TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)							
精嚢腺炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
子宮ポリープ	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
子宮脱	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腟分泌物	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)
腟出血	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
精索静脈瘤	0	0	0	0	0	1 (0.6)	1 (<0.1)
外陰腟不快感	0	0	0	1 (0.1)	1 (<0.1)	1 (0.6)	2 (<0.1)
外陰腟の炎症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
外陰腟痛	0	1 (4.4)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)							
外陰腟そう痒症	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	57 (17.8)	12 (53.3)	159 (12.4)	92 (10.5)	251 (11.6)	47 (27.8)	310 (13.2)
急性呼吸不全	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
胞隔炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
失声症	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
喘息	0	2 (8.9)	7 (0.5)	2 (0.2)	9 (0.4)	0	11 (0.5)
無気肺	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
気管支反応性亢進	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
気管支拡張症	1 (0.3)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
カタル	1 (0.3)	0	0	0	0	0	0
慢性閉塞性肺疾患	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	2 (1.2)	4 (0.2)
咳嗽	11 (3.4)	3 (13.3)	36 (2.8)	14 (1.6)	50 (2.3)	16 (9.5)	69 (2.9)
嚢胞性肺疾患	0	0	0	0	0	1 (0.6)	1 (<0.1)
横隔膜痛	1 (0.3)	0	0	0	0	0	0
咽喉乾燥	0	0	0	0	0	1 (0.6)	1 (<0.1)
発声障害	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
呼吸困難	0	0	13 (1.0)	5 (0.6)	18 (0.8)	3 (1.8)	21 (0.9)
労作性呼吸困難	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
肺気腫	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
鼻出血	0	0	8 (0.6)	7 (0.8)	15 (0.7)	0	15 (0.6)
喀血	1 (0.3)	0	0	0	0	0	0
しゃっくり	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
過換気	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
上気道分泌増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
間質性肺疾患	1 (0.3)	0	0	0	0	0	0
肺過膨脹	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
肺浸潤	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
鼻閉	4 (1.2)	1 (4.4)	3 (0.2)	8 (0.9)	11 (0.5)	1 (0.6)	13 (0.6)
鼻中隔弯曲	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
鼻中隔障害	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
鼻中隔穿孔	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
鼻甲介肥大	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
鼻潰瘍	0	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
非感染性気管支炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
口腔咽頭不快感	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
口腔咽頭痛	8 (2.5)	2 (8.9)	34 (2.7)	16 (1.8)	50 (2.3)	8 (4.7)	60 (2.6)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
呼吸時疼痛	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
副鼻腔不快感	1 (0.3)	0	0	0	0	0	0
副鼻腔分泌過多	0	1 (4.4)	0	0	0	0	1 (<0.1)
咽頭紅斑	0	0	0	0	0	1 (0.6)	1 (<0.1)
咽頭病変	0	1 (4.4)	0	0	0	0	1 (<0.1)
胸膜障害	1 (0.3)	0	0	0	0	0	0
胸水	0	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
胸膜痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肺臓炎	2 (0.6)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
気胸	1 (0.3)	0	0	0	0	0	0
湿性咳嗽	1 (0.3)	0	4 (0.3)	2 (0.2)	6 (0.3)	2 (1.2)	8 (0.3)
肺塞栓症	1 (0.3)	0	6 (0.5)	4 (0.5)	10 (0.5)	1 (0.6)	11 (0.5)
肺出血	1 (0.3)	0	0	0	0	0	0
肺腫瘤	2 (0.6)	2 (8.9)	2 (0.2)	0	2 (<0.1)	1 (0.6)	5 (0.2)
逆流性喉頭炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
気道うっ血	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
鼻痛	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
アレルギー性鼻炎	2 (0.6)	0	4 (0.3)	4 (0.5)	8 (0.4)	2 (1.2)	10 (0.4)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
鼻漏	2 (0.6)	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)
低音性連続性ラ音	0	0	0	0	0	1 (0.6)	1 (<0.1)
副鼻腔うっ血	5 (1.6)	0	4 (0.3)	4 (0.5)	8 (0.4)	1 (0.6)	9 (0.4)
副鼻腔障害	0	0	0	0	0	1 (0.6)	1 (<0.1)
副鼻腔痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
睡眠時無呼吸症候群	0	0	7 (0.5)	1 (0.1)	8 (0.4)	0	8 (0.3)
咽喉刺激感	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
扁桃肥大	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
