redacted]

TABLE 2.4 6.1.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=0)	UPA 15 mg QD (N=0)	UPA 30 mg QD (N=0)	UPA 15 mg QD (N=24)	UPA 30 mg QD (N=16)
Subgroup: >= 24 Month (Cont.)					
Any lymphopenia	0	0	0	2 (8.1) [1.0, 29.2]	1 (17.4) [0.4, 96.9]
Any creatine phosphokinase (CPK) elevation	0	0	0	0	0
Any hepatic disorder	0	0	0	0	0
Any renal dysfunction	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.
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.

Program Source Code: [redacted]

TABLE 2.4 3.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		
	Placebo QD (N=245) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 15 mg QD (N=250) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 30 mg QD (N=251) n/PYs (n/100 PYs) [SSA n/100 PYs]
Any serious infections	8/125.9 (6.4) [6.3]	8/178.5 (4.5) [4.5]	6/197.3 (3.0) [3.1]
Any opportunistic infection excluding tuberculosis and herpes zoster	2/127.7 (1.6) [1.7]	2/182.1 (1.1) [1.0]	1/198.6 (0.5) [0.5]
Any active tuberculosis	0/128.1	0/182.4	0/198.7
Any herpes zoster	0/128.1	11/178.1 (6.2) [6.0]	10/194.4 (5.1) [5.1]
Any adjudicated gastrointestinal perforations	1/128.1 (0.8) [0.8]	0/182.4	0/198.7
Any anemia	15/121.4 (12.4) [12.1]	10/175.7 (5.7) [5.8]	8/195.3 (4.1) [4.1]
Any neutropenia	5/125.4 (4.0) [3.9]	7/178.6 (3.9) [3.9]	15/189.8 (7.9) [7.9]
Any lymphopenia	4/126.2 (3.2) [3.0]	6/179.3 (3.3) [3.4]	5/196.9 (2.5) [2.5]
Any creatine phosphokinase (CPK) elevation	5/126.3 (4.0) [4.2]	14/174.0 (8.0) [8.1]	19/187.8 (10.1) [10.2]
Any hepatic disorder	5/125.5 (4.0) [4.0]	17/174.3 (9.8) [9.9]	12/193.6 (6.2) [6.2]
Any renal dysfunction	1/128.1 (0.8) [0.8]	1/182.4 (0.5) [0.5]	1/198.7 (0.5) [0.5]
Any malignancy	1/128.1 (0.8) [0.8]	1/182.4 (0.5) [0.6]	5/198.0 (2.5) [2.5]
Any malignancies excluding non-melanoma skin cancer (NMSC)	1/128.1 (0.8) [0.8]	1/182.4 (0.5) [0.6]	2/198.7 (1.0) [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.
n/100PYs = Number of subjects 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.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set)

	---M14-234 Substudy 3 (Cohorts 1 and 3) [B]--- UPA 15 mg QD (N=285) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 30 mg QD (N=291) n/PYs (n/100 PYs) [SSA n/100 PYs]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
Any serious infections	12/307.4 (3.9) [3.9]	12/299.3 (4.0) [3.8]	-1.9 (-7.3, 3.5)	-3.3 (-8.3, 1.8)
Any opportunistic infection excluding tuberculosis and herpes zoster	2/316.1 (0.6) [0.6]	1/303.9 (0.3) [0.3]	-0.7 (-3.4, 2.1)	-1.2 (-3.7, 1.4)
Any active tuberculosis	0/316.9	0/304.0	0.0	0.0
Any herpes zoster	18/296.4 (6.1) [6.0]	16/293.2 (5.5) [5.3]	6.0 (2.5, 9.6)	5.1 (2.0, 8.3)
Any adjudicated gastrointestinal perforations	0/316.9	0/304.0	-0.8 (-2.5, 0.8)	-0.8 (-2.5, 0.8)
Any anemia	16/303.9 (5.3) [5.5]	15/293.9 (5.1) [5.1]	-6.3 (-13.5, 0.8)	-8.1 (-14.8, -1.3)
Any neutropenia	11/306.1 (3.6) [3.6]	20/287.1 (7.0) [6.7]	0.0 (-4.5, 4.5)	4.0 (-1.3, 9.3)
Any lymphopenia	9/310.8 (2.9) [2.9]	7/300.7 (2.3) [2.7]	0.3 (-3.7, 4.4)	-0.5 (-4.2, 3.2)
Any creatine phosphokinase (CPK) elevation	18/292.1 (6.2) [6.2]	28/284.5 (9.8) [9.5]	3.9 (-1.7, 9.5)	6.0 (0.2, 11.9)
Any hepatic disorder	22/296.0 (7.4) [7.7]	18/293.0 (6.1) [6.1]	5.9 (-0.0, 11.8)	2.1 (-2.8, 7.1)
Any renal dysfunction	1/316.9 (0.3) [0.3]	1/304.0 (0.3) [0.3]	-0.3 (-2.3, 1.6)	-0.3 (-2.3, 1.6)
Any malignancy	1/316.9 (0.3) [0.3]	8/300.2 (2.7) [2.7]	-0.3 (-2.3, 1.8)	1.7 (-1.1, 4.5)
Any malignancies excluding non-melanoma skin cancer (NMSC)	1/316.9 (0.3) [0.3]	3/303.9 (1.0) [1.1]	-0.3 (-2.3, 1.8)	0.2 (-2.0, 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.
n/100PYs = Number of subjects 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.

[C] Study-size adjusted risk differences between treatment groups.

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		
	Placebo QD (N=245) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 15 mg QD (N=250) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 30 mg QD (N=251) n/PYs (n/100 PYs) [SSA n/100 PYs]
Any NMSC	0/128.1	0/182.4	3/198.1 (1.5) [1.5]
Any lymphoma	0/128.1	0/182.4	0/198.7
Any adjudicated MACE *	1/128.1 (0.8) [0.7]	0/182.4	1/197.9 (0.5) [0.5]
Any adjudicated VTE **	0/128.1	2/182.1 (1.1) [1.1]	2/198.7 (1.0) [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.
n/100PYs = Number of subjects 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.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set)

	---M14-234 Substudy 3 (Cohorts 1 and 3) [B]---		Differences [C] Cohort 1	
	UPA 15 mg QD (N=285) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 30 mg QD (N=291) n/PYs (n/100 PYs) [SSA n/100 PYs]	15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
Any NMSC	0/316.9	5/300.3 (1.7) [1.6]	0.0	1.5 (-0.2, 3.3)
Any lymphoma	0/316.9	0/304.0	0.0	0.0
Any adjudicated MACE *	0/316.9	2/301.5 (0.7) [0.6]	-0.7 (-2.1, 0.7)	-0.2 (-1.9, 1.5)
Any adjudicated VTE **	3/313.3 (1.0) [0.9]	2/303.9 (0.7) [0.6]	1.1 (-0.4, 2.7)	1.0 (-0.4, 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.
n/100PYs = Number of subjects 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.

[C] Study-size adjusted risk differences between treatment groups.

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-53.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 3.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		
	Placebo QD (N=41) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 15 mg QD (N=45) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 30 mg QD (N=45) n/PYs (n/100 PYs) [SSA n/100 PYs]
Any serious infections	2/21.4 (9.3) [9.1]	2/36.9 (5.4) [6.3]	1/36.9 (2.7) [2.9]
Any opportunistic infection excluding tuberculosis and herpes zoster	1/21.9 (4.6) [4.8]	0/37.8	0/37.1
Any active tuberculosis	0/21.9	0/37.8	0/37.1
Any herpes zoster	0/21.9	4/36.9 (10.9) [10.5]	3/36.7 (8.2) [8.4]
Any adjudicated gastrointestinal perforations	0/21.9	0/37.8	0/37.1
Any anemia	4/20.6 (19.4) [19.0]	1/36.9 (2.7) [3.1]	3/35.3 (8.5) [8.6]
Any neutropenia	2/20.8 (9.6) [9.4]	1/37.2 (2.7) [3.0]	8/32.8 (24.4) [24.5]
Any lymphopenia	1/21.6 (4.6) [4.3]	0/37.8	2/37.0 (5.4) [5.4]
Any creatine phosphokinase (CPK) elevation	1/21.6 (4.6) [4.3]	5/34.2 (14.6) [15.3]	6/33.2 (18.1) [18.4]
Any hepatic disorder	1/21.3 (4.7) [8.8]	5/35.1 (14.2) [15.4]	3/35.6 (8.4) [8.6]
Any renal dysfunction	0/21.9	0/37.8	1/37.1 (2.7) [2.5]
Any malignancy	0/21.9	0/37.8	1/37.1 (2.7) [2.5]
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/21.9	0/37.8	1/37.1 (2.7) [2.5]

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.
n/100PYs = Number of subjects 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.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set - Japan Analysis Set)

	---M14-234 Substudy 3 (Cohorts 1 and 3) [B]---		Differences [C] Cohort 1	
	UPA 15 mg QD (N=46) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 30 mg QD (N=54) n/PYs (n/100 PYs) [SSA n/100 PYs]	15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
Any serious infections	2/59.9 (3.3) [4.1]	4/57.5 (7.0) [6.5]	-2.9 (-18.2, 12.5)	-6.2 (-20.1, 7.7)
Any opportunistic infection excluding tuberculosis and herpes zoster	0/60.8	0/59.0	-4.8 (-14.1, 4.6)	-4.8 (-14.1, 4.6)
Any active tuberculosis	0/60.8	0/59.0	0.0	0.0
Any herpes zoster	5/52.7 (9.5) [8.9]	6/56.7 (10.6) [10.0]	10.5 (0.2, 20.9)	8.4 (-1.1, 17.9)
Any adjudicated gastrointestinal perforations	0/60.8	0/59.0	0.0	0.0
Any anemia	2/58.9 (3.4) [4.4]	3/55.3 (5.4) [6.8]	-15.9 (-35.4, 3.7)	-10.4 (-31.4, 10.6)
Any neutropenia	2/58.3 (3.4) [4.1]	11/50.7 (21.7) [19.6]	-6.4 (-20.8, 8.0)	15.1 (-6.4, 36.6)
Any lymphopenia	0/60.8	3/58.1 (5.2) [6.1]	-4.3 (-12.6, 4.1)	1.1 (-10.1, 12.4)
Any creatine phosphokinase (CPK) elevation	5/49.0 (10.2) [10.3]	8/53.1 (15.1) [15.2]	11.0 (-4.8, 26.9)	14.2 (-2.8, 31.2)
Any hepatic disorder	6/52.9 (11.4) [12.2]	4/56.1 (7.1) [6.7]	6.5 (-15.5, 28.5)	-0.2 (-20.1, 19.7)
Any renal dysfunction	0/60.8	1/59.1 (1.7) [1.4]	0.0	2.5 (-2.4, 7.5)
Any malignancy	0/60.8	1/59.1 (1.7) [1.4]	0.0	2.5 (-2.4, 7.5)
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/60.8	1/59.1 (1.7) [1.4]	0.0	2.5 (-2.4, 7.5)

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.
n/100PYs = Number of subjects 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.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set - Japan Analysis Set)

	M14-234 Substudy 3 (Cohort 1) [A]		
	Placebo QD (N=41) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 15 mg QD (N=45) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 30 mg QD (N=45) n/PYs (n/100 PYs) [SSA n/100 PYs]
Any NMSC	0/21.9	0/37.8	0/37.1
Any lymphoma	0/21.9	0/37.8	0/37.1
Any adjudicated MACE *	0/21.9	0/37.8	1/36.3 (2.8) [3.0]
Any adjudicated VTE **	0/21.9	0/37.8	0/37.1

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.
n/100PYs = Number of subjects 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.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 3.2.3 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(Responders Maintenance Analysis Set - Japan Analysis Set)

	---M14-234 Substudy 3 (Cohorts 1 and 3) [B]---		Differences [C] Cohort 1	
	UPA 15 mg QD (N=46) n/PYs (n/100 PYs) [SSA n/100 PYs]	UPA 30 mg QD (N=54) n/PYs (n/100 PYs) [SSA n/100 PYs]	15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
Any NMSC	0/60.8	0/59.0	0.0	0.0
Any lymphoma	0/60.8	0/59.0	0.0	0.0
Any adjudicated MACE *	0/60.8	1/58.3 (1.7) [1.8]	0.0	3.0 (-2.8, 8.8)
Any adjudicated VTE **	0/60.8	0/59.0	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.
n/100PYs = Number of subjects 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.
[C] Study-size adjusted risk differences between treatment groups.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-54.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.2.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set)

	Induction = PBO [A]	Induction Dose < 45 mg QD [B]	
	PBO (N=378) n/PYs (n/100 PYs)	UPA 15-30 mg / PBO (N=36) n/PYs (n/100 PYs)	UPA < 45 mg / <= 30 mg (N=281) n/PYs (n/100 PYs)
Any serious infections	8/118.1 (6.8)	2/105.5 (1.9)	21/553.1 (3.8)
Any opportunistic infection excluding tuberculosis and herpes zoster	1/120.5 (0.8)	0/108.2	2/580.0 (0.3)
Any active tuberculosis	0/120.5	0/108.2	1/586.0 (0.2)
Any herpes zoster	0/120.5	3/102.2 (2.9)	17/560.0 (3.0)
Any adjudicated gastrointestinal perforations	1/120.5 (0.8)	0/108.2	1/585.1 (0.2)
Any anemia	29/114.5 (25.3)	7/90.6 (7.7)	26/549.7 (4.7)
Any neutropenia	2/119.9 (1.7)	1/106.2 (0.9)	11/574.5 (1.9)
Any lymphopenia	4/119.5 (3.3)	1/105.1 (1.0)	15/564.7 (2.7)
Any creatine phosphokinase (CPK) elevation	6/118.4 (5.1)	9/86.3 (10.4)	21/546.8 (3.8)
Any hepatic disorder	13/114.0 (11.4)	4/98.4 (4.1)	24/543.3 (4.4)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set)

	Induction Dose = 45 mg QD [C]				
	UPA 45 mg / NM (N=129) n/PYs (n/100 PYs)	UPA 45 mg / PBO (N=245) n/PYs (n/100 PYs)	UPA 45 mg / 15 mg (N=306) n/PYs (n/100 PYs)	UPA 45 mg / 30 mg (N=307) n/PYs (n/100 PYs)	Any UPA (N=1304) n/PYs (n/100 PYs)
Any serious infections	3/23.8 (12.6)	13/350.9 (3.7)	20/447.7 (4.5)	18/433.9 (4.1)	69/1756.9 (3.9)
Any opportunistic infection excluding tuberculosis and herpes zoster	2/23.8 (8.4)	2/358.5 (0.6)	2/464.4 (0.4)	2/442.7 (0.5)	8/1812.5 (0.4)
Any active tuberculosis	0/24.1	0/358.9	0/466.1	0/443.4	1/1821.1 (<0.1)
Any herpes zoster	7/23.7 (29.5)	7/350.5 (2.0)	27/436.9 (6.2)	18/427.8 (4.2)	78/1739.8 (4.5)
Any adjudicated gastrointestinal perforations	0/24.1	1/358.9 (0.3)	0/466.1	0/443.4	1/1820.1 (<0.1)
Any anemia	17/22.3 (76.4)	27/334.5 (8.1)	30/436.5 (6.9)	25/423.5 (5.9)	119/1713.3 (6.9)
Any neutropenia	4/23.7 (16.9)	16/339.8 (4.7)	24/433.8 (5.5)	30/411.6 (7.3)	85/1736.9 (4.9)
Any lymphopenia	3/24.1 (12.5)	11/339.4 (3.2)	15/441.7 (3.4)	13/431.2 (3.0)	55/1750.1 (3.1)
Any creatine phosphokinase (CPK) elevation	8/23.5 (34.0)	22/333.5 (6.6)	35/416.4 (8.4)	49/384.3 (12.8)	138/1648.1 (8.4)
Any hepatic disorder	4/23.5 (17.0)	17/342.3 (5.0)	33/425.4 (7.8)	29/404.4 (7.2)	106/1686.6 (6.3)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set)

	Induction = PBO [A]	Induction Dose < 45 mg QD [B]	
	PBO (N=378) n/PYs (n/100 PYs)	UPA 15-30 mg / PBO (N=36) n/PYs (n/100 PYs)	UPA < 45 mg / <= 30 mg (N=281) n/PYs (n/100 PYs)
Any renal dysfunction	0/120.5	0/108.2	1/583.6 (0.2)
Any malignancy	0/120.5	3/106.2 (2.8)	4/583.8 (0.7)
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/120.5	2/108.1 (1.8)	3/584.4 (0.5)
Any NMSC	0/120.5	2/106.3 (1.9)	2/585.2 (0.3)
Any lymphoma	0/120.5	0/108.2	0/586.0
Any adjudicated MACE *	0/120.5	0/108.2	1/585.5 (0.2)
Any adjudicated VTE **	1/120.5 (0.8)	1/107.3 (0.9)	4/582.2 (0.7)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set)

	Induction Dose = 45 mg QD [C]				
	UPA 45 mg / NM (N=129)	UPA 45 mg / PBO (N=245)	UPA 45 mg / 15 mg (N=306)	UPA 45 mg / 30 mg (N=307)	Any UPA (N=1304)
	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)
Any renal dysfunction	0/24.1	1/358.9 (0.3)	3/462.8 (0.6)	1/443.4 (0.2)	5/1815.4 (0.3)
Any malignancy	0/24.1	4/356.1 (1.1)	2/466.1 (0.4)	9/439.6 (2.0)	21/1812.4 (1.2)
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/24.1	2/358.6 (0.6)	2/466.1 (0.4)	4/443.3 (0.9)	12/1820.5 (0.7)
Any NMSC	0/24.1	2/356.4 (0.6)	0/466.1	5/439.7 (1.1)	11/1812.8 (0.6)
Any lymphoma	0/24.1	0/358.9	0/466.1	0/443.4	0/1821.1
Any adjudicated MACE *	0/24.1	1/358.9 (0.3)	0/466.1	3/440.9 (0.7)	4/1818.0 (0.2)
Any adjudicated VTE **	1/24.1 (4.1)	0/358.9	3/462.5 (0.6)	2/443.3 (0.5)	11/1813.1 (0.6)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-55.