上気道うっ血	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
上気道の炎症	4 (1.2)	0	3 (0.2)	1 (0.1)	4 (0.2)	0	4 (0.2)
上気道咳症候群	2 (0.6)	0	1 (<0.1)	3 (0.3)	4 (0.2)	0	4 (0.2)
声帯ポリープ	1 (0.3)	0	0	0	0	0	0
喘鳴	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
皮膚および皮下組織障害	140 (43.7)	9 (40.0)	223 (17.4)	196 (22.4)	419 (19.4)	145 (85.7)	573 (24.4)
ざ瘡	11 (3.4)	1 (4.4)	31 (2.4)	33 (3.8)	64 (3.0)	54 (31.9)	119 (5.1)
嚢胞性ざ瘡	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
光線性弾性線維症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
光線角化症	0	0	3 (0.2)	3 (0.3)	6 (0.3)	0	6 (0.3)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
脱毛症	2 (0.6)	0	15 (1.2)	8 (0.9)	23 (1.1)	12 (7.1)	35 (1.5)
円形脱毛症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
アンドロゲン性脱毛症	0	0	0	0	0	1 (0.6)	1 (<0.1)
皮脂欠乏症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
水疱	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
皮膚嚢腫	0	0	3 (0.2)	2 (0.2)	5 (0.2)	0	5 (0.2)
皮膚炎	6 (1.9)	0	5 (0.4)	4 (0.5)	9 (0.4)	2 (1.2)	11 (0.5)
ざ瘡様皮膚炎	1 (0.3)	1 (4.4)	5 (0.4)	4 (0.5)	9 (0.4)	5 (3.0)	15 (0.6)
アレルギー性皮膚炎	1 (0.3)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
アトピー性皮膚炎	4 (1.2)	0	4 (0.3)	2 (0.2)	6 (0.3)	0	6 (0.3)
接触皮膚炎	5 (1.6)	0	6 (0.5)	1 (0.1)	7 (0.3)	0	7 (0.3)
剥脱性皮膚炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
乾癬様皮膚炎	1 (0.3)	0	0	0	0	0	0
皮膚症	0	0	0	0	0	1 (0.6)	1 (<0.1)
びまん性脱毛症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
薬疹	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮膚乾燥	9 (2.8)	0	3 (0.2)	5 (0.6)	8 (0.4)	0	8 (0.3)
異汗性湿疹	4 (1.2)	0	1 (<0.1)	2 (0.2)	3 (0.1)	0	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
斑状出血	1 (0.3)	0	2 (0.2)	1 (0.1)	3 (0.1)	2 (1.2)	5 (0.2)
湿疹	9 (2.8)	0	16 (1.2)	12 (1.4)	28 (1.3)	4 (2.4)	32 (1.4)
皮脂欠乏性湿疹	1 (0.3)	0	1 (<0.1)	4 (0.5)	5 (0.2)	0	5 (0.2)
紅斑	5 (1.6)	0	8 (0.6)	6 (0.7)	14 (0.6)	1 (0.6)	15 (0.6)
環状紅斑	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
多形紅斑	0	0	0	0	0	1 (0.6)	1 (<0.1)
結節性紅斑	2 (0.6)	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
固定疹	0	0	0	0	0	1 (0.6)	1 (<0.1)
多汗症	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
過角化	0	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
多毛症	1 (0.3)	0	0	0	0	0	0
嵌入爪	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
内方発育毛	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
間擦疹	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
瘢痕そう痒感	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
毛孔性角化症	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
黒子	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
扁平苔癬	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
機械性蕁麻疹	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
汗疹	0	0	3 (0.2)	0	3 (0.1)	1 (0.6)	4 (0.2)
爪床の炎症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
爪肥厚	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
神経皮膚炎	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
寝汗	2 (0.6)	1 (4.4)	7 (0.5)	3 (0.3)	10 (0.5)	1 (0.6)	12 (0.5)
爪破損	1 (0.3)	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
爪甲剥離症	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
皮膚疼痛	0	0	0	0	0	2 (1.2)	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
掌蹠膿疱症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脂肪織炎	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
丘疹	1 (0.3)	0	2 (0.2)	1 (0.1)	3 (0.1)	5 (3.0)	8 (0.3)
口囲皮膚炎	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
点状出血	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
光線性皮膚症	1 (0.3)	0	0	0	0	0	0
光線過敏性反応	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	2 (1.2)	4 (0.2)
そう痒症	19 (5.9)	2 (8.9)	13 (1.0)	10 (1.1)	23 (1.1)	3 (1.8)	28 (1.2)
乾癬	0	0	2 (0.2)	1 (0.1)	3 (0.1)	0	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
壊疽性膿皮症	2 (0.6)	0	0	0	0	1 (0.6)	1 (<0.1)
発疹	19 (5.9)	3 (13.3)	33 (2.6)	35 (4.0)	68 (3.2)	21 (12.4)	92 (3.9)
紅斑性皮疹	2 (0.6)	0	3 (0.2)	3 (0.3)	6 (0.3)	0	6 (0.3)
毛孔性皮疹	0	0	3 (0.2)	0	3 (0.1)	1 (0.6)	4 (0.2)
斑状皮疹	0	0	1 (<0.1)	3 (0.3)	4 (0.2)	1 (0.6)	5 (0.2)
斑状丘疹状皮疹	3 (0.9)	0	1 (<0.1)	5 (0.6)	6 (0.3)	2 (1.2)	8 (0.3)
丘疹性皮疹	0	0	2 (0.2)	1 (0.1)	3 (0.1)	3 (1.8)	6 (0.3)
そう痒性皮疹	0	0	1 (<0.1)	4 (0.5)	5 (0.2)	0	5 (0.2)
酒さ	2 (0.6)	1 (4.4)	10 (0.8)	3 (0.3)	13 (0.6)	1 (0.6)	15 (0.6)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
脂腺過形成	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
脂漏性皮膚炎	8 (2.5)	0	2 (0.2)	4 (0.5)	6 (0.3)	5 (3.0)	11 (0.5)
皮膚灼熱感	1 (0.3)	0	0	0	0	0	0
皮膚変色	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
皮膚不快感	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮膚びらん	1 (0.3)	0	0	0	0	0	0
皮膚剥脱	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	1 (0.6)	3 (0.1)
皮膚亀裂	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
皮膚色素過剰	1 (0.3)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
皮膚病変	0	0	5 (0.4)	7 (0.8)	12 (0.6)	2 (1.2)	14 (0.6)
皮膚腫瘤	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮膚線条	0	0	0	0	0	1 (0.6)	1 (<0.1)
皮膚潰瘍	1 (0.3)	0	1 (<0.1)	1 (0.1)	2 (<0.1)	2 (1.2)	4 (0.2)
日光皮膚炎	1 (0.3)	0	0	0	0	0	0
毛細血管拡張症	0	0	0	0	0	1 (0.6)	1 (<0.1)
蕁麻疹	5 (1.6)	0	3 (0.2)	7 (0.8)	10 (0.5)	0	10 (0.4)
尋常性白斑	1 (0.3)	0	0	0	0	0	0
乾皮症	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
社会環境	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)
閉経	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
閉経後	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
外科および内科処置	0	0	9 (0.7)	5 (0.6)	14 (0.6)	0	14 (0.6)
人工流産	0	0	3 (0.2)	0	3 (0.1)	0	3 (0.1)
歯科インプラント埋込み	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
植込み型除細動器挿入	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
抜歯	0	0	3 (0.2)	2 (0.2)	5 (0.2)	0	5 (0.2)
智歯抜歯	0	0	2 (0.2)	2 (0.2)	4 (0.2)	0	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害	21 (6.6)	2 (8.9)	58 (4.5)	38 (4.3)	96 (4.4)	19 (11.2)	117 (5.0)
大動脈瘤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
大動脈硬化症	0	0	1 (<0.1)	1 (0.1)	2 (<0.1)	0	2 (<0.1)
動脈硬化症	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (<0.1)
出血性静脈瘤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
コントロール不良の血圧	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
深部静脈血栓症	1 (0.3)	0	3 (0.2)	4 (0.5)	7 (0.3)	1 (0.6)	8 (0.3)
本態性高血圧症	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
潮紅	0	1 (4.4)	1 (<0.1)	0	1 (<0.1)	1 (0.6)	3 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害 (Cont.)							
血腫	1 (0.3)	1 (4.4)	0	1 (0.1)	1 (<0.1)	0	2 (<0.1)
出血	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ほてり	0	0	4 (0.3)	0	4 (0.2)	1 (0.6)	5 (0.2)
高血圧	10 (3.1)	0	35 (2.7)	26 (3.0)	61 (2.8)	9 (5.3)	70 (3.0)
高血圧クリーゼ	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
低血圧	2 (0.6)	0	0	1 (0.1)	1 (<0.1)	2 (1.2)	3 (0.1)
起立性低血圧	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
蒼白	0	0	0	0	0	1 (0.6)	1 (<0.1)
骨盤静脈血栓症	1 (0.3)	0	0	0	0	0	0

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害 (Cont.)							
末梢動脈閉塞性疾患	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
末梢冷感	1 (0.3)	0	0	0	0	0	0
末梢静脈疾患	0	0	2 (0.2)	0	2 (<0.1)	0	2 (<0.1)
静脈炎	0	0	0	1 (0.1)	1 (<0.1)	0	1 (<0.1)
レイノー現象	1 (0.3)	0	2 (0.2)	0	2 (<0.1)	1 (0.6)	3 (0.1)
血栓性静脈炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
表在性血栓性静脈炎	1 (0.3)	0	0	0	0	0	0
静脈瘤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
静脈血栓症	1 (0.3)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [DOSE] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=320.1) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=22.5) Events (E/100 PYs)	UPA 15 mg QD (N=850) (PYs=1283.0) Events (E/100 PYs)	UPA 30 mg QD (N=653) (PYs=875.5) Events (E/100 PYs)	UPA 15/30 mg QD (N=1114) (PYs=2158.5) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害 (Cont.)							
白衣性高血圧	0	0	0	2 (0.2)	2 (<0.1)	0	2 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are defined as specified for the ALL TRT UC[Dose] Analysis. Events are assigned to study drug treatment most recently received at the onset of the event, including up to 30 days past the last study drug dose for subjects who withdrew from treatment.

Program Source Code: [redacted]

表 2.7.4.7-102.