[redacted]20[redacted] 16:56 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 6.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Event Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	----Induction Dose = 45 mg QD [A]---- UPA 45 mg / 15 mg - 30 mg (N=103) (PYs=158.7) Events (E/100 PYs)
Any serious infections	7 (4.4)
Any opportunistic infection excluding tuberculosis and herpes zoster	1 (0.6)
Any active tuberculosis	0
Any herpes zoster	14 (8.8)
Any adjudicated gastrointestinal perforations	0
Any anemia	9 (5.7)
Any neutropenia	30 (18.9)
Any lymphopenia	8 (5.0)
Any creatine phosphokinase (CPK) elevation	26 (16.4)
Any hepatic disorder	28 (17.6)
Any renal dysfunction	2 (1.3)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100 PYs = Events per 100 patient-years.
UPA = Upadacitinib.
[A] Includes all subjects who received at least one dose of 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 2.7.4.7-56.

[redacted]20[redacted] 16:56 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	Induction = PBO [A]	Induction Dose < 45 mg QD [B]	
	PBO (N=56) n/PYs (n/100 PYs)	UPA 15-30 mg / PBO (N=3) n/PYs (n/100 PYs)	UPA < 45 mg / <= 30 mg (N=29) n/PYs (n/100 PYs)
Any serious infections	0/16.7	2/5.1 (39.1)	1/64.9 (1.5)
Any opportunistic infection excluding tuberculosis and herpes zoster	0/16.7	0/7.8	0/66.1
Any active tuberculosis	0/16.7	0/7.8	0/66.1
Any herpes zoster	0/16.7	1/5.4 (18.4)	4/63.6 (6.3)
Any adjudicated gastrointestinal perforations	0/16.7	0/7.8	0/66.1
Any anemia	4/16.6 (24.2)	1/3.5 (28.6)	1/65.5 (1.5)
Any neutropenia	0/16.7	0/7.8	2/60.8 (3.3)
Any lymphopenia	1/16.5 (6.1)	0/7.8	2/62.7 (3.2)
Any creatine phosphokinase (CPK) elevation	0/16.7	2/1.6 (121.8)	2/62.8 (3.2)
Any hepatic disorder	1/16.7 (6.0)	0/7.8	5/55.3 (9.0)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	Induction Dose = 45 mg QD [C]				
	UPA 45 mg / NM (N=16)	UPA 45 mg / PBO (N=41)	UPA 45 mg / 15 mg (N=49)	UPA 45 mg / 30 mg (N=54)	Any UPA (N=192)
	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)
Any serious infections	1/2.5 (40.8)	3/59.6 (5.0)	3/82.0 (3.7)	4/73.6 (5.4)	11/265.4 (4.1)
Any opportunistic infection excluding tuberculosis and herpes zoster	0/2.5	1/61.4 (1.6)	0/83.5	1/74.6 (1.3)	1/271.1 (0.4)
Any active tuberculosis	0/2.5	0/61.4	0/83.5	0/75.2	0/271.7
Any herpes zoster	3/2.5 (120.8)	1/61.1 (1.6)	6/72.9 (8.2)	6/72.9 (8.2)	20/254.2 (7.9)
Any adjudicated gastrointestinal perforations	0/2.5	0/61.4	0/83.5	0/75.2	0/271.7
Any anemia	1/2.5 (40.2)	5/58.0 (8.6)	5/79.2 (6.3)	4/71.0 (5.6)	14/258.8 (5.4)
Any neutropenia	2/2.2 (92.1)	4/54.3 (7.4)	7/71.7 (9.8)	16/59.5 (26.9)	31/234.4 (13.2)
Any lymphopenia	1/2.4 (41.1)	3/55.1 (5.4)	3/75.9 (4.0)	5/72.7 (6.9)	13/254.6 (5.1)
Any creatine phosphokinase (CPK) elevation	2/2.3 (85.7)	4/57.2 (7.0)	10/64.8 (15.4)	9/65.4 (13.8)	28/232.6 (12.0)
Any hepatic disorder	1/2.4 (41.6)	3/56.4 (5.3)	9/70.4 (12.8)	6/67.1 (8.9)	24/236.2 (10.2)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	Induction = PBO [A]	Induction Dose < 45 mg QD [B]	
	PBO (N=56) n/PYs (n/100 PYs)	UPA 15-30 mg / PBO (N=3) n/PYs (n/100 PYs)	UPA < 45 mg / <= 30 mg (N=29) n/PYs (n/100 PYs)
Any renal dysfunction	0/16.7	0/7.8	1/63.7 (1.6)
Any malignancy	0/16.7	0/7.8	0/66.1
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/16.7	0/7.8	0/66.1
Any NMSC	0/16.7	0/7.8	0/66.1
Any lymphoma	0/16.7	0/7.8	0/66.1
Any adjudicated MACE *	0/16.7	0/7.8	0/66.1
Any adjudicated VTE **	0/16.7	0/7.8	0/66.1

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

TABLE 2.4 4.2.2 J

Overview of Treatment-Emergent Adverse Events of Special Interest in Exposure-Adjusted Incidence Rate per 100 Patient Years
(All Treated [SUBJ] Analysis Set - Japan Analysis Set)

	Induction Dose = 45 mg QD [C]				
	UPA 45 mg / NM (N=16)	UPA 45 mg / PBO (N=41)	UPA 45 mg / 15 mg (N=49)	UPA 45 mg / 30 mg (N=54)	Any UPA (N=192)
	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)
Any renal dysfunction	0/2.5	0/61.4	1/81.3 (1.2)	1/75.2 (1.3)	3/267.0 (1.1)
Any malignancy	0/2.5	0/61.4	0/83.5	1/75.2 (1.3)	1/271.7 (0.4)
Any malignancies excluding non-melanoma skin cancer (NMSC)	0/2.5	0/61.4	0/83.5	1/75.2 (1.3)	1/271.7 (0.4)
Any NMSC	0/2.5	0/61.4	0/83.5	0/75.2	0/271.7
Any lymphoma	0/2.5	0/61.4	0/83.5	0/75.2	0/271.7
Any adjudicated MACE *	0/2.5	0/61.4	0/83.5	1/74.4 (1.3)	1/270.9 (0.4)
Any adjudicated VTE **	0/2.5	0/61.4	0/83.5	0/75.2	0/271.7

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
NM = Subject did not receive any dose of study drug during maintenance or long-term extension.
PBO = Placebo; UPA = Upadacitinib.

[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.

[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).

[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

** VTE: Venous Thromboembolic Events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) (fatal and non-fatal).

Program Source Code: [redacted]

表 2.7.4.7-57.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.2

Treatment-Emergent Opportunistic Infections Excluding Tuberculosis and Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	1 (0.8)	0	2 (0.3)
感染症および寄生虫症	1 (0.8)	0	2 (0.3)
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
食道カンジダ症	0	0	0
口腔真菌感染	0	0	1 (0.2)
ニューモシスチス・イロベチイ感染	0	0	1 (0.2)
ニューモシスチス・イロベチイ肺炎	0	0	0
クリプトコッカス性肺炎	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 4.4.1.2

Treatment-Emergent Opportunistic Infections Excluding Tuberculosis and Herpes Zoster
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	2 (8.3)	2 (0.6)	2 (0.4)	2 (0.5)	8 (0.4)
感染症および寄生虫症	2 (8.3)	2 (0.6)	2 (0.4)	2 (0.5)	8 (0.4)
サイトメガロウイルス性大腸炎	0	0	0	1 (0.2)	1 (<0.1)
サイトメガロウイルス感染	1 (4.2)	1 (0.3)	1 (0.2)	0	2 (0.1)
食道カンジダ症	0	0	1 (0.2)	0	1 (<0.1)
口腔真菌感染	1 (4.2)	0	0	0	2 (0.1)
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 (0.3)	0	0	0
クリプトコッカス性肺炎	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]

表 2.7.4.7-58.

[redacted]20[redacted] 10:52 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 2.4.4

Treatment-Emergent Herpes Zoster in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Extended Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mgQD (N=127) End of DB Induction[1] (Week 8) (PYs=20.0) Events(E/100 PYs)	UPA 45 mgQD (N=127) End of OL Extended Induction[2] (Week 16) (PYs=39.1) Events(E/100 PYs)
Any adverse event	1 (5.0)	6 (15.3)
感染症および寄生虫症	1 (5.0)	6 (15.3)
帯状疱疹	1 (5.0)	6 (15.3)

Note: E/100 PYs = Number of events per 100 patient-years.
Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the induction period (Part 2) or until one day prior to the first dose of study drug in any subsequent maintenance or long-term extension period.
PYs is defined as the sum of the study drug duration of all subjects in the respective time periods (8-week induction period [for Week 8], and 8-week induction period plus 8-week extended period [for Week 16]) normalized by 365.25.
[1] All events and exposure time from Part 1 induction studies (for the extended induction analysis set).
[2] All events and exposure time from Parts 1 and 2 induction studies (for the extended induction analysis set).
DB = double blind. OL = open label.

Program Source Code: [redacted]

表 2.7.4.7-59.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 2.4 4.4.1.4

Treatment-Emergent Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	0	4 (3.7)	18 (3.1)
感染症および寄生虫症	0	4 (3.7)	18 (3.1)
帯状疱疹	0	4 (3.7)	17 (2.9)
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 (0.2)
帯状疱疹性髄膜炎	0	0	0
耳帯状疱疹	0	0	0
水痘帯状疱疹ウイルス感染	0	0	0
神経系障害	0	0	0
ヘルペス後神経痛	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 4.4.1.4

Treatment-Emergent Herpes Zoster
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	8 (33.2)	8 (2.2)	30 (6.4)	22 (5.0)	88 (4.8)
感染症および寄生虫症	7 (29.1)	8 (2.2)	30 (6.4)	21 (4.7)	86 (4.7)
帯状疱疹	7 (29.1)	7 (2.0)	28 (6.0)	20 (4.5)	81 (4.4)
播種性帯状疱疹	0	1 (0.3)	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)
水痘帯状疱疹ウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
神経系障害	1 (4.2)	0	0	1 (0.2)	2 (0.1)
ヘルペス後神経痛	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]

表 2.7.4.7-60.

[redacted]20[redacted] 11:08 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 1.4.1.10

Number and Percentage of Subjects with Treatment-Emergent Hepatic Disorders
by Primary MedDRA System Organ Class and Preferred Term
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
Any adverse event	9 (2.4) [2.4]	25 (3.5) [3.6]
肝胆道系障害	2 (0.5) [0.5]	3 (0.4) [0.4]
胆汁うっ滞	1 (0.3) [0.3]	0
薬物性肝障害	0	1 (0.1) [0.2]
肝機能異常	0	2 (0.3) [0.3]
高ビリルビン血症	1 (0.3) [0.3]	0
臨床検査	8 (2.1) [2.1]	22 (3.1) [3.2]
アラニンアミノトランスフェラーゼ増加	4 (1.1) [1.0]	7 (1.0) [1.0]
アスパラギン酸アミノトランスフェラーゼ増加	5 (1.3) [1.3]	13 (1.8) [1.9]
血中ビリルビン増加	0	4 (0.6) [0.6]
血中非抱合ビリルビン増加	0	1 (0.1) [0.1]
γ-グルタミルトランスフェラーゼ増加	5 (1.3) [1.3]	2 (0.3) [0.3]
肝酵素上昇	0	2 (0.3) [0.3]
肝機能検査値上昇	1 (0.3) [0.3]	0
トランスアミナーゼ上昇	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
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]

表 2.7.4.7-61.

[redacted]20[redacted] 10:52 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 2.4.10

Treatment-Emergent Hepatic Disorders in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Extended Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mgQD (N=127) End of DB Induction[1] (Week 8) (PYs=20.0) Events(E/100 PYs)	UPA 45 mgQD (N=127) End of OL Extended Induction[2] (Week 16) (PYs=39.1) Events(E/100 PYs)
Any adverse event	4 (20.0)	9 (23.0)
臨床検査	4 (20.0)	9 (23.0)
アラニンアミノトランスフェラーゼ増加	2 (10.0)	3 (7.7)
アスパラギン酸アミノトランスフェラーゼ増加	1 (5.0)	2 (5.1)
肝酵素上昇	1 (5.0)	4 (10.2)

Note: E/100 PYs = Number of events per 100 patient-years.
Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the induction period (Part 2) or until one day prior to the first dose of study drug in any subsequent maintenance or long-term extension period.
PYs is defined as the sum of the study drug duration of all subjects in the respective time periods (8-week induction period [for Week 8], and 8-week induction period plus 8-week extended period [for Week 16]) normalized by 365.25.
[1] All events and exposure time from Part 1 induction studies (for the extended induction analysis set).
[2] All events and exposure time from Parts 1 and 2 induction studies (for the extended induction analysis set).
DB = double blind. OL = open label.

Program Source Code: [redacted]

表 2.7.4.7-62.

[redacted]20[redacted] 11:17 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 3.4.1.20

Treatment-Emergent Hepatic Disorders 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=128.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events(E/100 PYs) [SSA E/100 PYs]
Any adverse event	7 (5.5) [5.4]	32 (17.5) [17.9]	18 (9.1) [9.1]	41 (12.9) [13.5]	29 (9.5) [9.3]
肝胆道系障害	3 (2.3) [2.3]	6 (3.3) [3.2]	2 (1.0) [1.0]	9 (2.8) [2.9]	3 (1.0) [1.1]
薬物性肝障害	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.3) [0.3]	1 (0.3) [0.3]
肝機能異常	2 (1.6) [1.4]	3 (1.6) [1.5]	0	4 (1.3) [1.2]	1 (0.3) [0.3]
脂肪肝	0	1 (0.5) [0.6]	0	3 (0.9) [1.0]	0
高トランスアミナーゼ血症	0	1 (0.5) [0.5]	0	1 (0.3) [0.3]	0
肝障害	0	0	1 (0.5) [0.5]	0	1 (0.3) [0.5]
肝損傷	1 (0.8) [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 3.4.1.20

Treatment-Emergent Hepatic Disorders 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=128.1)	UPA 15 mg QD (N=250) (PYs=182.4)	UPA 30 mg QD (N=251) (PYs=198.7)	UPA 15 mg QD (N=285) (PYs=316.9)	UPA 30 mg QD (N=291) (PYs=304.0)
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	4 (3.1) [3.1]	26 (14.3) [14.7]	16 (8.1) [8.1]	32 (10.1) [10.7]	26 (8.6) [8.2]
アラニンアミノトランスフェラーゼ増加	1 (0.8) [0.7]	8 (4.4) [4.6]	6 (3.0) [3.0]	9 (2.8) [3.0]	8 (2.6) [2.5]
アスパラギン酸アミノトランスフェラーゼ増加	2 (1.6) [1.6]	9 (4.9) [5.2]	4 (2.0) [2.0]	9 (2.8) [3.0]	6 (2.0) [1.9]
血中ビリルビン増加	0	3 (1.6) [1.6]	3 (1.5) [1.5]	3 (0.9) [1.0]	5 (1.6) [1.7]
γ-グルタミルトランスフェラーゼ増加	1 (0.8) [0.8]	5 (2.7) [2.8]	1 (0.5) [0.5]	9 (2.8) [3.0]	3 (1.0) [0.9]
肝酵素上昇	0	1 (0.5) [0.6]	1 (0.5) [0.5]	1 (0.3) [0.3]	1 (0.3) [0.3]
肝機能検査値上昇	0	0	1 (0.5) [0.5]	0	2 (0.7) [0.6]
トランスアミナーゼ上昇	0	0	0	1 (0.3) [0.3]	1 (0.3) [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.
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 2.7.4.7-63.

[redacted]20[redacted] 10:46 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	25 (20.8)	8 (7.4)	45 (7.7)
肝胆道系障害	5 (4.2)	2 (1.8)	10 (1.7)
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 (0.2)
肝機能異常	0	0	3 (0.5)
脂肪肝	0	2 (1.8)	2 (0.3)
肝炎	0	0	1 (0.2)
肝細胞損傷	0	0	1 (0.2)
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 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	6 (24.9)	29 (8.1)	67 (14.4)	53 (12.0)	199 (10.9)
肝胆道系障害	1 (4.2)	8 (2.2)	12 (2.6)	5 (1.1)	35 (1.9)
胆汁うっ滞	0	0	0	0	0
薬物性肝障害	0	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
肝嚢胞	0	0	0	0	1 (<0.1)
肝機能異常	0	2 (0.6)	6 (1.3)	3 (0.7)	12 (0.7)
脂肪肝	0	1 (0.3)	3 (0.6)	0	8 (0.4)
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 (0.3)	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 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
高ビリルビン血症	2 (1.7)	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 (0.2)
非アルコール性脂肪性肝疾患	0	0	1 (0.2)
臨床検査	20 (16.6)	6 (5.5)	35 (6.0)
アラニンアミノトランスフェラーゼ増加	6 (5.0)	2 (1.8)	10 (1.7)
アスパラギン酸アミノトランスフェラーゼ増加	7 (5.8)	1 (0.9)	10 (1.7)
血中ビリルビン増加	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 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) 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	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
肝損傷	0	1 (0.3)	0	0	0
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 (0.3)	0	0	2 (0.1)
臨床検査	5 (20.8)	21 (5.9)	55 (11.8)	48 (10.8)	164 (9.0)
アラニンアミノトランスフェラーゼ増加	0	5 (1.4)	14 (3.0)	15 (3.4)	44 (2.4)
アスパラギン酸アミノトランスフェラーゼ増加	1 (4.2)	9 (2.5)	16 (3.4)	13 (2.9)	48 (2.6)
血中ビリルビン増加	0	0	7 (1.5)	8 (1.8)	17 (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 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
血中非抱合ビリルビン増加	0	0	0
γ-グルタミルトランスフェラーゼ増加	6 (5.0)	2 (1.8)	2 (0.3)
肝酵素上昇	0	0	9 (1.5)
肝機能検査異常	0	1 (0.9)	0
肝機能検査値上昇	1 (0.8)	0	2 (0.3)
トランスアミナーゼ上昇	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 4.4.1.10

Treatment-Emergent Hepatic Disorders
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
血中非抱合ビリルビン増加	0	0	0	1 (0.2)	1 (<0.1)
γ-グルタミルトランスフェラーゼ増加	0	4 (1.1)	11 (2.4)	4 (0.9)	21 (1.2)
肝酵素上昇	4 (16.6)	1 (0.3)	4 (0.9)	4 (0.9)	22 (1.2)
肝機能検査異常	0	0	0	0	1 (<0.1)
肝機能検査値上昇	0	1 (0.3)	0	2 (0.5)	5 (0.3)
トランスアミナーゼ上昇	0	1 (0.3)	3 (0.6)	1 (0.2)	5 (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]

表 2.7.4.7-64.