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
Any adverse event	77 (391.5)	20 (234.7)	205 (260.9)
血液およびリンパ系障害	5 (25.4)	1 (11.7)	6 (7.6)
貧血	4 (20.3)	1 (11.7)	1 (1.3)
鉄欠乏性貧血	0	0	0
白血球減少症	0	0	3 (3.8)
リンパ節症	0	0	0
リンパ球減少症	1 (5.1)	0	1 (1.3)
小球性貧血	0	0	0
好中球減少症	0	0	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
Any adverse event	49 (1999.7)	330 (400.2)	293 (264.2)	389 (385.5)	1154 (324.8)
血液およびリンパ系障害	3 (122.4)	22 (26.7)	13 (11.7)	16 (15.9)	51 (14.4)
貧血	1 (40.8)	4 (4.9)	3 (2.7)	3 (3.0)	10 (2.8)
鉄欠乏性貧血	0	4 (4.9)	3 (2.7)	0	4 (1.1)
白血球減少症	0	5 (6.1)	3 (2.7)	2 (2.0)	12 (3.4)
リンパ節症	0	1 (1.2)	0	0	1 (0.3)
リンパ球減少症	1 (40.8)	2 (2.4)	1 (0.9)	1 (1.0)	5 (1.4)
小球性貧血	0	0	0	1 (1.0)	1 (0.3)
好中球減少症	1 (40.8)	5 (6.1)	3 (2.7)	9 (8.9)	18 (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 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)			
血小板減少症	0	0	0
心臓障害	0	0	0
不整脈	0	0	0
完全房室ブロック	0	0	0
僧帽弁閉鎖不全症	0	0	0
上室性期外収縮	0	0	0
心室性期外収縮	0	0	0
先天性、家族性および遺伝性障害	0	0	0
歯原性嚢胞	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)					
血小板減少症	0	1 (1.2)	0	0	0
心臓障害	0	0	3 (2.7)	3 (3.0)	6 (1.7)
不整脈	0	0	1 (0.9)	0	1 (0.3)
完全房室ブロック	0	0	1 (0.9)	0	1 (0.3)
僧帽弁閉鎖不全症	0	0	0	1 (1.0)	1 (0.3)
上室性期外収縮	0	0	1 (0.9)	0	1 (0.3)
心室性期外収縮	0	0	0	2 (2.0)	2 (0.6)
先天性、家族性および遺伝性障害	0	1 (1.2)	0	0	1 (0.3)
歯原性嚢胞	0	1 (1.2)	0	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
耳および迷路障害	0	0	0
感音性難聴	0	0	0
片耳難聴	0	0	0
メニエール病	0	0	0
耳漏	0	0	0
耳鳴	0	0	0
回転性めまい	0	0	0
内分泌障害	0	0	2 (2.5)
副腎機能不全	0	0	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
耳および迷路障害	0	0	7 (6.3)	5 (5.0)	12 (3.4)
感音性難聴	0	0	1 (0.9)	0	1 (0.3)
片耳難聴	0	0	0	1 (1.0)	1 (0.3)
メニエール病	0	0	0	2 (2.0)	2 (0.6)
耳漏	0	0	0	1 (1.0)	1 (0.3)
耳鳴	0	0	2 (1.8)	0	2 (0.6)
回転性めまい	0	0	4 (3.6)	1 (1.0)	5 (1.4)
内分泌障害	0	0	0	1 (1.0)	3 (0.8)
副腎機能不全	0	0	0	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
内分泌障害 (Cont.)			
甲状腺腫	0	0	1 (1.3)
甲状腺腫瘤	0	0	0
眼障害	2 (10.2)	1 (11.7)	1 (1.3)
眼瞼炎	0	0	0
白内障	0	1 (11.7)	0
霰粒腫	0	0	0
結膜嚢胞	0	0	0
結膜出血	0	0	0
アレルギー性結膜炎	1 (5.1)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
内分泌障害 (Cont.)					
甲状腺腫	0	0	0	0	1 (0.3)
甲状腺腫瘤	0	0	0	1 (1.0)	1 (0.3)
眼障害	0	9 (10.9)	5 (4.5)	9 (8.9)	21 (5.9)
眼瞼炎	0	1 (1.2)	0	0	0
白内障	0	1 (1.2)	1 (0.9)	0	3 (0.8)
霰粒腫	0	0	0	1 (1.0)	1 (0.3)
結膜嚢胞	0	1 (1.2)	0	0	1 (0.3)
結膜出血	0	0	0	2 (2.0)	2 (0.6)
アレルギー性結膜炎	0	3 (3.6)	1 (0.9)	2 (2.0)	5 (1.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
眼障害 (Cont.)			
ドライアイ	0	0	0
緑内障	0	0	0
角膜炎	0	0	0
黄斑浮腫	0	0	0
眼充血	0	0	1 (1.3)
翼状片	1 (5.1)	0	0
網膜静脈閉塞	0	0	0
潰瘍性角膜炎	0	0	0
ぶどう膜炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
眼障害 (Cont.)					
ドライアイ	0	1 (1.2)	0	2 (2.0)	3 (0.8)
緑内障	0	0	0	1 (1.0)	1 (0.3)
角膜炎	0	0	0	1 (1.0)	1 (0.3)
黄斑浮腫	0	0	1 (0.9)	0	1 (0.3)
眼充血	0	0	0	0	1 (0.3)
翼状片	0	0	0	0	0
網膜静脈閉塞	0	0	1 (0.9)	0	1 (0.3)
潰瘍性角膜炎	0	1 (1.2)	0	0	0
ぶどう膜炎	0	1 (1.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
眼障害 (Cont.)			
硝子体浮遊物	0	0	0
胃腸障害	17 (86.4)	5 (58.7)	28 (35.6)
腹部膨満	0	0	4 (5.1)
腹痛	0	0	2 (2.5)
下腹部痛	0	0	1 (1.3)
上腹部痛	0	0	0
肛門の炎症	1 (5.1)	0	0
肛門ポリープ	0	0	0
肛門そう痒症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
眼障害 (Cont.)					
硝子体浮遊物	0	0	1 (0.9)	0	1 (0.3)
胃腸障害	7 (285.7)	60 (72.8)	30 (27.0)	37 (36.7)	137 (38.6)
腹部膨満	1 (40.8)	1 (1.2)	0	0	5 (1.4)
腹痛	0	0	2 (1.8)	1 (1.0)	5 (1.4)
下腹部痛	0	0	1 (0.9)	0	2 (0.6)
上腹部痛	0	2 (2.4)	1 (0.9)	1 (1.0)	3 (0.8)
肛門の炎症	0	0	0	0	0
肛門ポリープ	0	0	0	1 (1.0)	1 (0.3)
肛門そう痒症	0	1 (1.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
胃腸障害 (Cont.)			
口角口唇炎	0	0	1 (1.3)
アフタ性潰瘍	0	0	1 (1.3)
虚血性大腸炎	0	0	0
潰瘍性大腸炎	11 (55.9)	0	5 (6.4)
便秘	1 (5.1)	0	0
齲歯	1 (5.1)	0	1 (1.3)
歯嚢胞	0	0	0
下痢	0	0	0
消化不良	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
胃腸障害 (Cont.)					
口角口唇炎	0	0	0	0	1 (0.3)
アフタ性潰瘍	0	1 (1.2)	0	0	1 (0.3)
虚血性大腸炎	0	0	1 (0.9)	0	1 (0.3)
潰瘍性大腸炎	3 (122.4)	15 (18.2)	3 (2.7)	3 (3.0)	16 (4.5)
便秘	1 (40.8)	7 (8.5)	1 (0.9)	8 (7.9)	17 (4.8)
齲歯	0	3 (3.6)	1 (0.9)	1 (1.0)	6 (1.7)
歯嚢胞	0	0	0	1 (1.0)	1 (0.3)
下痢	0	1 (1.2)	1 (0.9)	0	2 (0.6)
消化不良	0	4 (4.9)	1 (0.9)	0	5 (1.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
胃腸障害 (Cont.)			
腸炎	0	0	0
胃ポリープ	0	0	0
胃炎	0	0	0
胃食道逆流性疾患	0	0	2 (2.5)
歯肉痛	0	0	1 (1.3)
歯肉腫脹	0	0	0
舌痛	0	0	0
痔出血	0	0	0
痔核	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
胃腸障害 (Cont.)					
腸炎	0	1 (1.2)	0	2 (2.0)	3 (0.8)
胃ポリープ	0	1 (1.2)	0	0	1 (0.3)
胃炎	0	2 (2.4)	0	0	2 (0.6)
胃食道逆流性疾患	0	1 (1.2)	2 (1.8)	1 (1.0)	5 (1.4)
歯肉痛	0	0	0	0	1 (0.3)
歯肉腫脹	0	1 (1.2)	1 (0.9)	0	1 (0.3)
舌痛	0	1 (1.2)	0	0	0
痔出血	0	1 (1.2)	0	0	0
痔核	0	2 (2.4)	4 (3.6)	1 (1.0)	6 (1.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
胃腸障害 (Cont.)			
血栓性痔核	0	0	0
胃酸過多	0	0	0
単径ヘルニア	0	0	0
腸管ポリープ	0	0	0
過敏性腸症候群	0	0	1 (1.3)
大腸ポリープ	0	5 (58.7)	1 (1.3)
口唇障害	0	0	0
口唇乾燥	0	0	0
口腔嚢胞	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
胃腸障害 (Cont.)					
血栓性痔核	0	1 (1.2)	0	0	0
胃酸過多	0	0	0	1 (1.0)	1 (0.3)
単径ヘルニア	0	0	1 (0.9)	0	1 (0.3)
腸管ポリープ	0	0	1 (0.9)	0	1 (0.3)
過敏性腸症候群	0	0	0	0	1 (0.3)
大腸ポリープ	0	2 (2.4)	2 (1.8)	0	10 (2.8)
口唇障害	0	0	1 (0.9)	0	1 (0.3)
口唇乾燥	1 (40.8)	0	0	0	1 (0.3)
口腔嚢胞	0	1 (1.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
胃腸障害 (Cont.)			
悪心	1 (5.1)	0	1 (1.3)
口腔扁平苔癬	0	0	1 (1.3)
膵炎	0	0	0
歯周病	0	0	1 (1.3)
肛門周囲痛	0	0	0
直腸炎	0	0	2 (2.5)
直腸ポリープ	0	0	0
口内炎	2 (10.2)	0	1 (1.3)
埋伏歯	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
胃腸障害 (Cont.)					
悪心	0	1 (1.2)	3 (2.7)	0	4 (1.1)
口腔扁平苔癬	0	0	0	0	1 (0.3)
膵炎	1 (40.8)	1 (1.2)	0	0	1 (0.3)
歯周病	0	1 (1.2)	0	2 (2.0)	3 (0.8)
肛門周囲痛	0	1 (1.2)	0	0	1 (0.3)
直腸炎	0	1 (1.2)	0	0	2 (0.6)
直腸ポリープ	0	0	1 (0.9)	0	1 (0.3)
口内炎	0	6 (7.3)	2 (1.8)	9 (8.9)	16 (4.5)
埋伏歯	0	0	0	1 (1.0)	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
胃腸障害 (Cont.)			