[redacted]20[redacted] 11:08 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 1.4.1.6

Number and Percentage of Subjects with Treatment-Emergent Anemia
by Primary MedDRA System Organ Class and Preferred Term
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
Any adverse event	21 (5.6) [5.6]	25 (3.5) [3.4]
血液およびリンパ系障害	18 (4.8) [4.7]	24 (3.3) [3.3]
貧血	16 (4.2) [4.2]	22 (3.1) [3.0]
失血性貧血	0	1 (0.1) [0.1]
鉄欠乏性貧血	1 (0.3) [0.3]	2 (0.3) [0.3]
正球性貧血	1 (0.3) [0.3]	0
臨床検査	3 (0.8) [0.8]	1 (0.1) [0.1]
ヘモグロビン減少	3 (0.8) [0.8]	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
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]

表 2.7.4.7-65.

[redacted]20[redacted] 10:52 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 2.4.6

Treatment-Emergent Anemia in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Extended Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mgQD (N=127) End of DB Induction[1] (Week 8) (PYs=20.0) Events(E/100 PYs)	UPA 45 mgQD (N=127) End of OL Extended Induction[2] (Week 16) (PYs=39.1) Events(E/100 PYs)
Any adverse event	10 (50.0)	16 (40.9)
血液およびリンパ系障害	10 (50.0)	15 (38.4)
貧血	10 (50.0)	15 (38.4)
臨床検査	0	1 (2.6)
ヘモグロビン減少	0	1 (2.6)

Note: E/100 PYs = Number of events per 100 patient-years.
Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the induction period (Part 2) or until one day prior to the first dose of study drug in any subsequent maintenance or long-term extension period.
PYs is defined as the sum of the study drug duration of all subjects in the respective time periods (8-week induction period [for Week 8], and 8-week induction period plus 8-week extended period [for Week 16]) normalized by 365.25.
[1] All events and exposure time from Part 1 induction studies (for the extended induction analysis set).
[2] All events and exposure time from Parts 1 and 2 induction studies (for the extended induction analysis set).
DB = double blind. OL = open label.

Program Source Code: [redacted]

表 2.7.4.7-66.

[redacted] 11:17 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 3.4.1.12

Treatment-Emergent Anemia 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=128.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events(E/100 PYs) [SSA E/100 PYs]
Any adverse event	19 (14.8) [14.6]	11 (6.0) [6.1]	8 (4.0) [4.0]	19 (6.0) [6.1]	18 (5.9) [5.9]
血液およびリンパ系障害	18 (14.1) [13.8]	9 (4.9) [5.1]	7 (3.5) [3.5]	15 (4.7) [5.0]	11 (3.6) [3.6]
貧血	13 (10.1) [9.8]	9 (4.9) [5.1]	6 (3.0) [3.0]	13 (4.1) [4.3]	9 (3.0) [2.8]
鉄欠乏性貧血	5 (3.9) [4.0]	0	0	1 (0.3) [0.3]	1 (0.3) [0.3]
小球性貧血	0	0	1 (0.5) [0.5]	1 (0.3) [0.3]	1 (0.3) [0.5]
臨床検査	1 (0.8) [0.8]	2 (1.1) [1.0]	1 (0.5) [0.5]	4 (1.3) [1.1]	7 (2.3) [2.3]
ヘマトクリット減少	0	0	0	1 (0.3) [0.2]	0
ヘモグロビン減少	1 (0.8) [0.8]	2 (1.1) [1.0]	1 (0.5) [0.5]	3 (0.9) [0.9]	5 (1.6) [1.7]
平均赤血球容積異常	0	0	0	0	1 (0.3) [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.
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 3.4.1.12

Treatment-Emergent Anemia 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=128.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events(E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
平均赤血球容積増加	0	0	0	0	1 (0.3) [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.
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 2.7.4.7-67.

[redacted]20[redacted] 10:46 [redacted]

TABLE 2.4 4.4.1.6

Treatment-Emergent Anemia
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	32 (26.6)	9 (8.3)	32 (5.5)
血液およびリンパ系障害	28 (23.2)	8 (7.4)	26 (4.4)
貧血	26 (21.6)	8 (7.4)	23 (3.9)
大球性貧血	0	0	0
失血性貧血	0	0	0
鉄欠乏性貧血	1 (0.8)	0	3 (0.5)
小球性貧血	0	0	0
正球性貧血	1 (0.8)	0	0
臨床検査	4 (3.3)	1 (0.9)	6 (1.0)
ヘマトクリット減少	0	0	1 (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 4.4.1.6

Treatment-Emergent Anemia
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	19 (78.9)	35 (9.8)	39 (8.4)	32 (7.2)	145 (8.0)
血液およびリンパ系障害	18 (74.8)	32 (8.9)	31 (6.7)	25 (5.6)	120 (6.6)
貧血	17 (70.6)	23 (6.4)	25 (5.4)	18 (4.1)	99 (5.4)
大球性貧血	0	0	2 (0.4)	0	2 (0.1)
失血性貧血	0	0	0	2 (0.5)	2 (0.1)
鉄欠乏性貧血	1 (4.2)	8 (2.2)	3 (0.6)	4 (0.9)	14 (0.8)
小球性貧血	0	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
正球性貧血	0	0	0	0	0
臨床検査	1 (4.2)	3 (0.8)	8 (1.7)	7 (1.6)	25 (1.4)
ヘマトクリット減少	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 4.4.1.6

Treatment-Emergent Anemia
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
ヘモグロビン減少	4 (3.3)	1 (0.9)	5 (0.9)
平均赤血球容積異常	0	0	0
平均赤血球容積増加	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 4.4.1.6

Treatment-Emergent Anemia
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
ヘモグロビン減少	1 (4.2)	3 (0.8)	6 (1.3)	5 (1.1)	20 (1.1)
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of 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 2.7.4.7-68.

[redacted]20[redacted] 11:08 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 1.4.1.7

Number and Percentage of Subjects with Treatment-Emergent Neutropenia
by Primary MedDRA System Organ Class and Preferred Term
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
Any adverse event	1 (0.3) [0.3]	33 (4.6) [4.6]
血液およびリンパ系障害	1 (0.3) [0.3]	13 (1.8) [1.8]
好中球減少症	1 (0.3) [0.3]	13 (1.8) [1.8]
臨床検査	0	20 (2.8) [2.8]
好中球数減少	0	20 (2.8) [2.8]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
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]

表 2.7.4.7-69.

[redacted]20[redacted] 10:52 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 2.4.7

Treatment-Emergent Neutropenia in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Extended Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mgQD (N=127) End of DB Induction[1] (Week 8) (PYs=20.0) Events(E/100 PYs)	UPA 45 mgQD (N=127) End of OL Extended Induction[2] (Week 16) (PYs=39.1) Events(E/100 PYs)
Any adverse event	3 (15.0)	5 (12.8)
臨床検査	3 (15.0)	5 (12.8)
好中球数減少	3 (15.0)	5 (12.8)

Note: E/100 PYs = Number of events per 100 patient-years.
Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the induction period (Part 2) or until one day prior to the first dose of study drug in any subsequent maintenance or long-term extension period.
PYs is defined as the sum of the study drug duration of all subjects in the respective time periods (8-week induction period [for Week 8], and 8-week induction period plus 8-week extended period [for Week 16]) normalized by 365.25.
[1] All events and exposure time from Part 1 induction studies (for the extended induction analysis set).
[2] All events and exposure time from Parts 1 and 2 induction studies (for the extended induction analysis set).
DB = double blind. OL = open label.

Program Source Code: [redacted]

表 2.7.4.7-70.

[redacted]20[redacted] 11:17 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
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TABLE 2.4 3.4.1.14

Treatment-Emergent Neutropenia 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=128.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events(E/100 PYs) [SSA E/100 PYs]
Any adverse event	7 (5.5) [5.4]	11 (6.0) [6.0]	18 (9.1) [9.1]	15 (4.7) [4.8]	25 (8.2) [7.9]
血液およびリンパ系障害	3 (2.3) [2.3]	6 (3.3) [3.2]	6 (3.0) [3.0]	6 (1.9) [2.0]	9 (3.0) [2.7]
好中球減少症	3 (2.3) [2.3]	6 (3.3) [3.2]	6 (3.0) [3.0]	6 (1.9) [2.0]	9 (3.0) [2.7]
臨床検査	4 (3.1) [3.1]	5 (2.7) [2.8]	12 (6.0) [6.0]	9 (2.8) [2.8]	16 (5.3) [5.1]
顆粒球数減少	0	0	1 (0.5) [0.5]	0	1 (0.3) [0.3]
好中球数減少	4 (3.1) [3.1]	5 (2.7) [2.8]	11 (5.5) [5.5]	9 (2.8) [2.8]	15 (4.9) [4.8]

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]

表 2.7.4.7-71.

[redacted]20[redacted] 10:46 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.7

Treatment-Emergent Neutropenia
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	3 (2.5)	1 (0.9)	12 (2.0)
血液およびリンパ系障害	3 (2.5)	0	7 (1.2)
周期性好中球減少症	0	0	0
好中球減少症	3 (2.5)	0	7 (1.2)
臨床検査	0	1 (0.9)	5 (0.9)
顆粒球数減少	0	0	0
好中球数減少	0	1 (0.9)	5 (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 4.4.1.7

Treatment-Emergent Neutropenia
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	5 (20.8)	29 (8.1)	37 (7.9)	40 (9.0)	117 (6.4)
血液およびリンパ系障害	1 (4.2)	12 (3.3)	16 (3.4)	16 (3.6)	49 (2.7)
周期性好中球減少症	0	1 (0.3)	0	0	1 (<0.1)
好中球減少症	1 (4.2)	11 (3.1)	16 (3.4)	16 (3.6)	48 (2.6)
臨床検査	4 (16.6)	17 (4.7)	21 (4.5)	24 (5.4)	68 (3.7)
顆粒球数減少	0	0	0	1 (0.2)	1 (<0.1)
好中球数減少	4 (16.6)	17 (4.7)	21 (4.5)	23 (5.2)	67 (3.7)

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]

表 2.7.4.7-72.

[redacted]20[redacted] 11:08 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
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TABLE 2.4 1.4.1.8

Number and Percentage of Subjects with Treatment-Emergent Lymphopenia
by Primary MedDRA System Organ Class and Preferred Term
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
Any adverse event	2 (0.5) [0.5]	18 (2.5) [2.5]
血液およびリンパ系障害	2 (0.5) [0.5]	11 (1.5) [1.5]
リンパ球減少症	2 (0.5) [0.5]	11 (1.5) [1.5]
臨床検査	0	7 (1.0) [1.0]
リンパ球数減少	0	5 (0.7) [0.7]
リンパ球百分率減少	0	4 (0.6) [0.6]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
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]

表 2.7.4.7-73.

[redacted]20[redacted] 10:52 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 2.4.8

Treatment-Emergent Lymphopenia in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Extended Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mgQD (N=127) End of DB Induction[1] (Week 8) (PYs=20.0) Events(E/100 PYs)	UPA 45 mgQD (N=127) End of OL Extended Induction[2] (Week 16) (PYs=39.1) Events(E/100 PYs)
Any adverse event	2 (10.0)	4 (10.2)
血液およびリンパ系障害	2 (10.0)	3 (7.7)
リンパ球減少症	2 (10.0)	3 (7.7)
臨床検査	0	1 (2.6)
リンパ球数減少	0	1 (2.6)

Note: E/100 PYs = Number of events per 100 patient-years.
Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the induction period (Part 2) or until one day prior to the first dose of study drug in any subsequent maintenance or long-term extension period.
PYs is defined as the sum of the study drug duration of all subjects in the respective time periods (8-week induction period [for Week 8], and 8-week induction period plus 8-week extended period [for Week 16]) normalized by 365.25.
[1] All events and exposure time from Part 1 induction studies (for the extended induction analysis set).
[2] All events and exposure time from Parts 1 and 2 induction studies (for the extended induction analysis set).
DB = double blind. OL = open label.

Program Source Code: [redacted]

表 2.7.4.7-74.

[redacted]20[redacted] 11:17 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 3.4.1.16

Treatment-Emergent Lymphopenia 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=128.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events(E/100 PYs) [SSA E/100 PYs]
Any adverse event	5 (3.9) [3.7]	9 (4.9) [4.9]	7 (3.5) [3.5]	13 (4.1) [4.0]	10 (3.3) [3.7]
血液およびリンパ系障害	3 (2.3) [2.2]	3 (1.6) [1.6]	1 (0.5) [0.5]	4 (1.3) [1.3]	2 (0.7) [0.6]
リンパ球減少症	3 (2.3) [2.2]	3 (1.6) [1.6]	1 (0.5) [0.5]	4 (1.3) [1.3]	2 (0.7) [0.6]
臨床検査	2 (1.6) [1.6]	6 (3.3) [3.3]	6 (3.0) [3.0]	9 (2.8) [2.7]	8 (2.6) [3.1]
リンパ球数減少	2 (1.6) [1.6]	5 (2.7) [2.8]	5 (2.5) [2.5]	8 (2.5) [2.4]	7 (2.3) [2.8]
リンパ球百分率減少	0	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.3) [0.3]	1 (0.3) [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.
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 2.7.4.7-75.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.8

Treatment-Emergent Lymphopenia
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	5 (4.2)	1 (0.9)	19 (3.2)
血液およびリンパ系障害	4 (3.3)	1 (0.9)	8 (1.4)
リンパ球減少症	4 (3.3)	1 (0.9)	8 (1.4)
臨床検査	1 (0.8)	0	11 (1.9)
リンパ球数減少	1 (0.8)	0	11 (1.9)
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 4.4.1.8

Treatment-Emergent Lymphopenia
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	3 (12.5)	15 (4.2)	29 (6.2)	18 (4.1)	80 (4.4)
血液およびリンパ系障害	3 (12.5)	10 (2.8)	8 (1.7)	7 (1.6)	34 (1.9)
リンパ球減少症	3 (12.5)	10 (2.8)	8 (1.7)	7 (1.6)	34 (1.9)
臨床検査	0	5 (1.4)	21 (4.5)	11 (2.5)	46 (2.5)
リンパ球数減少	0	5 (1.4)	15 (3.2)	9 (2.0)	38 (2.1)
リンパ球百分率減少	0	0	6 (1.3)	2 (0.5)	8 (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]

表 2.7.4.7-76.

[redacted]20[redacted] 11:08 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 1.4.1.9

Number and Percentage of Subjects with Treatment-Emergent Creatine Phosphokinase (CPK) Elevations
by Primary MedDRA System Organ Class and Preferred Term
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
Any adverse event	5 (1.3) [1.4]	37 (5.1) [5.2]
臨床検査	5 (1.3) [1.4]	37 (5.1) [5.2]
血中クレアチンホスホキナーゼ増加	5 (1.3) [1.4]	37 (5.1) [5.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
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]

表 2.7.4.7-77.

[redacted]20[redacted] 10:52 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 2.4.9

Treatment-Emergent Creatine Phosphokinase (CPK) Elevations in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Extended Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mgQD (N=127) End of DB Induction[1] (Week 8) (PYs=20.0) Events(E/100 PYs)	UPA 45 mgQD (N=127) End of OL Extended Induction[2] (Week 16) (PYs=39.1) Events(E/100 PYs)
Any adverse event	8 (40.0)	16 (40.9)
臨床検査	8 (40.0)	16 (40.9)
血中クレアチンホスホキナーゼ増加	8 (40.0)	16 (40.9)

Note: E/100 PYs = Number of events per 100 patient-years.
Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the induction period (Part 2) or until one day prior to the first dose of study drug in any subsequent maintenance or long-term extension period.
PYs is defined as the sum of the study drug duration of all subjects in the respective time periods (8-week induction period [for Week 8], and 8-week induction period plus 8-week extended period [for Week 16]) normalized by 365.25.
[1] All events and exposure time from Part 1 induction studies (for the extended induction analysis set).
[2] All events and exposure time from Parts 1 and 2 induction studies (for the extended induction analysis set).
DB = double blind. OL = open label.

Program Source Code: [redacted]

表 2.7.4.7-78.

[redacted]20[redacted] 11:17 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 3.4.1.18

Treatment-Emergent Creatine Phosphokinase (CPK) Elevations 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=128.1)	UPA 15 mg QD (N=250) (PYs=182.4)	UPA 30 mg QD (N=251) (PYs=198.7)	UPA 15 mg QD (N=285) (PYs=316.9)	UPA 30 mg QD (N=291) (PYs=304.0)
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]
Any adverse event	5 (3.9) [4.1]	14 (7.7) [7.7]	22 (11.1) [11.1]	21 (6.6) [6.6]	33 (10.9) [10.4]
臨床検査	5 (3.9) [4.1]	14 (7.7) [7.7]	22 (11.1) [11.1]	21 (6.6) [6.6]	33 (10.9) [10.4]
血中クレアチンホスホキナーゼ増加	5 (3.9) [4.1]	14 (7.7) [7.7]	22 (11.1) [11.1]	21 (6.6) [6.6]	33 (10.9) [10.4]

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 2.7.4.7-79.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.9

Treatment-Emergent Creatine Phosphokinase (CPK) Elevations
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	6 (5.0)	11 (10.2)	30 (5.1)
臨床検査	6 (5.0)	11 (10.2)	30 (5.1)
血中クレアチンホスホキナーゼ増加	6 (5.0)	11 (10.2)	30 (5.1)

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 4.4.1.9

Treatment-Emergent Creatine Phosphokinase (CPK) Elevations
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	8 (33.2)	27 (7.5)	46 (9.9)	63 (14.2)	178 (9.8)
臨床検査	8 (33.2)	27 (7.5)	46 (9.9)	63 (14.2)	178 (9.8)
血中クレアチンホスホキナーゼ増加	8 (33.2)	27 (7.5)	46 (9.9)	63 (14.2)	178 (9.8)

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]

表 2.7.4.7-80.

[redacted]20[redacted] 11:17 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 3.4.1.22

Treatment-Emergent Renal Dysfunction 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=128.1) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event	1 (0.8) [0.8]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.3) [0.3]	1 (0.3) [0.3]
腎および尿路障害	1 (0.8) [0.8]	1 (0.5) [0.5]	1 (0.5) [0.5]	1 (0.3) [0.3]	1 (0.3) [0.3]
急性腎障害	1 (0.8) [0.8]	0	1 (0.5) [0.5]	0	1 (0.3) [0.3]
腎機能障害	0	1 (0.5) [0.5]	0	1 (0.3) [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]

表 2.7.4.7-81.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 2.4 4.4.1.11

Treatment-Emergent Renal Dysfunction
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	0	0	1 (0.2)
腎および尿路障害	0	0	1 (0.2)
急性腎障害	0	0	0
腎機能障害	0	0	1 (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 4.4.1.11

Treatment-Emergent Renal Dysfunction
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	0	1 (0.3)	3 (0.6)	1 (0.2)	5 (0.3)
腎および尿路障害	0	1 (0.3)	3 (0.6)	1 (0.2)	5 (0.3)
急性腎障害	0	1 (0.3)	1 (0.2)	1 (0.2)	2 (0.1)
腎機能障害	0	0	2 (0.4)	0	3 (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]

表 2.7.4.7-82.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.5

Treatment-Emergent Adjudicated Gastrointestinal Perforations
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	1 (0.8)	0	1 (0.2)
胃腸障害	1 (0.8)	0	1 (0.2)
大腸穿孔	1 (0.8)	0	1 (0.2)
感染症および寄生虫症	0	0	0
腹部膿瘍	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 4.4.1.5

Treatment-Emergent Adjudicated Gastrointestinal Perforations
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	0	2 (0.6)	0	0	1 (<0.1)
胃腸障害	0	1 (0.3)	0	0	1 (<0.1)
大腸穿孔	0	1 (0.3)	0	0	1 (<0.1)
感染症および寄生虫症	0	1 (0.3)	0	0	0
腹部膿瘍	0	1 (0.3)	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]

表 2.7.4.7-83.

[redacted]20[redacted] 11:17 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
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TABLE 2.4 3.4.1.24

Treatment-Emergent Malignancies 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=128.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events(E/100 PYs) [SSA E/100 PYs]
Any adverse event	1 (0.8) [0.8]	1 (0.5) [0.6]	5 (2.5) [2.5]	1 (0.3) [0.3]	9 (3.0) [2.9]
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 (0.8) [0.8]	1 (0.5) [0.6]	5 (2.5) [2.5]	1 (0.3) [0.3]	9 (3.0) [2.9]
結腸腺癌	0	0	1 (0.5) [0.5]	0	1 (0.3) [0.3]
基底細胞癌	0	0	3 (1.5) [1.5]	0	5 (1.6) [1.6]
ボーエン病	0	0	0	0	1 (0.3) [0.3]
浸潤性乳癌	1 (0.8) [0.8]	1 (0.5) [0.6]	0	1 (0.3) [0.3]	0
小細胞癌	0	0	1 (0.5) [0.5]	0	1 (0.3) [0.3]
子宮頚部扁平上皮癌	0	0	0	0	1 (0.3) [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]

表 2.7.4.7-84.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	0	5 (4.6)	5 (0.9)
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）	0	5 (4.6)	5 (0.9)
結腸腺癌	0	1 (0.9)	0
膵腺癌	0	0	1 (0.2)
基底細胞癌	0	3 (2.8)	0
ボーエン病	0	0	1 (0.2)
浸潤性乳癌	0	0	0
喉頭扁平上皮癌	0	1 (0.9)	0
悪性黒色腫	0	0	1 (0.2)
前立腺癌	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 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	0	4 (1.1)	2 (0.4)	10 (2.3)	25 (1.4)
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)	0	4 (1.1)	2 (0.4)	10 (2.3)	25 (1.4)
結腸腺癌	0	0	0	1 (0.2)	2 (0.1)
膵腺癌	0	0	0	0	1 (<0.1)
基底細胞癌	0	1 (0.3)	0	5 (1.1)	9 (0.5)
ボーエン病	0	0	0	1 (0.2)	2 (0.1)
浸潤性乳癌	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
喉頭扁平上皮癌	0	0	0	0	1 (<0.1)
悪性黒色腫	0	0	0	0	1 (<0.1)
前立腺癌	0	1 (0.3)	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 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) 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.)			
小細胞癌	0	0	0
扁平上皮癌	0	0	1 (0.2)
皮膚有棘細胞癌	0	0	1 (0.2)
子宮頚部扁平上皮癌	0	0	0
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 4.4.1.12

Treatment-Emergent Malignancies
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) 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.)					
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 (0.3)	0	0	2 (0.1)
子宮頚部扁平上皮癌	0	0	0	1 (0.2)	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]

表 2.7.4.7-85.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 4

TABLE 2.4 4.4.1.13

Treatment-Emergent Malignancies Excluding Non-Melanoma Skin Cancer (NMSC)
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	0	2 (1.8)	3 (0.5)
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）	0	2 (1.8)	3 (0.5)
結腸腺癌	0	1 (0.9)	0
膵腺癌	0	0	1 (0.2)
浸潤性乳癌	0	0	0
喉頭扁平上皮癌	0	1 (0.9)	0
悪性黒色腫	0	0	1 (0.2)
前立腺癌	0	0	0
小細胞癌	0	0	0
扁平上皮癌	0	0	1 (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 4.4.1.13

Treatment-Emergent Malignancies Excluding Non-Melanoma Skin Cancer (NMSC)
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	0	2 (0.6)	2 (0.4)	4 (0.9)	12 (0.7)
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)	0	2 (0.6)	2 (0.4)	4 (0.9)	12 (0.7)
結腸腺癌	0	0	0	1 (0.2)	2 (0.1)
膵腺癌	0	0	0	0	1 (<0.1)
浸潤性乳癌	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
喉頭扁平上皮癌	0	0	0	0	1 (<0.1)
悪性黒色腫	0	0	0	0	1 (<0.1)
前立腺癌	0	1 (0.3)	0	0	1 (<0.1)
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.4.1.13

Treatment-Emergent Malignancies Excluding Non-Melanoma Skin Cancer (NMSC)
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) 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.)			
子宮頚部扁平上皮癌	0	0	0
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 4.4.1.13

Treatment-Emergent Malignancies Excluding Non-Melanoma Skin Cancer (NMSC)
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) 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.)					
子宮頚部扁平上皮癌	0	0	0	1 (0.2)	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]

表 2.7.4.7-86.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 2.4 4.4.1.14

Treatment-Emergent NMSC
in Exposure-Adjusted Event Rate per 100 Patient 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	0	3 (2.8)	2 (0.3)
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）	0	3 (2.8)	2 (0.3)
基底細胞癌	0	3 (2.8)	0
ボーエン病	0	0	1 (0.2)
皮膚有棘細胞癌	0	0	1 (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 4.4.1.14

Treatment-Emergent NMSC
in Exposure-Adjusted Event Rate per 100 Patient 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	0	2 (0.6)	0	6 (1.4)	13 (0.7)
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）	0	2 (0.6)	0	6 (1.4)	13 (0.7)
基底細胞癌	0	1 (0.3)	0	5 (1.1)	9 (0.5)
ボーエン病	0	0	0	1 (0.2)	2 (0.1)
皮膚有棘細胞癌	0	1 (0.3)	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]

表 2.7.4.7-87.

[redacted]20[redacted] 11:09 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 3.4.1.32

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(Responders Maintenance Analysis Set)

Event Category Adjudicated Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=128.1) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event	2 (1.6) [1.6]	0	1 (0.5) [0.5]	0	2 (0.7) [0.6]
MACE *	1 (0.8) [0.7]	0	1 (0.5) [0.5]	0	2 (0.7) [0.6]
Cardiovascular death	0	0	0	0	0
Fatal acute myocardial infarction	0	0	0	0	0
Sudden cardiac death	0	0	0	0	0
Heart failure	0	0	0	0	0
Cardiovascular procedure-related death	0	0	0	0	0
Death due to cardiovascular hemorrhage	0	0	0	0	0
Fatal stroke	0	0	0	0	0
Pulmonary embolism **	0	0	0	0	0
Venous thrombosis **	0	0	0	0	0
Non-cardiac/Non-neurologic arterial thrombosis	0	0	0	0	0
Other	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.
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.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

Program Source Code: [redacted]

TABLE 2.4 3.4.1.32

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(Responders Maintenance Analysis Set)

Event Category Adjudicated Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=128.1) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events (E/100 PYs) [SSA E/100 PYs]
MACE * (Cont.)					
Non-fatal myocardial infarction	1 (0.8) [0.7]	0	0	0	0
Non-fatal stroke	0	0	1 (0.5) [0.5]	0	2 (0.7) [0.6]
Undetermined/UNK cause of death	0	0	0	0	0
Other cardiovascular events (non-fatal)	1 (0.8) [0.8]	0	0	0	0
Cardiovascular procedures	0	0	0	0	0
Unstable angina requiring hospitalization	0	0	0	0	0
Hospital based treatment for heart failure	1 (0.8) [0.8]	0	0	0	0
Transient ischemic attack	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.
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.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

Program Source Code: [redacted]

表 2.7.4.7-88.

[redacted]20[redacted] 10:40 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.16

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

Event Category Adjudicated Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	0	2 (1.8)	2 (0.3)
MACE *	0	0	1 (0.2)
Cardiovascular death	0	0	0
Fatal acute myocardial infarction	0	0	0
Sudden cardiac death	0	0	0
Heart failure	0	0	0
Cardiovascular procedure-related death	0	0	0
Death due to cardiovascular hemorrhage	0	0	0
Fatal stroke	0	0	0
Pulmonary embolism **	0	0	0
Venous thrombosis **	0	0	0
Non-cardiac/Non-neurologic arterial thrombosis	0	0	0
Other	0	0	0

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.16

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

Event Category Adjudicated 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	0	2 (0.6)	0	3 (0.7)	7 (0.4)
MACE *	0	1 (0.3)	0	3 (0.7)	4 (0.2)
Cardiovascular death	0	0	0	0	0
Fatal acute myocardial infarction	0	0	0	0	0
Sudden cardiac death	0	0	0	0	0
Heart failure	0	0	0	0	0
Cardiovascular procedure-related death	0	0	0	0	0
Death due to cardiovascular hemorrhage	0	0	0	0	0
Fatal stroke	0	0	0	0	0
Pulmonary embolism **	0	0	0	0	0
Venous thrombosis **	0	0	0	0	0
Non-cardiac/Non-neurologic arterial thrombosis	0	0	0	0	0
Other	0	0	0	0	0

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

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TABLE 2.4 4.4.1.16

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

Event Category Adjudicated Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
MACE * (Cont.)			
Non-fatal myocardial infarction	0	0	1 (0.2)
Non-fatal stroke	0	0	0
Undetermined/UNK cause of death	0	0	0
Other cardiovascular events (non-fatal)	0	2 (1.8)	1 (0.2)
Cardiovascular procedures	0	1 (0.9)	1 (0.2)
Unstable angina requiring hospitalization	0	1 (0.9)	0
Hospital based treatment for heart failure	0	0	0
Transient ischemic attack	0	0	0

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

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TABLE 2.4 4.4.1.16

Treatment-Emergent Adjudicated MACE and Other Cardiovascular Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

Event Category Adjudicated 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
MACE * (Cont.)					
Non-fatal myocardial infarction	0	1 (0.3)	0	0	1 (<0.1)
Non-fatal stroke	0	0	0	3 (0.7)	3 (0.2)
Undetermined/UNK cause of death	0	0	0	0	0
Other cardiovascular events (non-fatal)	0	1 (0.3)	0	0	3 (0.2)
Cardiovascular procedures	0	0	0	0	2 (0.1)
Unstable angina requiring hospitalization	0	0	0	0	1 (<0.1)
Hospital based treatment for heart failure	0	1 (0.3)	0	0	0
Transient ischemic attack	0	0	0	0	0

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** Pulmonary embolism and venous thrombosis (under cardiovascular death) are also included in the adjudicated thromboembolic events table.

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表 2.7.4.7-89.

[redacted]20[redacted] 11:03 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 2.4 1.4.1.17

Number and Percentage of Subjects with Treatment-Emergent Adjudicated Thrombotic Events by Adjudicated Term
(Placebo-Controlled Induction Analysis Set)

Event Category Adjudicated Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
Any adverse event	1 (0.3) [0.3]	1 (0.1) [0.2]
Venous thromboembolic events (fatal and non-fatal)	1 (0.3) [0.3]	1 (0.1) [0.2]
Venous thromboembolic events (fatal) *	0	0
Pulmonary embolism	0	0
Venous thrombosis	0	0
Venous thromboembolic events (non-fatal) **	1 (0.3) [0.3]	1 (0.1) [0.2]
Deep vein thrombosis (DVT)	1 (0.3) [0.3]	1 (0.1) [0.2]
Pulmonary embolism (PE)	1 (0.3) [0.3]	1 (0.1) [0.2]
DVT and PE (concurrent)	1 (0.3) [0.3]	1 (0.1) [0.2]
Other venous thrombosis (non-fatal)	0	0
Arterial thromboembolic events (non-cardiac, non-neurologic)(non-fatal)	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

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表 2.7.4.7-90.

[redacted]20[redacted] 11:09 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 3.4.1.34

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(Responders Maintenance Analysis Set)

Event Category Adjudicated Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=128.1) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event	1 (0.8) [0.8]	2 (1.1) [1.1]	2 (1.0) [1.0]	3 (0.9) [0.8]	2 (0.7) [0.6]
Venous thromboembolic events (fatal and non-fatal)	0	2 (1.1) [1.1]	2 (1.0) [1.0]	3 (0.9) [0.8]	2 (0.7) [0.6]
Venous thromboembolic events (fatal) *	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0
Venous thrombosis	0	0	0	0	0
Venous thromboembolic events (non-fatal) **	0	2 (1.1) [1.1]	2 (1.0) [1.0]	3 (0.9) [0.8]	2 (0.7) [0.6]
Deep vein thrombosis (DVT)	0	0	2 (1.0) [1.0]	1 (0.3) [0.3]	2 (0.7) [0.6]
Pulmonary embolism (PE)	0	2 (1.1) [1.1]	0	2 (0.6) [0.5]	0
DVT and PE (concurrent)	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.
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.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

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TABLE 2.4 3.4.1.34

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(Responders Maintenance Analysis Set)

Event Category Adjudicated Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=128.1) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=182.4) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=198.7) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=316.9) Events (E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=304.0) Events (E/100 PYs) [SSA E/100 PYs]
Other venous thrombosis (non-fatal)	1 (0.8) [0.8]	0	0	0	0
Arterial thromboembolic events (non-cardiac, non-neurologic)(non-fatal)	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.
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.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

表 2.7.4.7-91.

[redacted]20[redacted] 10:40 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.4.1.17

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

Event Category Adjudicated Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	1 (0.8)	1 (0.9)	4 (0.7)
Venous thromboembolic events (fatal and non-fatal)	1 (0.8)	1 (0.9)	4 (0.7)
Venous thromboembolic events (fatal) *	0	0	0
Pulmonary embolism	0	0	0
Venous thrombosis	0	0	0
Venous thromboembolic events (non-fatal) **	1 (0.8)	1 (0.9)	4 (0.7)
Deep vein thrombosis (DVT)	1 (0.8)	1 (0.9)	2 (0.3)
Pulmonary embolism (PE)	1 (0.8)	0	3 (0.5)
DVT and PE (concurrent)	1 (0.8)	0	1 (0.2)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.17

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

Event Category Adjudicated 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	1 (4.2)	1 (0.3)	3 (0.6)	2 (0.5)	11 (0.6)
Venous thromboembolic events (fatal and non-fatal)	1 (4.2)	0	3 (0.6)	2 (0.5)	11 (0.6)
Venous thromboembolic events (fatal) *	0	0	0	0	0
Pulmonary embolism	0	0	0	0	0
Venous thrombosis	0	0	0	0	0
Venous thromboembolic events (non-fatal) **	1 (4.2)	0	3 (0.6)	2 (0.5)	11 (0.6)
Deep vein thrombosis (DVT)	1 (4.2)	0	1 (0.2)	2 (0.5)	7 (0.4)
Pulmonary embolism (PE)	1 (4.2)	0	2 (0.4)	0	6 (0.3)
DVT and PE (concurrent)	1 (4.2)	0	0	0	2 (0.1)

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.17

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

Event Category Adjudicated Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Other venous thrombosis (non-fatal)	0	0	0
Arterial thromboembolic events (non-cardiac, non-neurologic)(non-fatal)	0	0	0

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

TABLE 2.4 4.4.1.17

Treatment-Emergent Adjudicated Thrombotic Events in Exposure-Adjusted Event Rate per 100 Patient Years by Adjudicated Term
(All Treated [SUBJ] Analysis Set)

Event Category Adjudicated 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Other venous thrombosis (non-fatal)	0	1 (0.3)	0	0	0
Arterial thromboembolic events (non-cardiac, non-neurologic)(non-fatal)	0	0	0	0	0

Note: Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).
NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
* Venous thromboembolic events (fatal) are also counted under cardiovascular death in the MACE table.
** Venous thromboembolic events (non-fatal) include deep vein thrombosis (DVT) and pulmonary embolism (PE). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row.