歯の脱落	0	0	0
歯痛	0	0	2 (2.5)
嘔吐	0	0	0
一般・全身障害および投与部位の状態	5 (25.4)	0	11 (14.0)
医薬品副作用	0	0	0
胸痛	0	0	1 (1.3)
疲労	0	0	0
異常感	0	0	1 (1.3)
炎症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
胃腸障害 (Cont.)					
歯の脱落	0	0	0	1 (1.0)	1 (0.3)
歯痛	0	0	0	1 (1.0)	3 (0.8)
嘔吐	0	0	0	2 (2.0)	2 (0.6)
一般・全身障害および投与部位の状態	4 (163.2)	17 (20.6)	12 (10.8)	26 (25.8)	64 (18.0)
医薬品副作用	0	0	1 (0.9)	0	1 (0.3)
胸痛	0	0	0	3 (3.0)	4 (1.1)
疲労	0	0	0	1 (1.0)	1 (0.3)
異常感	0	0	0	0	1 (0.3)
炎症	0	0	0	1 (1.0)	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
注射部位疼痛	0	0	0
倦怠感	0	0	0
非心臓性胸痛	0	0	0
末梢性浮腫	1 (5.1)	0	0
発熱	4 (20.3)	0	8 (10.2)
腫脹	0	0	0
評価不能の事象	0	0	1 (1.3)
肝胆道系障害	1 (5.1)	0	4 (5.1)
胆嚢炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
注射部位疼痛	0	2 (2.4)	4 (3.6)	6 (5.9)	12 (3.4)
倦怠感	1 (40.8)	2 (2.4)	1 (0.9)	0	2 (0.6)
非心臓性胸痛	0	1 (1.2)	0	0	0
末梢性浮腫	0	2 (2.4)	0	2 (2.0)	3 (0.8)
発熱	3 (122.4)	10 (12.1)	5 (4.5)	13 (12.9)	37 (10.4)
腫脹	0	0	1 (0.9)	0	1 (0.3)
評価不能の事象	0	0	0	0	1 (0.3)
肝胆道系障害	0	4 (4.9)	7 (6.3)	3 (3.0)	16 (4.5)
胆嚢炎	0	0	1 (0.9)	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
胆石症	0	0	0
薬物性肝障害	0	0	0
肝機能異常	0	0	2 (2.5)
脂肪肝	0	0	2 (2.5)
肝障害	0	0	0
肝損傷	0	0	0
門脈血栓症	1 (5.1)	0	0
免疫系障害	0	0	1 (1.3)
アナフィラキシー反応	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
肝胆道系障害 (Cont.)					
胆石症	0	0	1 (0.9)	0	1 (0.3)
薬物性肝障害	0	1 (1.2)	0	0	1 (0.3)
肝機能異常	0	1 (1.2)	3 (2.7)	3 (3.0)	8 (2.3)
脂肪肝	0	0	1 (0.9)	0	3 (0.8)
肝障害	0	1 (1.2)	1 (0.9)	0	2 (0.6)
肝損傷	0	1 (1.2)	0	0	0
門脈血栓症	0	0	0	0	0
免疫系障害	0	0	1 (0.9)	2 (2.0)	4 (1.1)
アナフィラキシー反応	0	0	0	1 (1.0)	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
免疫系障害 (Cont.)			
季節性アレルギー	0	0	1 (1.3)
感染症および寄生虫症	8 (40.7)	4 (46.9)	81 (103.1)
膿瘍	1 (5.1)	0	0
ダニ皮膚炎	0	0	0
肛門膿瘍	0	0	0
虫垂炎	0	0	0
細菌性関節炎	0	0	0
無症候性細菌尿	0	0	0
細菌感染	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
免疫系障害 (Cont.)					
季節性アレルギー	0	0	1 (0.9)	1 (1.0)	3 (0.8)
感染症および寄生虫症	8 (326.5)	77 (93.4)	73 (65.8)	102 (101.1)	324 (91.2)
膿瘍	0	0	0	0	0
ダニ皮膚炎	0	0	2 (1.8)	0	2 (0.6)
肛門膿瘍	0	0	2 (1.8)	0	2 (0.6)
虫垂炎	0	0	1 (0.9)	1 (1.0)	2 (0.6)
細菌性関節炎	0	0	1 (0.9)	0	1 (0.3)
無症候性細菌尿	0	0	1 (0.9)	0	1 (0.3)
細菌感染	0	2 (2.4)	0	0	2 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
細菌性膣症	0	0	0
バルトリン腺炎	0	0	0
気管支炎	0	0	2 (2.5)
COVID-19	0	0	0
COVID-19肺炎	0	0	0
カンピロバクター胃腸炎	0	0	1 (1.3)
カンジダ感染	0	0	0
蜂巣炎	0	0	0
クロストリジウム・ディフィシレ感染	0	1 (11.7)	5 (6.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code:[redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
細菌性膣症	0	1 (1.2)	0	0	0
バルトリン腺炎	0	1 (1.2)	0	0	1 (0.3)
気管支炎	0	0	0	2 (2.0)	4 (1.1)
COVID-19	0	0	0	1 (1.0)	1 (0.3)
COVID-19肺炎	0	0	0	1 (1.0)	1 (0.3)