Program Source Code: [redacted]

表 2.7.4.7-92.

[redacted]20[redacted] 08:54 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)

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

R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 5.1.1

Overview of Number and Percentage of Subjects with Treatment-Emergent Adverse Events
(All Treated [DOSE] Analysis Set)

	PBO (N=608) n (%)	UPA 7.5 mg QD (N=47) n (%)	UPA 15 mg QD (N=850) n (%)	UPA 30 mg QD (N=653) n (%)	UPA 15/30 mg QD (N=1114) n (%)	UPA 45 mg QD (N=987) n (%)	Any UPA (N=1308) n (%)
Subjects with:							
Any adverse event (AE)	428 (70.4)	37 (78.7)	669 (78.7)	517 (79.2)	973 (87.3)	567 (57.4)	1138 (87.0)
COVID-19 infection related AE	16 (2.6)	0	67 (7.9)	65 (10.0)	132 (11.8)	3 (0.3)	135 (10.3)
Any serious AE	59 (9.7)	1 (2.1)	101 (11.9)	95 (14.5)	185 (16.6)	34 (3.4)	214 (16.4)
Any AE leading to discontinuation of study drug	56 (9.2)	4 (8.5)	55 (6.5)	62 (9.5)	117 (10.5)	30 (3.0)	151 (11.5)
Any severe AE	62 (10.2)	4 (8.5)	86 (10.1)	78 (11.9)	158 (14.2)	32 (3.2)	192 (14.7)
Any AE with reasonable possibility of being related to study drug$	176 (28.9)	13 (27.7)	318 (37.4)	280 (42.9)	532 (47.8)	270 (27.4)	660 (50.5)
Any AE leading to death	0	0	1 (0.1)	3 (0.5)	4 (0.4)	0	4 (0.3)
Deaths#	0	0	1 (0.1)	3 (0.5)	4 (0.4)	0	4 (0.3)
Deaths occurring <= 30 days after last dose of study drug	0	0	1 (0.1)	3 (0.5)	4 (0.4)	0	4 (0.3)
Deaths occurring > 30 days after last dose of study drug	0	0	0	0	0	0	0
COVID-19 infection related deaths	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)

Note: 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.

$ As assessed by investigator.

Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

表 2.7.4.7-93.

[redacted]20[redacted] 08:55 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 5.1.2

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
(All Treated [DOSE] Analysis Set)

	Placebo (N=608)	UPA 7.5 mg QD (N=47)	UPA 15 mg QD (N=850)	UPA 30 mg QD (N=653)	UPA 15/30 mg QD (N=1114)	UPA 45 mg QD (N=987)	Any UPA (N=1308)
Exposure-adjusted event rate:	(PYs=320.1) Events (E/100 PYs)	(PYs=22.5) Events (E/100 PYs)	(PYs=1283.0) Events (E/100 PYs)	(PYs=875.5) Events (E/100 PYs)	(PYs=2158.5) Events (E/100 PYs)	(PYs=169.2) Events (E/100 PYs)	(PYs=2350.2) Events (E/100 PYs)
Any adverse event (AE)	1558 (486.7)	150 (666.1)	3663 (285.5)	2602 (297.2)	6265 (290.2)	1372 (810.9)	7787 (331.3)
COVID-19 infection related AE	16 (5.0)	0	72 (5.6)	73 (8.3)	145 (6.7)	3 (1.8)	148 (6.3)
Any serious AE	80 (25.0)	1 (4.4)	152 (11.8)	142 (16.2)	294 (13.6)	42 (24.8)	337 (14.3)
Any AE leading to discontinuation of study drug	64 (20.0)	7 (31.1)	62 (4.8)	77 (8.8)	139 (6.4)	37 (21.9)	183 (7.8)
Any severe AE	84 (26.2)	5 (22.2)	111 (8.7)	107 (12.2)	218 (10.1)	42 (24.8)	265 (11.3)
Any AE with reasonable possibility of being related to study drug$	402 (125.6)	25 (111.0)	851 (66.3)	757 (86.5)	1608 (74.5)	549 (324.5)	2182 (92.8)
Any AE leading to death	0	0	1 (<0.1)	4 (0.5)	5 (0.2)	0	5 (0.2)
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)
Deaths#	0/320.1	0/22.5	1/1283.0 (<0.1)	3/875.5 (0.3)	4/2158.5 (0.2)	0/169.2	4/2350.2 (0.2)
Deaths occurring <= 30 days after last dose of study drug	0/320.1	0/22.5	1/1283.0 (<0.1)	3/875.5 (0.3)	4/2158.5 (0.2)	0/169.2	4/2350.2 (0.2)
Deaths occurring > 30 days after last dose of study drug	0/320.1	0/22.5	0/1283.0	0/875.5	0/2158.5	0/169.2	0/2350.2
COVID-19 infection related deaths	0/320.1	0/22.5	0/1283.0	1/875.5 (0.1)	1/2158.5 (<0.1)	0/169.2	1/2350.2 (<0.1)

Note: 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.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
PBO = Placebo; UPA = Upadacitinib.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

表 2.7.4.7-94.

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

TABLE 2.4 3.3.1

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
Any adverse event	186 (75.9) [75.5]	193 (77.2) [77.2]	199 (79.3) [79.3]	238 (83.5) [83.5]	245 (84.2) [84.2]
血液およびリンパ系障害	23 (9.4) [9.3]	17 (6.8) [6.9]	17 (6.8) [6.8]	29 (10.2) [10.2]	26 (8.9) [8.9]
貧血	10 (4.1) [4.0]	9 (3.6) [3.7]	8 (3.2) [3.2]	15 (5.3) [5.3]	11 (3.8) [3.8]
好酸球増加症	1 (0.4) [0.4]	0	0	0	0
内出血発生の増加傾向	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
鉄欠乏性貧血	5 (2.0) [2.1]	0	0	1 (0.4) [0.4]	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
血液およびリンパ系障害 (Cont.)					
白血球増加症	1 (0.4) [0.4]	0	0	0	0
白血球減少症	3 (1.2) [1.2]	5 (2.0) [2.0]	1 (0.4) [0.4]	7 (2.5) [2.4]	5 (1.7) [1.7]
リンパ節症	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]
リンパ球増加症	1 (0.4) [0.4]	0	0	0	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]
小球性貧血	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
血液およびリンパ系障害 (Cont.)					
好中球減少症	3 (1.2) [1.2]	4 (1.6) [1.6]	6 (2.4) [2.4]	4 (1.4) [1.4]	9 (3.1) [3.0]
汎血球減少症	0	0	0	1 (0.4) [0.4]	0
脾腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
血小板減少症	1 (0.4) [0.4]	0	0	0	0
血小板増加症	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
心臓障害	5 (2.0) [2.0]	4 (1.6) [1.6]	8 (3.2) [3.2]	6 (2.1) [2.1]	13 (4.5) [4.5]
急性心筋梗塞	1 (0.4) [0.4]	0	0	0	0
不整脈	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]
心房細動	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
完全房室ブロック	0	0	0	1 (0.4) [0.4]	0
第一度房室ブロック	0	0	0	0	1 (0.3) [0.3]
二束ブロック	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
心臓障害 (Cont.)					
心不全	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
うっ血性心不全	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
慢性左室不全	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
僧帽弁閉鎖不全症	0	0	0	0	1 (0.3) [0.3]
動悸	2 (0.8) [0.8]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
心膜炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
心臓障害 (Cont.)					
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]
上室性頻脈	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
頻脈	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0
心室性期外収縮	0	0	1 (0.4) [0.4]	0	3 (1.0) [1.0]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
先天性、家族性および遺伝性障害	0	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.7) [0.7]	2 (0.7) [0.7]
皮様嚢腫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
胃腸管動静脈奇形	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
ジルベール症候群	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
陰嚢水瘤	0	0	0	1 (0.4) [0.3]	0
耳および迷路障害	3 (1.2) [1.2]	4 (1.6) [1.6]	1 (0.4) [0.4]	7 (2.5) [2.5]	6 (2.1) [2.0]
感音性難聴	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
耳および迷路障害 (Cont.)					
片耳難聴	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
耳痛	0	1 (0.4) [0.4]	0	3 (1.1) [1.1]	0
耳部腫脹	1 (0.4) [0.4]	0	0	0	0
外耳道の外骨腫	1 (0.4) [0.4]	0	0	0	0
聴力低下	0	0	0	0	1 (0.3) [0.3]
メニエール病	0	0	0	0	1 (0.3) [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).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
耳および迷路障害 (Cont.)					
中耳滲出液	1 (0.4) [0.4]	0	0	0	0
耳漏	0	0	0	0	1 (0.3) [0.3]
耳鳴	0	0	0	0	1 (0.3) [0.3]
回転性めまい	0	2 (0.8) [0.8]	0	3 (1.1) [1.1]	2 (0.7) [0.7]
内分泌障害	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.4]	2 (0.7) [0.7]
クッシング症候群	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
内分泌障害 (Cont.)					
甲状腺腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
続発性副腎皮質機能不全	0	0	0	0	1 (0.3) [0.3]
甲状腺腫瘤	0	0	0	0	1 (0.3) [0.3]
眼障害	12 (4.9) [4.9]	7 (2.8) [2.7]	9 (3.6) [3.6]	12 (4.2) [4.2]	12 (4.1) [4.1]
無水晶体眼	0	0	0	0	1 (0.3) [0.3]
眼瞼炎	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
眼障害 (Cont.)					
白内障	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.8) [0.8]	4 (1.4) [1.4]	3 (1.0) [1.0]
霰粒腫	0	0	3 (1.2) [1.2]	0	3 (1.0) [1.0]
結膜充血	1 (0.4) [0.4]	0	0	0	0
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]
角膜浮腫	0	0	0	0	1 (0.3) [0.3]
角膜混濁	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
眼障害 (Cont.)					
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]
上強膜炎	1 (0.4) [0.4]	0	0	0	0
眼刺激	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
眼そう痒症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
眼部腫脹	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
眼瞼障害	1 (0.4) [0.4]	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).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
眼障害 (Cont.)					
眼瞼発疹	1 (0.4) [0.4]	0	0	0	0
緑内障	0	0	0	0	1 (0.3) [0.3]
角膜炎	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
流涙増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
黄斑浮腫	0	0	0	1 (0.4) [0.4]	0
近視	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
眼障害 (Cont.)					
眼充血	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.4]
眼窩周囲腫脹	1 (0.4) [0.4]	0	0	0	0
網膜静脈閉塞	0	0	0	1 (0.4) [0.4]	0
潰瘍性角膜炎	1 (0.4) [0.4]	0	0	0	0
ぶどう膜炎	1 (0.4) [0.4]	0	0	0	0
硝子体浮遊物	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害	110 (44.9) [44.6]	62 (24.8) [24.7]	58 (23.1) [23.2]	92 (32.3) [32.2]	94 (32.3) [32.3]
腹部膨満	1 (0.4) [0.4]	2 (0.8) [0.8]	5 (2.0) [2.0]	2 (0.7) [0.7]	6 (2.1) [2.1]
腹部腫瘤	1 (0.4) [0.4]	0	0	0	0
腹痛	6 (2.4) [2.5]	6 (2.4) [2.4]	4 (1.6) [1.6]	10 (3.5) [3.5]	7 (2.4) [2.4]
下腹部痛	3 (1.2) [1.2]	0	0	1 (0.4) [0.3]	0
上腹部痛	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.8) [0.8]	5 (1.8) [1.8]	4 (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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
腹部圧痛	0	0	2 (0.8) [0.8]	1 (0.4) [0.3]	3 (1.0) [1.0]
異常便	1 (0.4) [0.4]	0	0	0	0
裂肛	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0
痔瘻	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]
肛門の炎症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肛門ポリープ	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
肛門そう痒症	2 (0.8) [0.8]	0	0	0	0
アフタ性潰瘍	2 (0.8) [0.8]	1 (0.4) [0.4]	3 (1.2) [1.2]	1 (0.4) [0.3]	4 (1.4) [1.3]
大腸炎	3 (1.2) [1.2]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0
虚血性大腸炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
潰瘍性大腸炎	74 (30.2) [29.8]	31 (12.4) [12.4]	20 (8.0) [8.0]	43 (15.1) [15.1]	31 (10.7) [10.7]
結腸異形成	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	2 (0.7) [0.7]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
便秘	2 (0.8) [0.8]	3 (1.2) [1.2]	6 (2.4) [2.4]	5 (1.8) [1.8]	10 (3.4) [3.4]
便意切迫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
齲歯	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	2 (0.7) [0.7]
歯嚢胞	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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]
口内乾燥	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
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]
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]
小腸炎	0	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]
腸炎	0	0	0	0	2 (0.7) [0.7]
変色便	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
大腿ヘルニア	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
鼓腸	3 (1.2) [1.2]	0	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]
胃潰瘍	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
胃炎	0	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.1) [1.0]	1 (0.3) [0.3]
消化器痛	0	0	0	1 (0.4) [0.4]	0
胃食道逆流性疾患	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.2) [1.2]	3 (1.1) [1.1]	3 (1.0) [1.0]
歯肉腫脹	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
舌痛	1 (0.4) [0.4]	0	0	0	0
血便排泄	1 (0.4) [0.4]	0	0	0	0
痔出血	2 (0.8) [0.8]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
痔核	1 (0.4) [0.4]	3 (1.2) [1.2]	2 (0.8) [0.8]	6 (2.1) [2.1]	4 (1.4) [1.4]
血栓性痔核	1 (0.4) [0.4]	0	0	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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
腸閉塞	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
腸管ポリープ	0	0	0	1 (0.4) [0.3]	0
過敏性腸症候群	0	0	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.4]
大腸穿孔	1 (0.4) [0.4]	0	0	0	0
大腸ポリープ	2 (0.8) [0.8]	0	1 (0.4) [0.4]	2 (0.7) [0.7]	5 (1.7) [1.7]
口唇障害	0	0	0	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
口唇腫脹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
口腔嚢胞	1 (0.4) [0.4]	0	0	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]
粘液便	1 (0.4) [0.4]	0	0	0	0
悪心	5 (2.0) [2.1]	4 (1.6) [1.5]	5 (2.0) [2.0]	12 (4.2) [4.2]	7 (2.4) [2.4]
非感染性歯肉炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
嚥下痛	1 (0.4) [0.4]	0	0	0	2 (0.7) [0.7]
食道炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
口腔障害	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
膵炎	1 (0.4) [0.4]	0	0	0	0
歯周病	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肛門周囲痛	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
直腸炎	1 (0.4) [0.4]	0	0	0	0
直腸分泌物	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
直腸異形成	0	0	0	1 (0.4) [0.4]	0
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]
直腸ポリープ	0	0	0	0	1 (0.3) [0.3]
直腸攣縮	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
直腸しぶり	1 (0.4) [0.4]	0	0	0	0
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]
埋伏歯	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]
歯の脱落	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
歯痛	0	4 (1.6) [1.6]	3 (1.2) [1.2]	7 (2.5) [2.5]	7 (2.4) [2.4]
臍ヘルニア	1 (0.4) [0.4]	0	0	0	1 (0.3) [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).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
胃腸障害 (Cont.)					
嘔吐	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	4 (1.4) [1.4]
一般・全身障害および投与部位の状態	22 (9.0) [9.0]	16 (6.4) [6.4]	28 (11.2) [11.2]	36 (12.6) [12.6]	48 (16.5) [16.5]
無力症	0	0	0	1 (0.4) [0.4]	0
胸部不快感	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
胸痛	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.8) [0.8]	2 (0.7) [0.7]	4 (1.4) [1.4]
悪寒	2 (0.8) [0.8]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	2 (0.7) [0.7]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
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 (0.4) [0.4]	0	0	0	0
薬効欠如	1 (0.4) [0.4]	0	0	0	0
異形成	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]
疲労	5 (2.0) [2.1]	2 (0.8) [0.8]	4 (1.6) [1.6]	9 (3.2) [3.1]	10 (3.4) [3.4]
全身性浮腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
高体温症	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
一般・全身障害および投与部位の状態 (Cont.)					
炎症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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]
注射部位疼痛	0	1 (0.4) [0.4]	2 (0.8) [0.8]	9 (3.2) [3.1]	9 (3.1) [3.1]
倦怠感	1 (0.4) [0.4]	0	2 (0.8) [0.8]	3 (1.1) [1.1]	2 (0.7) [0.7]
腫瘤	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
粘膜乾燥	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
一般・全身障害および投与部位の状態 (Cont.)					
小結節	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
非心臓性胸痛	1 (0.4) [0.4]	0	0	0	0
浮腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
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]
疼痛	1 (0.4) [0.4]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	2 (0.7) [0.7]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
一般・全身障害および投与部位の状態 (Cont.)					
発熱	7 (2.9) [2.9]	8 (3.2) [3.2]	15 (6.0) [6.0]	15 (5.3) [5.3]	22 (7.6) [7.6]
異物感	1 (0.4) [0.4]	0	0	0	0
腫脹	0	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]
顔面腫脹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
ワクチン接種部位疼痛	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
肝胆道系障害	3 (1.2) [1.2]	6 (2.4) [2.3]	2 (0.8) [0.8]	13 (4.6) [4.5]	3 (1.0) [1.0]
胆道ジスキネジア	0	0	0	1 (0.4) [0.3]	0
硬化性胆管炎	0	0	0	3 (1.1) [1.1]	0
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]
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]
脂肪肝	0	2 (0.8) [0.8]	0	4 (1.4) [1.4]	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

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
肝胆道系障害 (Cont.)					
肝障害	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
肝損傷	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
免疫系障害	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	2 (0.7) [0.7]
アナフィラキシー反応	0	0	0	0	1 (0.3) [0.3]
薬物過敏症	1 (0.4) [0.4]	0	0	0	0
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症	92 (37.6) [37.1]	98 (39.2) [39.1]	105 (41.8) [41.8]	137 (48.1) [48.1]	153 (52.6) [52.5]
腹部膿瘍	1 (0.4) [0.4]	0	0	0	0
腹壁膿瘍	0	0	0	1 (0.4) [0.3]	0
ダニ皮膚炎	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0
急性心内膜炎	1 (0.4) [0.4]	0	0	0	0
肛門膿瘍	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	2 (0.7) [0.7]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
肛門直腸感染	1 (0.4) [0.4]	0	0	0	0
虫垂炎	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]
細菌性関節炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
無症候性COVID-19	0	0	0	1 (0.4) [0.4]	2 (0.7) [0.7]
細菌感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
細菌性膣症	1 (0.4) [0.4]	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).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
ブラストシスティス感染	0	0	0	1 (0.4) [0.4]	0
乳房膿瘍	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
気管支炎	3 (1.2) [1.2]	5 (2.0) [1.9]	1 (0.4) [0.4]	6 (2.1) [2.1]	3 (1.0) [1.0]
感染性滑液包炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
カンピロバクター胃腸炎	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]
カンピロバクター感染	0	1 (0.4) [0.4]	0	3 (1.1) [1.0]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
カンジダ感染	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0
蜂巣炎	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	1 (0.3) [0.3]
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
クロストリジウム・ディフィシレ感染	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.1) [1.1]	3 (1.0) [1.0]
結膜炎	0	2 (0.8) [0.8]	1 (0.4) [0.4]	4 (1.4) [1.4]	2 (0.7) [0.7]
コロナウイルス感染	0	0	0	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
COVID-19	8 (3.3) [3.4]	5 (2.0) [2.0]	10 (4.0) [4.0]	16 (5.6) [5.6]	27 (9.3) [9.3]
COVID-19肺炎	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	5 (1.8) [1.8]	6 (2.1) [2.1]
膀胱炎	0	3 (1.2) [1.2]	2 (0.8) [0.8]	8 (2.8) [2.8]	2 (0.7) [0.7]
サイトメガロウイルス性大腸炎	0	0	0	0	1 (0.3) [0.3]
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
毛嚢虫症	0	3 (1.2) [1.2]	2 (0.8) [0.8]	3 (1.1) [1.0]	3 (1.0) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
皮膚糸状菌症	1 (0.4) [0.4]	0	0	0	0
爪の皮膚糸状菌症	0	0	0	0	1 (0.3) [0.3]
憩室炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
耳感染	0	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.1) [1.0]	3 (1.0) [1.0]
感染性腸炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
エンテロウイルス感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
大腸菌性尿路感染	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
眼感染	0	0	0	1 (0.4) [0.4]	0
毛包炎	4 (1.6) [1.6]	4 (1.6) [1.6]	9 (3.6) [3.6]	4 (1.4) [1.4]	11 (3.8) [3.8]
真菌感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
皮膚真菌感染	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
せつ	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
胃腸炎	4 (1.6) [1.6]	5 (2.0) [2.1]	3 (1.2) [1.2]	5 (1.8) [1.8]	8 (2.7) [2.8]
ウイルス性胃腸炎	0	0	2 (0.8) [0.8]	2 (0.7) [0.7]	4 (1.4) [1.4]
陰部単純ヘルペス	0	0	0	0	1 (0.3) [0.3]
歯肉膿瘍	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
歯肉炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]
単径部膿瘍	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
ヘモフィルス感染	1 (0.4) [0.4]	0	0	0	0
手足口病	0	0	0	0	1 (0.3) [0.3]
ヘリコバクター感染	0	0	0	1 (0.4) [0.3]	0
ヘルペス性皮膚炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
ヘルペス眼感染	0	0	0	0	1 (0.3) [0.3]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
帯状疱疹	0	11 (4.4) [4.3]	14 (5.6) [5.6]	20 (7.0) [7.0]	25 (8.6) [8.6]
帯状疱疹性髄膜炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
耳帯状疱疹	0	0	0	1 (0.4) [0.4]	0
麦粒腫	3 (1.2) [1.2]	0	2 (0.8) [0.8]	2 (0.7) [0.7]	2 (0.7) [0.7]
膿痂疹	1 (0.4) [0.4]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
咬傷感染	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
感染性皮膚嚢腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
インフルエンザ	3 (1.2) [1.2]	7 (2.8) [2.8]	8 (3.2) [3.2]	10 (3.5) [3.5]	10 (3.4) [3.4]
大腸感染	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]
喉頭炎	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
潜伏結核	0	0	2 (0.8) [0.8]	1 (0.4) [0.3]	4 (1.4) [1.4]
下気道感染	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
乳腺炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
伝染性軟属腫	1 (0.4) [0.4]	0	0	0	0
上咽頭炎	20 (8.2) [8.0]	23 (9.2) [9.4]	26 (10.4) [10.4]	31 (10.9) [10.9]	32 (11.0) [11.0]
食道カンジダ症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
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]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	3 (1.2) [1.2]	5 (2.0) [2.0]	7 (2.8) [2.8]	5 (1.8) [1.7]	10 (3.4) [3.5]
外耳炎	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0
乳頭腫ウイルス感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
爪囲炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]
歯周炎	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]
扁桃周囲炎	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
咽頭炎	4 (1.6) [1.6]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	3 (1.0) [1.0]
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]
毛巣嚢胞	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
胸膜感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
ニューモシスチス・イロベチイ肺炎	1 (0.4) [0.4]	0	0	0	0
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
クリプトコッカス性肺炎	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
ウイルス性肺炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
歯髄炎	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]
膿疱	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]
腎盂腎炎	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
膿皮症	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
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]
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]
セラチア感染	1 (0.4) [0.4]	0	0	0	0
副鼻腔炎	4 (1.6) [1.6]	2 (0.8) [0.8]	3 (1.2) [1.2]	6 (2.1) [2.1]	6 (2.1) [2.1]
ブドウ球菌感染	1 (0.4) [0.4]	0	0	0	0
皮下組織膿瘍	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
股部白癬	0	0	0	0	1 (0.3) [0.3]
白癬感染	2 (0.8) [0.8]	0	0	0	1 (0.3) [0.4]
足部白癬	2 (0.8) [0.8]	3 (1.2) [1.2]	1 (0.4) [0.4]	4 (1.4) [1.4]	3 (1.0) [1.0]
癜風	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]
扁桃炎	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.2) [1.2]	4 (1.4) [1.4]	3 (1.0) [1.0]
細菌性扁桃炎	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
歯膿瘍	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]
歯感染	2 (0.8) [0.8]	0	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.0) [1.0]
トリコモナス症	1 (0.4) [0.4]	0	0	0	0
上気道感染	8 (3.3) [3.2]	12 (4.8) [4.8]	11 (4.4) [4.4]	14 (4.9) [4.9]	12 (4.1) [4.1]
尿路感染	6 (2.4) [2.5]	7 (2.8) [2.8]	3 (1.2) [1.2]	12 (4.2) [4.2]	8 (2.7) [2.8]
ガードネレラ菌性腟炎	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
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 (0.4) [0.4]	0	1 (0.4) [0.3]	0
ウイルス血症	1 (0.4) [0.4]	0	0	0	0
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]
ウイルス性咽頭炎	0	0	0	1 (0.4) [0.4]	0
ウイルス性上気道感染	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.2) [1.2]	1 (0.4) [0.4]	4 (1.4) [1.4]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
感染症および寄生虫症 (Cont.)					
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]
創傷感染	0	0	0	0	1 (0.3) [0.3]
傷害、中毒および処置合併症	11 (4.5) [4.4]	12 (4.8) [4.8]	12 (4.8) [4.8]	20 (7.0) [7.0]	16 (5.5) [5.5]
動物による引っかき傷	1 (0.4) [0.4]	0	0	0	0
足関節部骨折	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]
節足動物咬傷	0	0	0	1 (0.4) [0.3]	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
傷害、中毒および処置合併症 (Cont.)					
骨挫傷	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
挫傷	0	0	3 (1.2) [1.2]	2 (0.7) [0.7]	4 (1.4) [1.4]
毒性物質曝露	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
眼外傷	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
転倒	0	0	0	0	1 (0.3) [0.3]
足骨折	0	0	0	1 (0.4) [0.3]	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
傷害、中毒および処置合併症 (Cont.)					
仙骨骨折	0	0	0	1 (0.4) [0.3]	0
熱中症	1 (0.4) [0.4]	0	0	0	0
熱射病	0	0	0	1 (0.4) [0.4]	0
損傷	1 (0.4) [0.4]	0	0	0	0
関節損傷	0	2 (0.8) [0.8]	0	3 (1.1) [1.0]	0
靭帯断裂	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
傷害、中毒および処置合併症 (Cont.)					
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]
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]
四肢外傷性切断	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
腰椎骨折	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
筋断裂	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]
肉離れ	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
傷害、中毒および処置合併症 (Cont.)					
過量投与	0	0	0	2 (0.7) [0.7]	0
処置後出血	0	0	0	0	1 (0.3) [0.3]
外傷後疼痛	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0
肺挫傷	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
肋骨骨折	1 (0.4) [0.4]	0	0	0	0
交通事故	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
傷害、中毒および処置合併症 (Cont.)					
皮膚裂傷	1 (0.4) [0.4]	3 (1.2) [1.2]	0	3 (1.1) [1.1]	0
脊椎圧迫骨折	1 (0.4) [0.4]	0	0	0	0
スポーツ損傷	0	0	0	1 (0.4) [0.4]	0
ストレス骨折	0	0	0	1 (0.4) [0.3]	0
皮下血腫	1 (0.4) [0.4]	0	0	0	0
胸椎骨折	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
傷害、中毒および処置合併症 (Cont.)					
脛骨骨折	0	0	0	1 (0.4) [0.4]	0
歯牙破折	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
創傷	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
手首関節骨折	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
臨床検査	16 (6.5) [6.5]	42 (16.8) [16.8]	53 (21.1) [21.1]	58 (20.4) [20.3]	75 (25.8) [25.7]
アラニンアミノトランスフェラーゼ増加	1 (0.4) [0.4]	7 (2.8) [2.9]	7 (2.8) [2.8]	9 (3.2) [3.2]	10 (3.4) [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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
アミラーゼ増加	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
抗核抗体増加	1 (0.4) [0.4]	0	0	0	0
大動脈雑音	0	0	0	0	1 (0.3) [0.3]
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.8) [0.8]	9 (3.6) [3.7]	5 (2.0) [2.0]	10 (3.5) [3.6]	8 (2.7) [2.7]
細菌検査陽性	0	0	0	1 (0.4) [0.3]	0
血中アルブミン減少	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
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]
血中アルカリホスファターゼ増加	0	0	0	0	1 (0.3) [0.3]
血中重炭酸塩減少	0	0	0	1 (0.4) [0.3]	0
血中ビリルビン増加	0	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.7) [0.7]	4 (1.4) [1.4]
血中カルシウム増加	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	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

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
血中コレステロール増加	0	2 (0.8) [0.8]	6 (2.4) [2.4]	2 (0.7) [0.7]	8 (2.7) [2.7]
血中クレアチンホスホキナーゼ増加	5 (2.0) [2.1]	15 (6.0) [6.0]	19 (7.6) [7.6]	19 (6.7) [6.7]	34 (11.7) [11.6]
血中クレアチニン増加	2 (0.8) [0.8]	0	4 (1.6) [1.6]	0	4 (1.4) [1.4]
血中葉酸減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
血中ブドウ糖減少	0	0	0	0	1 (0.3) [0.3]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
血中鉄減少	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]
血中リン減少	0	0	0	0	2 (0.7) [0.7]
血中カリウム減少	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0
血中カリウム増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
血圧上昇	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]
血中ナトリウム増加	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
血中トリグリセリド異常	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
血中トリグリセリド増加	0	0	0	0	1 (0.3) [0.3]
尿中血陽性	0	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]
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]
骨密度減少	0	0	0	1 (0.4) [0.3]	0
炭水化物耐性低下	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
γ-グルタミルトランスフェラーゼ増加	1 (0.4) [0.4]	5 (2.0) [2.0]	1 (0.4) [0.4]	6 (2.1) [2.1]	4 (1.4) [1.4]
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
尿中ブドウ糖陽性	0	0	0	1 (0.4) [0.4]	0
顆粒球数減少	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
握力低下	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
ヘマトクリット減少	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
ヘモグロビン減少	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	4 (1.4) [1.4]	4 (1.4) [1.4]
尿中ヘモグロビン陽性	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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]
B型肝炎DNA測定陽性	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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]
リパーゼ増加	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
肝機能検査値上昇	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
低比重リポ蛋白減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
低比重リポ蛋白増加	0	1 (0.4) [0.4]	5 (2.0) [2.0]	1 (0.4) [0.3]	5 (1.7) [1.7]
リンパ球数減少	2 (0.8) [0.8]	4 (1.6) [1.6]	4 (1.6) [1.6]	6 (2.1) [2.1]	7 (2.4) [2.4]
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]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
リンパ球百分率増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
平均赤血球容積異常	0	0	0	0	1 (0.3) [0.3]
平均赤血球容積増加	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]
単球数増加	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
好中球数減少	2 (0.8) [0.8]	5 (2.0) [2.0]	8 (3.2) [3.2]	10 (3.5) [3.5]	11 (3.8) [3.8]
好中球数増加	2 (0.8) [0.8]	2 (0.8) [0.8]	2 (0.8) [0.8]	4 (1.4) [1.4]	3 (1.0) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
好中球百分率増加	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
血小板数減少	1 (0.4) [0.4]	0	0	0	0
血小板数増加	0	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]
プレアルブミン減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
前立腺特異性抗原増加	0	0	0	1 (0.4) [0.4]	0
総蛋白減少	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
総蛋白増加	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
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]
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]
血沈亢進	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
網状赤血球数減少	0	0	0	1 (0.4) [0.4]	0
ブドウ球菌検査陽性	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
トランスアミナーゼ上昇	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]
尿検査異常	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
尿中ケトン体陽性	0	0	0	0	1 (0.3) [0.4]
尿中白血球エステラーゼ陽性	0	0	0	1 (0.4) [0.3]	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]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
臨床検査 (Cont.)					
白血球数減少	2 (0.8) [0.8]	5 (2.0) [2.0]	6 (2.4) [2.4]	8 (2.8) [2.8]	9 (3.1) [3.1]
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]
尿中白血球陽性	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.4]
代謝および栄養障害	16 (6.5) [6.4]	16 (6.4) [6.5]	15 (6.0) [6.0]	26 (9.1) [9.2]	25 (8.6) [8.6]
食欲減退	1 (0.4) [0.4]	0	0	2 (0.7) [0.7]	1 (0.3) [0.3]
糖尿病	0	0	0	0	2 (0.7) [0.7]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
代謝および栄養障害 (Cont.)					
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]
葉酸欠乏	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
耐糖能障害	1 (0.4) [0.4]	0	0	0	0
痛風	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
高カルシウム血症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
高コレステロール血症	2 (0.8) [0.8]	4 (1.6) [1.7]	4 (1.6) [1.6]	6 (2.1) [2.1]	9 (3.1) [3.1]