カンピロバクター胃腸炎	0	0	1 (0.9)	1 (1.0)	3 (0.8)
カンジダ感染	0	0	0	1 (1.0)	1 (0.3)
蜂巣炎	0	0	1 (0.9)	0	1 (0.3)
クロストリジウム・ディフィシレ感染	0	0	0	0	6 (1.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
結膜炎	1 (5.1)	0	0
ウイルス性結膜炎	0	0	0
膀胱炎	0	0	4 (5.1)
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	0	0	0
感染性皮膚炎	0	0	0
爪の皮膚糸状菌症	0	0	1 (1.3)
感染性腸炎	0	0	1 (1.3)
毛包炎	0	0	2 (2.5)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
結膜炎	0	0	1 (0.9)	1 (1.0)	2 (0.6)
ウイルス性結膜炎	0	1 (1.2)	0	0	1 (0.3)
膀胱炎	0	3 (3.6)	1 (0.9)	4 (4.0)	12 (3.4)
サイトメガロウイルス性大腸炎	0	0	0	1 (1.0)	1 (0.3)
サイトメガロウイルス感染	0	0	1 (0.9)	0	1 (0.3)
感染性皮膚炎	0	1 (1.2)	0	0	1 (0.3)
爪の皮膚糸状菌症	0	0	0	1 (1.0)	2 (0.6)
感染性腸炎	0	0	0	1 (1.0)	2 (0.6)
毛包炎	1 (40.8)	1 (1.2)	2 (1.8)	5 (5.0)	10 (2.8)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
胃腸炎	0	0	1 (1.3)
ウイルス性胃腸炎	0	0	2 (2.5)
歯肉炎	0	0	0
ヘリコバクター感染	0	0	0
ヘルペス性皮膚炎	0	0	0
ヘルペス眼感染	0	0	0
単純ヘルペス	0	0	0
帯状疱疹	0	2 (23.5)	6 (7.6)
帯状疱疹性髄膜炎	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 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
胃腸炎	0	2 (2.4)	3 (2.7)	1 (1.0)	6 (1.7)
ウイルス性胃腸炎	0	0	0	0	2 (0.6)
歯肉炎	0	2 (2.4)	1 (0.9)	1 (1.0)	4 (1.1)
ヘリコバクター感染	0	0	1 (0.9)	0	1 (0.3)
ヘルペス性皮膚炎	0	0	1 (0.9)	0	1 (0.3)
ヘルペス眼感染	0	0	0	1 (1.0)	1 (0.3)
単純ヘルペス	0	3 (3.6)	1 (0.9)	0	4 (1.1)
帯状疱疹	3 (122.4)	4 (4.9)	6 (5.4)	10 (9.9)	29 (8.2)
帯状疱疹性髄膜炎	0	0	0	1 (1.0)	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
麦粒腫	0	0	2 (2.5)
膿痂疹	0	0	0
インフルエンザ	0	0	3 (3.8)
クレブシエラ感染	0	0	1 (1.3)
大腸感染	0	0	0
潜伏結核	0	0	1 (1.3)
伝染性軟属腫	0	0	0
上咽頭炎	4 (20.3)	0	24 (30.5)
口腔カンジダ症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
麦粒腫	0	3 (3.6)	2 (1.8)	2 (2.0)	7 (2.0)
膿痂疹	0	0	1 (0.9)	0	1 (0.3)
インフルエンザ	1 (40.8)	2 (2.4)	4 (3.6)	3 (3.0)	13 (3.7)
クレブシエラ感染	0	0	0	0	1 (0.3)
大腸感染	0	0	1 (0.9)	1 (1.0)	2 (0.6)
潜伏結核	0	0	0	2 (2.0)	3 (0.8)
伝染性軟属腫	0	1 (1.2)	0	0	0
上咽頭炎	0	21 (25.5)	23 (20.7)	27 (26.8)	89 (25.0)
口腔カンジダ症	0	1 (1.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
口腔ヘルペス	0	0	11 (14.0)
骨髄炎	0	0	0
外耳炎	0	0	0
爪囲炎	0	0	1 (1.3)
歯冠周囲炎	0	0	0
歯周炎	0	0	1 (1.3)
扁桃周囲炎	0	0	0
咽頭炎	0	0	2 (2.5)
胸膜感染	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	0	7 (8.5)	6 (5.4)	13 (12.9)	37 (10.4)
骨髄炎	0	1 (1.2)	0	0	1 (0.3)
外耳炎	0	1 (1.2)	0	0	0
爪囲炎	0	0	0	0	1 (0.3)
歯冠周囲炎	0	2 (2.4)	0	0	2 (0.6)
歯周炎	0	4 (4.9)	0	3 (3.0)	7 (2.0)
扁桃周囲炎	0	0	1 (0.9)	0	1 (0.3)
咽頭炎	0	0	1 (0.9)	5 (5.0)	8 (2.3)
胸膜感染	0	0	0	1 (1.0)	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ニューモシスチス・イロベチイ肺炎	0	0	0
肺炎	0	0	2 (2.5)
歯髄炎	0	0	0
腎盂腎炎	0	1 (11.7)	0
鼻炎	0	0	1 (1.3)
副鼻腔炎	0	0	0
皮膚感染	0	0	0
白癬感染	0	0	0
足部白癬	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ニューモシスチス・イロベチイ肺炎	0	1 (1.2)	0	0	0