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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
代謝および栄養障害 (Cont.)					
高血糖	1 (0.4) [0.4]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	1 (0.3) [0.3]
高リパーゼ血症	1 (0.4) [0.4]	0	0	0	0
高脂血症	0	1 (0.4) [0.4]	2 (0.8) [0.8]	5 (1.8) [1.8]	3 (1.0) [1.1]
高ナトリウム血症	0	0	0	0	1 (0.3) [0.3]
高尿酸血症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
低カリウム血症	3 (1.2) [1.2]	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
代謝および栄養障害 (Cont.)					
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]
低リン酸血症	1 (0.4) [0.4]	0	0	0	0
鉄欠乏	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.4]
代謝症候群	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肥満	0	0	0	0	1 (0.3) [0.3]
2型糖尿病	1 (0.4) [0.4]	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
代謝および栄養障害 (Cont.)					
過少体重	0	0	0	1 (0.4) [0.3]	0
ビタミンD欠乏	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.8) [0.8]	4 (1.4) [1.4]	4 (1.4) [1.4]
筋骨格系および結合組織障害	51 (20.8) [20.7]	36 (14.4) [14.5]	27 (10.8) [10.8]	67 (23.5) [23.5]	46 (15.8) [15.9]
強直性脊椎炎	1 (0.4) [0.4]	0	0	0	0
関節痛	25 (10.2) [10.2]	13 (5.2) [5.3]	7 (2.8) [2.8]	26 (9.1) [9.1]	14 (4.8) [4.8]
関節炎	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
腸炎性関節炎	1 (0.4) [0.4]	0	0	0	0
関節障害	7 (2.9) [2.8]	1 (0.4) [0.4]	3 (1.2) [1.2]	2 (0.7) [0.7]	3 (1.0) [1.0]
背部痛	10 (4.1) [4.1]	7 (2.8) [2.9]	1 (0.4) [0.4]	13 (4.6) [4.6]	5 (1.7) [1.7]
骨痛	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
滑液包炎	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
軟骨萎縮	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
頚部脊柱管狭窄症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
軟骨軟化症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
ばち状指	0	0	0	1 (0.4) [0.3]	0
尾骨痛	1 (0.4) [0.4]	0	0	0	0
肋軟骨炎	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
外骨腫	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
四肢拘縮	0	0	0	1 (0.4) [0.4]	0
線維筋痛	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
側腹部痛	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
出血性関節症	1 (0.4) [0.4]	0	0	0	0
椎間板変性症	1 (0.4) [0.4]	0	0	0	0
椎間板突出	0	0	0	2 (0.7) [0.7]	2 (0.7) [0.7]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
関節滲出液	0	0	0	1 (0.4) [0.3]	0
関節硬直	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
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]
腰部脊柱管狭窄症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
筋拘縮	0	0	0	1 (0.4) [0.4]	0
筋痙縮	0	0	0	1 (0.4) [0.3]	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
筋力低下	1 (0.4) [0.4]	0	0	0	0
筋骨格系胸痛	2 (0.8) [0.8]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
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]
筋骨格硬直	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0
筋肉痛	2 (0.8) [0.8]	2 (0.8) [0.8]	1 (0.4) [0.4]	8 (2.8) [2.8]	6 (2.1) [2.1]
筋炎	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
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]
骨炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
変形性関節症	2 (0.8) [0.8]	0	0	3 (1.1) [1.1]	0
骨壊死	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
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]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
四肢痛	4 (1.6) [1.6]	1 (0.4) [0.4]	3 (1.2) [1.2]	2 (0.7) [0.7]	8 (2.7) [2.7]
関節周囲炎	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
足底筋膜炎	0	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]
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]
変形性脊椎症	1 (0.4) [0.4]	0	0	0	0
脊椎関節障害	1 (0.4) [0.4]	1 (0.4) [0.4]	0	2 (0.7) [0.7]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)					
軟骨下機能不全骨折	0	0	0	1 (0.4) [0.3]	0
腱痛	1 (0.4) [0.4]	0	0	0	0
腱炎	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
腱鞘炎	1 (0.4) [0.4]	0	0	0	0
弾発指	0	0	0	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
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 (1.2) [1.3]	5 (2.0) [2.0]	8 (3.2) [3.2]	9 (3.2) [3.1]	14 (4.8) [4.8]
結腸腺癌	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
基底細胞癌	0	0	3 (1.2) [1.2]	0	5 (1.7) [1.7]
肺の良性新生物	0	0	0	1 (0.4) [0.3]	0
良性脾腫瘍	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
ボーエン病	0	0	0	0	1 (0.3) [0.3]
気管支の良性新生物	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
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.)					
大腸腺腫	1 (0.4) [0.4]	0	0	0	0
線維腫	0	0	0	0	1 (0.3) [0.3]
線維性組織球腫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
血管腫	0	0	0	1 (0.4) [0.4]	0
皮膚血管腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
浸潤性乳癌	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
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.)					
メラノサイト性母斑	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
髄膜腫	0	0	0	0	1 (0.3) [0.3]
卵巣胚細胞良性奇形腫	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
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]
皮膚乳頭腫	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
小細胞癌	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
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 (0.3) [0.3]
子宮頚部扁平上皮癌	0	0	0	0	1 (0.3) [0.4]
甲状腺腺腫	0	0	0	1 (0.4) [0.3]	0
子宮平滑筋腫	0	0	0	1 (0.4) [0.4]	0
神経系障害	22 (9.0) [8.9]	18 (7.2) [7.2]	20 (8.0) [8.0]	29 (10.2) [10.1]	41 (14.1) [14.1]
脳損傷	0	0	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
神経系障害 (Cont.)					
灼熱感	0	0	0	1 (0.4) [0.3]	0
頚動脈硬化症	0	0	0	0	1 (0.3) [0.3]
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]
脳血管発作	0	0	0	0	1 (0.3) [0.3]
頚髄圧迫	0	0	0	0	1 (0.3) [0.3]
頚髄神経根障害	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
神経系障害 (Cont.)					
注意力障害	0	0	0	1 (0.4) [0.4]	0
浮動性めまい	3 (1.2) [1.2]	2 (0.8) [0.8]	2 (0.8) [0.8]	3 (1.1) [1.1]	6 (2.1) [2.1]
味覚不全	1 (0.4) [0.4]	0	0	0	0
てんかん	1 (0.4) [0.4]	0	0	0	0
本態性振戦	1 (0.4) [0.4]	0	0	0	0
頭痛	11 (4.5) [4.4]	8 (3.2) [3.2]	9 (3.6) [3.6]	17 (6.0) [5.9]	19 (6.5) [6.5]

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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
神経系障害 (Cont.)					
知覚過敏	1 (0.4) [0.4]	0	0	0	0
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]
腰仙部神経根障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
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]
前兆を伴う片頭痛	0	0	0	1 (0.4) [0.3]	0
脊髄症	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
神経系障害 (Cont.)					
神経圧迫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
末梢性ニューロパチー	1 (0.4) [0.4]	0	0	0	0
後頭神経痛	0	0	0	1 (0.4) [0.3]	0
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]
睡眠の質低下	0	0	0	0	1 (0.3) [0.3]
ヘルペス後神経痛	0	0	0	0	1 (0.3) [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).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
神経系障害 (Cont.)					
失神寸前の状態	0	0	0	0	2 (0.7) [0.7]
坐骨神経痛	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	3 (1.0) [1.0]
傾眠	0	0	0	0	2 (0.7) [0.7]
会話障害	0	0	0	1 (0.4) [0.4]	0
脊椎炎性脊髄症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
くも膜下出血	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
神経系障害 (Cont.)					
硬膜下滲出液	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
失神	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
緊張性頭痛	0	0	0	0	1 (0.3) [0.3]
視野欠損	0	0	0	0	1 (0.3) [0.3]
精神障害	14 (5.7) [5.7]	7 (2.8) [2.7]	13 (5.2) [5.2]	14 (4.9) [4.9]	19 (6.5) [6.5]
不安	6 (2.4) [2.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	4 (1.4) [1.4]	4 (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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
精神障害 (Cont.)					
不安障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
抑うつ気分	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
うつ病	2 (0.8) [0.8]	1 (0.4) [0.4]	4 (1.6) [1.6]	2 (0.7) [0.7]	6 (2.1) [2.1]
不眠症	7 (2.9) [2.9]	2 (0.8) [0.8]	8 (3.2) [3.2]	5 (1.8) [1.7]	11 (3.8) [3.8]
故意の自傷行為	0	0	0	0	1 (0.3) [0.3]
易刺激性	1 (0.4) [0.4]	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).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
精神障害 (Cont.)					
精神障害	1 (0.4) [0.4]	0	0	0	0
パニック発作	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
睡眠障害	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
自殺念慮	1 (0.4) [0.4]	0	0	0	0
腎および尿路障害	7 (2.9) [2.8]	6 (2.4) [2.4]	12 (4.8) [4.8]	8 (2.8) [2.8]	16 (5.5) [5.5]
急性腎障害	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
腎および尿路障害 (Cont.)					
膀胱結石	0	0	0	0	1 (0.3) [0.3]
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]
糖尿	1 (0.4) [0.4]	0	0	0	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]
水腎症	1 (0.4) [0.4]	0	0	0	0
緊張性膀胱	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
腎および尿路障害 (Cont.)					
白血球尿	1 (0.4) [0.4]	0	0	0	0
排尿異常	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
腎石灰沈着症	1 (0.4) [0.4]	0	0	0	0
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]
頻尿	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
蛋白尿	1 (0.4) [0.4]	0	0	0	2 (0.7) [0.7]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
腎および尿路障害 (Cont.)					
腎仙痛	0	0	4 (1.6) [1.6]	0	4 (1.4) [1.4]
腎機能障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
尿管結石症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
尿閉	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
生殖系および乳房障害	8 (3.3) [3.2]	10 (4.0) [4.0]	7 (2.8) [2.8]	17 (6.0) [6.0]	13 (4.5) [4.5]
無月経	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [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).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
生殖系および乳房障害 (Cont.)					
バルトリン嚢腫	1 (0.4) [0.4]	0	0	0	0
良性前立腺肥大症	0	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.1) [1.1]	3 (1.0) [1.0]
乳房嚢胞	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
乳房痛	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
子宮頚部上皮異形成	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
性交出血	0	0	0	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
生殖系および乳房障害 (Cont.)					
機能不全性子宮出血	1 (0.4) [0.4]	0	0	0	0
月経困難症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]
性交困難	0	0	0	1 (0.4) [0.4]	0
勃起不全	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]
閉経期症状	1 (0.4) [0.4]	0	0	0	0
月経過多	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
生殖系および乳房障害 (Cont.)					
不規則月経	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0
不正子宮出血	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	1 (0.3) [0.3]
卵巣静脈血栓症	1 (0.4) [0.4]	0	0	0	0
多嚢胞性卵巣	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
閉経後出血	0	0	0	0	1 (0.3) [0.3]
前立腺腫瘤	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
生殖系および乳房障害 (Cont.)					
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]
精液変色	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
腟分泌物	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]
腟出血	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
外陰腟そう痒症	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
呼吸器、胸郭および縦隔障害	18 (7.3) [7.2]	15 (6.0) [6.1]	20 (8.0) [8.0]	23 (8.1) [8.1]	27 (9.3) [9.3]
急性呼吸不全	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
失声症	0	0	0	0	1 (0.3) [0.3]
喘息	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]
気管支拡張症	1 (0.4) [0.4]	0	0	0	0
慢性閉塞性肺疾患	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
咳嗽	3 (1.2) [1.2]	3 (1.2) [1.2]	4 (1.6) [1.6]	6 (2.1) [2.1]	4 (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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)					
呼吸困難	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
労作性呼吸困難	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肺気腫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
鼻出血	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	3 (1.0) [1.0]
喀血	1 (0.4) [0.4]	0	0	0	0
しゃっくり	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)					
過換気	0	0	0	0	1 (0.3) [0.3]
間質性肺疾患	1 (0.4) [0.4]	0	0	0	0
肺過膨脹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肺浸潤	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
鼻閉	3 (1.2) [1.2]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
鼻潰瘍	0	0	0	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)					
非感染性気管支炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
口腔咽頭痛	5 (2.0) [2.0]	3 (1.2) [1.2]	6 (2.4) [2.4]	5 (1.8) [1.7]	7 (2.4) [2.4]
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]
肺塞栓症	0	2 (0.8) [0.8]	0	3 (1.1) [1.0]	3 (1.0) [1.0]
肺出血	1 (0.4) [0.4]	0	0	0	0
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)					
鼻漏	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
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]
睡眠時無呼吸症候群	0	0	0	1 (0.4) [0.3]	0
咽喉刺激感	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
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]
上気道咳症候群	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害	49 (20.0) [19.8]	38 (15.2) [15.1]	51 (20.3) [20.3]	56 (19.6) [19.6]	68 (23.4) [23.4]
ざ瘡	8 (3.3) [3.2]	6 (2.4) [2.3]	9 (3.6) [3.6]	9 (3.2) [3.1]	14 (4.8) [4.8]
嚢胞性ざ瘡	0	0	0	1 (0.4) [0.3]	0
光線角化症	0	0	0	0	2 (0.7) [0.7]
脱毛症	0	2 (0.8) [0.8]	3 (1.2) [1.2]	4 (1.4) [1.4]	4 (1.4) [1.4]
皮脂欠乏症	0	0	1 (0.4) [0.4]	0	1 (0.3) [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).
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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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
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]
皮膚炎	3 (1.2) [1.2]	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.7) [0.7]	3 (1.0) [1.0]
ざ瘡様皮膚炎	0	0	0	2 (0.7) [0.7]	1 (0.3) [0.3]
アレルギー性皮膚炎	0	0	0	0	1 (0.3) [0.3]
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]
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
びまん性脱毛症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
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]
異汗性湿疹	2 (0.8) [0.8]	0	0	0	2 (0.7) [0.7]
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]
湿疹	5 (2.0) [2.0]	2 (0.8) [0.8]	5 (2.0) [2.0]	4 (1.4) [1.4]	7 (2.4) [2.4]
皮脂欠乏性湿疹	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	3 (1.0) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
紅斑	2 (0.8) [0.8]	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.1) [1.0]	3 (1.0) [1.0]
結節性紅斑	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
多汗症	0	0	0	1 (0.4) [0.3]	0
間擦疹	0	0	0	1 (0.4) [0.3]	0
瘢痕そう痒感	0	0	0	0	1 (0.3) [0.3]
黒子	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
機械性蕁麻疹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
汗疹	0	0	0	1 (0.4) [0.4]	0
神経皮膚炎	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0
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]
爪破損	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
爪甲剥離症	0	0	1 (0.4) [0.4]	0	1 (0.3) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
掌蹠膿疱症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
脂肪織炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
丘疹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
口囲皮膚炎	0	0	0	1 (0.4) [0.3]	0
光線性皮膚症	1 (0.4) [0.4]	0	0	0	0
光線過敏性反応	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
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]
壊疽性膿皮症	1 (0.4) [0.4]	0	0	0	0
発疹	9 (3.7) [3.7]	8 (3.2) [3.2]	11 (4.4) [4.4]	13 (4.6) [4.5]	15 (5.2) [5.2]
紅斑性皮疹	1 (0.4) [0.4]	1 (0.4) [0.4]	0	3 (1.1) [1.0]	0
毛孔性皮疹	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
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]

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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
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]
丘疹性皮疹	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
そう痒性皮疹	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
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]
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]
皮膚灼熱感	1 (0.4) [0.4]	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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
皮膚びらん	1 (0.4) [0.4]	0	0	0	0
皮膚剥脱	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]
皮膚亀裂	1 (0.4) [0.4]	0	0	1 (0.4) [0.3]	0
皮膚色素過剰	1 (0.4) [0.4]	0	0	0	0
皮膚病変	0	0	2 (0.8) [0.8]	1 (0.4) [0.4]	5 (1.7) [1.7]
皮膚腫瘤	0	1 (0.4) [0.4]	0	1 (0.4) [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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
皮膚潰瘍	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
蕁麻疹	2 (0.8) [0.8]	0	5 (2.0) [2.0]	0	6 (2.1) [2.1]
乾皮症	0	0	0	0	1 (0.3) [0.3]
社会環境	0	0	0	0	1 (0.3) [0.3]
閉経後	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
外科および内科処置	0	2 (0.8) [0.8]	0	3 (1.1) [1.1]	2 (0.7) [0.7]
人工流産	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0
歯科インプラント埋込み	0	0	0	0	1 (0.3) [0.3]
抜歯	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]
血管障害	4 (1.6) [1.6]	8 (3.2) [3.3]	10 (4.0) [4.0]	14 (4.9) [5.0]	17 (5.8) [5.9]
大動脈瘤	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
大動脈硬化症	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
血管障害 (Cont.)					
出血性静脈瘤	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
深部静脈血栓症	0	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]
血腫	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
高血圧	2 (0.8) [0.8]	6 (2.4) [2.5]	6 (2.4) [2.4]	10 (3.5) [3.5]	9 (3.1) [3.1]
低血圧	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
起立性低血圧	0	0	0	0	1 (0.3) [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.
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

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] 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%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) n (%) [SSA%]
血管障害 (Cont.)					
末梢動脈閉塞性疾患	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
静脈炎	0	0	0	0	1 (0.3) [0.3]
レイノー現象	0	0	0	1 (0.4) [0.4]	0
静脈血栓症	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0
白衣性高血圧	0	0	0	0	2 (0.7) [0.7]

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 3.3.5

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)
Any adverse event	186 (75.9) [75.5]	193 (77.2) [77.2]	199 (79.3) [79.3]	238 (83.5) [83.5]	245 (84.2) [84.2]		
血中クレアチンホスホキナーゼ増加	5 (2.0) [2.1]	15 (6.0) [6.0]	19 (7.6) [7.6]	19 (6.7) [6.7]	34 (11.7) [11.6]	4.0 (0.4, 7.6)	5.5 (1.6, 9.3)
上咽頭炎	20 (8.2) [8.0]	23 (9.2) [9.4]	26 (10.4) [10.4]	31 (10.9) [10.9]	32 (11.0) [11.0]	1.4 (-3.6, 6.4)	2.4 (-2.7, 7.5)
潰瘍性大腸炎	74 (30.2) [29.8]	31 (12.4) [12.4]	20 (8.0) [8.0]	43 (15.1) [15.1]	31 (10.7) [10.7]	-17.4 (-24.4, -10.4)	-21.8 (-28.4, -15.3)
COVID-19	8 (3.3) [3.4]	5 (2.0) [2.0]	10 (4.0) [4.0]	16 (5.6) [5.6]	27 (9.3) [9.3]	-1.4 (-4.4, 1.7)	0.6 (-2.8, 4.1)
帯状疱疹	0	11 (4.4) [4.3]	14 (5.6) [5.6]	20 (7.0) [7.0]	25 (8.6) [8.6]	4.3 (1.6, 7.0)	5.6 (2.5, 8.6)
発熱	7 (2.9) [2.9]	8 (3.2) [3.2]	15 (6.0) [6.0]	15 (5.3) [5.3]	22 (7.6) [7.6]	0.3 (-2.9, 3.5)	3.1 (-0.6, 6.8)

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)
頭痛	11 (4.5) [4.4]	8 (3.2) [3.2]	9 (3.6) [3.6]	17 (6.0) [5.9]	19 (6.5) [6.5]	-1.2 (-4.7, 2.2)	-0.8 (-4.4, 2.7)
発疹	9 (3.7) [3.7]	8 (3.2) [3.2]	11 (4.4) [4.4]	13 (4.6) [4.5]	15 (5.2) [5.2]	-0.5 (-3.8, 2.9)	0.7 (-2.9, 4.3)
関節痛	25 (10.2) [10.2]	13 (5.2) [5.3]	7 (2.8) [2.8]	26 (9.1) [9.1]	14 (4.8) [4.8]	-4.9 (-9.7, -0.2)	-7.4 (-11.8, -3.0)
ざ瘡	8 (3.3) [3.2]	6 (2.4) [2.3]	9 (3.6) [3.6]	9 (3.2) [3.1]	14 (4.8) [4.8]	-0.9 (-3.9, 2.2)	0.4 (-3.0, 3.7)
上気道感染	8 (3.3) [3.2]	12 (4.8) [4.8]	11 (4.4) [4.4]	14 (4.9) [4.9]	12 (4.1) [4.1]	1.7 (-1.9, 5.2)	1.2 (-2.2, 4.7)
貧血	10 (4.1) [4.0]	9 (3.6) [3.7]	8 (3.2) [3.2]	15 (5.3) [5.3]	11 (3.8) [3.8]	-0.3 (-3.8, 3.2)	-0.8 (-4.2, 2.6)
好中球数減少	2 (0.8) [0.8]	5 (2.0) [2.0]	8 (3.2) [3.2]	10 (3.5) [3.5]	11 (3.8) [3.8]	1.2 (-1.1, 3.5)	2.4 (-0.3, 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.
[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)
不眠症	7 (2.9) [2.9]	2 (0.8) [0.8]	8 (3.2) [3.2]	5 (1.8) [1.7]	11 (3.8) [3.8]	-2.1 (-4.7, 0.5)	0.3 (-2.9, 3.5)
毛包炎	4 (1.6) [1.6]	4 (1.6) [1.6]	9 (3.6) [3.6]	4 (1.4) [1.4]	11 (3.8) [3.8]	-0.0 (-2.5, 2.5)	2.0 (-1.0, 4.9)
インフルエンザ	3 (1.2) [1.2]	7 (2.8) [2.8]	8 (3.2) [3.2]	10 (3.5) [3.5]	10 (3.4) [3.4]	1.6 (-1.0, 4.2)	2.0 (-0.8, 4.7)
疲労	5 (2.0) [2.1]	2 (0.8) [0.8]	4 (1.6) [1.6]	9 (3.2) [3.1]	10 (3.4) [3.4]	-1.3 (-3.6, 1.1)	-0.5 (-3.1, 2.1)
アラニンアミノトランスフェラーゼ増加	1 (0.4) [0.4]	7 (2.8) [2.9]	7 (2.8) [2.8]	9 (3.2) [3.2]	10 (3.4) [3.4]	2.5 (0.0, 5.0)	2.4 (-0.0, 4.8)
口腔ヘルペス	3 (1.2) [1.2]	5 (2.0) [2.0]	7 (2.8) [2.8]	5 (1.8) [1.7]	10 (3.4) [3.5]	0.7 (-1.7, 3.2)	1.6 (-1.1, 4.2)
便秘	2 (0.8) [0.8]	3 (1.2) [1.2]	6 (2.4) [2.4]	5 (1.8) [1.8]	10 (3.4) [3.4]	0.4 (-1.6, 2.5)	1.6 (-0.8, 4.0)

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)
高血圧	2 (0.8) [0.8]	6 (2.4) [2.5]	6 (2.4) [2.4]	10 (3.5) [3.5]	9 (3.1) [3.1]	1.6 (-0.8, 4.1)	1.6 (-0.9, 4.0)
注射部位疼痛	0	1 (0.4) [0.4]	2 (0.8) [0.8]	9 (3.2) [3.1]	9 (3.1) [3.1]	0.4 (-1.0, 1.7)	0.8 (-0.8, 2.3)
白血球数減少	2 (0.8) [0.8]	5 (2.0) [2.0]	6 (2.4) [2.4]	8 (2.8) [2.8]	9 (3.1) [3.1]	1.2 (-1.2, 3.5)	1.6 (-0.9, 4.0)
高コレステロール血症	2 (0.8) [0.8]	4 (1.6) [1.7]	4 (1.6) [1.6]	6 (2.1) [2.1]	9 (3.1) [3.1]	0.9 (-1.3, 3.1)	0.8 (-1.3, 3.0)
好中球減少症	3 (1.2) [1.2]	4 (1.6) [1.6]	6 (2.4) [2.4]	4 (1.4) [1.4]	9 (3.1) [3.0]	0.4 (-1.9, 2.7)	1.2 (-1.4, 3.7)
尿路感染	6 (2.4) [2.5]	7 (2.8) [2.8]	3 (1.2) [1.2]	12 (4.2) [4.2]	8 (2.7) [2.8]	0.3 (-2.7, 3.3)	-1.3 (-3.9, 1.3)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.8) [0.8]	9 (3.6) [3.7]	5 (2.0) [2.0]	10 (3.5) [3.6]	8 (2.7) [2.7]	2.9 (0.1, 5.7)	1.2 (-1.1, 3.5)

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)
胃腸炎	4 (1.6) [1.6]	5 (2.0) [2.1]	3 (1.2) [1.2]	5 (1.8) [1.8]	8 (2.7) [2.8]	0.4 (-2.2, 3.1)	-0.4 (-2.8, 1.9)
四肢痛	4 (1.6) [1.6]	1 (0.4) [0.4]	3 (1.2) [1.2]	2 (0.7) [0.7]	8 (2.7) [2.7]	-1.1 (-3.2, 0.9)	-0.4 (-2.6, 1.9)
血中コレステロール増加	0	2 (0.8) [0.8]	6 (2.4) [2.4]	2 (0.7) [0.7]	8 (2.7) [2.7]	0.8 (-0.8, 2.3)	2.4 (0.2, 4.6)
悪心	5 (2.0) [2.1]	4 (1.6) [1.5]	5 (2.0) [2.0]	12 (4.2) [4.2]	7 (2.4) [2.4]	-0.5 (-3.1, 2.0)	-0.1 (-2.8, 2.6)
腹痛	6 (2.4) [2.5]	6 (2.4) [2.4]	4 (1.6) [1.6]	10 (3.5) [3.5]	7 (2.4) [2.4]	-0.1 (-3.0, 2.8)	-0.9 (-3.6, 1.8)
歯痛	0	4 (1.6) [1.6]	3 (1.2) [1.2]	7 (2.5) [2.5]	7 (2.4) [2.4]	1.6 (-0.3, 3.5)	1.2 (-0.5, 2.9)
リンパ球数減少	2 (0.8) [0.8]	4 (1.6) [1.6]	4 (1.6) [1.6]	6 (2.1) [2.1]	7 (2.4) [2.4]	0.8 (-1.4, 3.0)	0.8 (-1.4, 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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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)
口腔咽頭痛	5 (2.0) [2.0]	3 (1.2) [1.2]	6 (2.4) [2.4]	5 (1.8) [1.7]	7 (2.4) [2.4]	-0.8 (-3.2, 1.7)	0.4 (-2.3, 3.2)
湿疹	5 (2.0) [2.0]	2 (0.8) [0.8]	5 (2.0) [2.0]	4 (1.4) [1.4]	7 (2.4) [2.4]	-1.2 (-3.6, 1.1)	-0.0 (-2.7, 2.6)
筋肉痛	2 (0.8) [0.8]	2 (0.8) [0.8]	1 (0.4) [0.4]	8 (2.8) [2.8]	6 (2.1) [2.1]	-0.0 (-1.9, 1.9)	-0.4 (-2.1, 1.3)
副鼻腔炎	4 (1.6) [1.6]	2 (0.8) [0.8]	3 (1.2) [1.2]	6 (2.1) [2.1]	6 (2.1) [2.1]	-0.8 (-3.1, 1.4)	-0.4 (-2.8, 1.9)
ＣＯＶＩＤ－１９肺炎	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	5 (1.8) [1.8]	6 (2.1) [2.1]	-0.0 (-1.6, 1.5)	0.4 (-1.4, 2.1)
浮動性めまい	3 (1.2) [1.2]	2 (0.8) [0.8]	2 (0.8) [0.8]	3 (1.1) [1.1]	6 (2.1) [2.1]	-0.4 (-2.5, 1.7)	-0.4 (-2.5, 1.6)
うつ病	2 (0.8) [0.8]	1 (0.4) [0.4]	4 (1.6) [1.6]	2 (0.7) [0.7]	6 (2.1) [2.1]	-0.4 (-2.2, 1.3)	0.8 (-1.4, 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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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)
腹部膨満	1 (0.4) [0.4]	2 (0.8) [0.8]	5 (2.0) [2.0]	2 (0.7) [0.7]	6 (2.1) [2.1]	0.4 (-1.3, 2.2)	1.6 (-0.6, 3.8)
蕁麻疹	2 (0.8) [0.8]	0	5 (2.0) [2.0]	0	6 (2.1) [2.1]	-0.8 (-2.3, 0.8)	1.2 (-1.1, 3.5)
背部痛	10 (4.1) [4.1]	7 (2.8) [2.9]	1 (0.4) [0.4]	13 (4.6) [4.6]	5 (1.7) [1.7]	-1.2 (-4.6, 2.2)	-3.7 (-6.4, -0.9)
白血球減少症	3 (1.2) [1.2]	5 (2.0) [2.0]	1 (0.4) [0.4]	7 (2.5) [2.4]	5 (1.7) [1.7]	0.8 (-1.6, 3.2)	-0.8 (-2.6, 1.1)
大腸ポリープ	2 (0.8) [0.8]	0	1 (0.4) [0.4]	2 (0.7) [0.7]	5 (1.7) [1.7]	-0.8 (-2.4, 0.8)	-0.4 (-2.2, 1.3)
低比重リポ蛋白増加	0	1 (0.4) [0.4]	5 (2.0) [2.0]	1 (0.4) [0.3]	5 (1.7) [1.7]	0.4 (-1.0, 1.7)	2.0 (-0.0, 4.0)
皮膚病変	0	0	2 (0.8) [0.8]	1 (0.4) [0.4]	5 (1.7) [1.7]	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)
基底細胞癌	0	0	3 (1.2) [1.2]	0	5 (1.7) [1.7]	0.0	1.2 (-0.5, 2.9)
咳嗽	3 (1.2) [1.2]	3 (1.2) [1.2]	4 (1.6) [1.6]	6 (2.1) [2.1]	4 (1.4) [1.4]	0.0 (-2.1, 2.2)	0.4 (-1.9, 2.7)
γ-グルタミルトランスフェラーゼ増加	1 (0.4) [0.4]	5 (2.0) [2.0]	1 (0.4) [0.4]	6 (2.1) [2.1]	4 (1.4) [1.4]	1.6 (-0.6, 3.8)	-0.0 (-1.6, 1.6)
痔核	1 (0.4) [0.4]	3 (1.2) [1.2]	2 (0.8) [0.8]	6 (2.1) [2.1]	4 (1.4) [1.4]	0.8 (-1.1, 2.6)	0.4 (-1.3, 2.1)
上腹部痛	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.8) [0.8]	5 (1.8) [1.8]	4 (1.4) [1.4]	0.4 (-1.7, 2.5)	-0.0 (-1.9, 1.9)
不安	6 (2.4) [2.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	4 (1.4) [1.4]	4 (1.4) [1.4]	-2.0 (-4.3, 0.3)	-1.6 (-4.0, 0.8)
ビタミンD欠乏	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.8) [0.8]	4 (1.4) [1.4]	4 (1.4) [1.4]	0.4 (-1.6, 2.4)	0.0 (-1.9, 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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 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)
ヘモグロビン減少	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	4 (1.4) [1.4]	4 (1.4) [1.4]	0.4 (-1.4, 2.1)	-0.0 (-1.6, 1.5)
脱毛症	0	2 (0.8) [0.8]	3 (1.2) [1.2]	4 (1.4) [1.4]	4 (1.4) [1.4]	0.8 (-0.8, 2.4)	1.2 (-0.5, 2.9)
胸痛	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.8) [0.8]	2 (0.7) [0.7]	4 (1.4) [1.4]	0.4 (-1.3, 2.2)	0.4 (-1.3, 2.1)
血中ビリルビン増加	0	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.7) [0.7]	4 (1.4) [1.4]	0.8 (-0.8, 2.4)	1.2 (-0.5, 2.9)
挫傷	0	0	3 (1.2) [1.2]	2 (0.7) [0.7]	4 (1.4) [1.4]	0.0	1.2 (-0.5, 2.9)
ウイルス性胃腸炎	0	0	2 (0.8) [0.8]	2 (0.7) [0.7]	4 (1.4) [1.4]	0.0	0.8 (-0.8, 2.4)
ウイルス性上気道感染	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.2) [1.2]	1 (0.4) [0.4]	4 (1.4) [1.4]	-0.8 (-2.7, 1.1)	-0.0 (-2.2, 2.2)

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

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)
アフタ性潰瘍	2 (0.8) [0.8]	1 (0.4) [0.4]	3 (1.2) [1.2]	1 (0.4) [0.3]	4 (1.4) [1.3]	-0.4 (-2.2, 1.3)	0.4 (-1.7, 2.4)
嘔吐	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	4 (1.4) [1.4]	-0.0 (-1.6, 1.5)	-0.0 (-1.6, 1.5)
潜伏結核	0	0	2 (0.8) [0.8]	1 (0.4) [0.3]	4 (1.4) [1.4]	0.0	0.8 (-0.8, 2.4)
血中クレアチニン増加	2 (0.8) [0.8]	0	4 (1.6) [1.6]	0	4 (1.4) [1.4]	-0.8 (-2.3, 0.8)	0.8 (-1.4, 3.0)
腎仙痛	0	0	4 (1.6) [1.6]	0	4 (1.4) [1.4]	0.0	1.6 (-0.3, 3.5)
気管支炎	3 (1.2) [1.2]	5 (2.0) [1.9]	1 (0.4) [0.4]	6 (2.1) [2.1]	3 (1.0) [1.0]	0.7 (-1.7, 3.1)	-0.8 (-2.7, 1.1)
高脂血症	0	1 (0.4) [0.4]	2 (0.8) [0.8]	5 (1.8) [1.8]	3 (1.0) [1.1]	0.4 (-1.0, 1.8)	0.8 (-0.7, 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)
好中球数増加	2 (0.8) [0.8]	2 (0.8) [0.8]	2 (0.8) [0.8]	4 (1.4) [1.4]	3 (1.0) [1.0]	0.0 (-1.9, 1.9)	-0.0 (-1.9, 1.9)
足部白癬	2 (0.8) [0.8]	3 (1.2) [1.2]	1 (0.4) [0.4]	4 (1.4) [1.4]	3 (1.0) [1.0]	0.4 (-1.6, 2.5)	-0.4 (-2.1, 1.3)
白内障	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.8) [0.8]	4 (1.4) [1.4]	3 (1.0) [1.0]	0.3 (-1.4, 2.1)	0.4 (-1.4, 2.1)
扁桃炎	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.2) [1.2]	4 (1.4) [1.4]	3 (1.0) [1.0]	0.4 (-1.3, 2.1)	0.8 (-1.1, 2.7)
胃食道逆流性疾患	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.2) [1.2]	3 (1.1) [1.1]	3 (1.0) [1.0]	-0.8 (-2.7, 1.1)	-0.0 (-2.2, 2.2)
クロストリジウム・ディフィシレ感染	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.1) [1.1]	3 (1.0) [1.0]	-0.4 (-2.2, 1.3)	-0.0 (-1.9, 1.9)
紅斑	2 (0.8) [0.8]	3 (1.2) [1.2]	1 (0.4) [0.4]	3 (1.1) [1.0]	3 (1.0) [1.0]	0.3 (-1.7, 2.4)	-0.4 (-2.2, 1.3)

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[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)
良性前立腺肥大症	0	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.1) [1.1]	3 (1.0) [1.0]	0.4 (-1.0, 1.7)	0.8 (-0.8, 2.4)
毛嚢虫症	0	3 (1.2) [1.2]	2 (0.8) [0.8]	3 (1.1) [1.0]	3 (1.0) [1.0]	1.2 (-0.5, 2.9)	0.8 (-0.8, 2.3)
耳感染	0	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.1) [1.0]	3 (1.0) [1.0]	0.4 (-1.0, 1.8)	0.8 (-0.8, 2.3)
肺塞栓症	0	2 (0.8) [0.8]	0	3 (1.1) [1.0]	3 (1.0) [1.0]	0.8 (-0.7, 2.3)	0.0
関節障害	7 (2.9) [2.8]	1 (0.4) [0.4]	3 (1.2) [1.2]	2 (0.7) [0.7]	3 (1.0) [1.0]	-2.4 (-4.9, 0.1)	-1.6 (-4.3, 1.0)
咽頭炎	4 (1.6) [1.6]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	3 (1.0) [1.0]	-0.8 (-3.0, 1.4)	-1.2 (-3.3, 0.8)
皮膚炎	3 (1.2) [1.2]	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.7) [0.7]	3 (1.0) [1.0]	-0.4 (-2.5, 1.6)	-0.0 (-2.2, 2.2)

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[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
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[C] Study-size adjusted risk difference between treatment groups.
SSA = Study-size adjusted.

Program Source Code: [redacted]