肺炎	1 (40.8)	1 (1.2)	0	1 (1.0)	4 (1.1)
歯髄炎	0	1 (1.2)	0	0	1 (0.3)
腎盂腎炎	0	1 (1.2)	0	0	2 (0.6)
鼻炎	0	0	0	0	1 (0.3)
副鼻腔炎	0	1 (1.2)	1 (0.9)	0	2 (0.6)
皮膚感染	0	0	0	3 (3.0)	3 (0.8)
白癬感染	1 (40.8)	1 (1.2)	0	0	1 (0.3)
足部白癬	0	2 (2.4)	2 (1.8)	2 (2.0)	5 (1.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
扁桃炎	0	0	3 (3.8)
上気道感染	1 (5.1)	0	3 (3.8)
水痘	0	0	1 (1.3)
ウイルス感染	0	0	0
外陰部腟カンジダ症	0	0	0
創傷感染	1 (5.1)	0	0
傷害、中毒および処置合併症	1 (5.1)	0	5 (6.4)
吻合部漏出	1 (5.1)	0	0
動物咬傷	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
扁桃炎	0	0	0	1 (1.0)	4 (1.1)
上気道感染	0	4 (4.9)	3 (2.7)	3 (3.0)	13 (3.7)
水痘	0	0	0	0	1 (0.3)
ウイルス感染	1 (40.8)	0	0	0	1 (0.3)
外陰部腟カンジダ症	0	1 (1.2)	1 (0.9)	0	2 (0.6)
創傷感染	0	0	0	1 (1.0)	1 (0.3)
傷害、中毒および処置合併症	1 (40.8)	7 (8.5)	10 (9.0)	6 (5.9)	25 (7.0)
吻合部漏出	0	0	0	0	0
動物咬傷	0	0	0	1 (1.0)	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
節足動物咬傷	0	0	0
節足動物刺傷	0	0	0
骨挫傷	0	0	0
挫傷	0	0	0
上顎炎	0	0	2 (2.5)
足骨折	0	0	0
熱中症	0	0	0
熱射病	0	0	0
関節損傷	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
節足動物咬傷	0	0	1 (0.9)	1 (1.0)	2 (0.6)
節足動物刺傷	0	0	1 (0.9)	0	1 (0.3)
骨挫傷	0	1 (1.2)	0	0	0
挫傷	0	0	1 (0.9)	1 (1.0)	2 (0.6)
上顆炎	0	0	0	0	2 (0.6)
足骨折	0	0	1 (0.9)	2 (2.0)	3 (0.8)
熱中症	0	1 (1.2)	0	0	0
熱射病	0	0	1 (0.9)	0	1 (0.3)
関節損傷	0	0	1 (0.9)	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
靱帯捻挫	0	0	1 (1.3)
過量投与	0	0	0
処置後出血	0	0	1 (1.3)
肺挫傷	0	0	0
肋骨骨折	0	0	0
皮膚擦過傷	0	0	0
皮膚裂傷	0	0	0
ストレス骨折	0	0	0
皮下血腫	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
靱帯捻挫	0	0	0	0	1 (0.3)
過量投与	0	0	1 (0.9)	0	1 (0.3)
処置後出血	0	0	0	0	1 (0.3)
肺挫傷	0	0	1 (0.9)	0	1 (0.3)
肋骨骨折	0	1 (1.2)	0	1 (1.0)	1 (0.3)
皮膚擦過傷	0	1 (1.2)	0	0	1 (0.3)
皮膚裂傷	1 (40.8)	0	0	0	1 (0.3)
ストレス骨折	0	0	1 (0.9)	0	1 (0.3)
皮下血腫	0	2 (2.4)	0	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
胸椎骨折	0	0	0
脛骨骨折	0	0	1 (1.3)
ワクチン接種合併症	0	0	0
臨床検査	6 (30.5)	3 (35.2)	14 (17.8)
アラニンアミノトランスフェラーゼ増加	1 (5.1)	0	0
アミラーゼ増加	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (5.1)	0	0
血中アルカリホスファターゼ増加	1 (5.1)	0	0
血中ビリルビン増加	0	0	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
胸椎骨折	0	0	1 (0.9)	0	1 (0.3)
脛骨骨折	0	0	0	0	1 (0.3)
ワクチン接種合併症	0	1 (1.2)	0	0	1 (0.3)
臨床検査	11 (448.9)	21 (25.5)	49 (44.2)	66 (65.4)	157 (44.2)
アラニンアミノトランスフェラーゼ増加	0	1 (1.2)	3 (2.7)	7 (6.9)	11 (3.1)
アミラーゼ増加	1 (40.8)	1 (1.2)	2 (1.8)	0	3 (0.8)
アスパラギン酸アミノトランスフェラーゼ増加	1 (40.8)	1 (1.2)	4 (3.6)	6 (5.9)	12 (3.4)
血中アルカリホスファターゼ増加	0	0	0	0	0
血中ビリルビン増加	0	0	0	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
臨床検査 (Cont.)			
血中コレステロール増加	0	0	0
血中クレアチンホスホキナーゼ増加	0	3 (35.2)	4 (5.1)
血中クレアチニン増加	0	0	0
血中尿酸増加	0	0	0
尿中血陽性	0	0	0
γ-グルタミルトランスフェラーゼ増加	1 (5.1)	0	2 (2.5)
高比重リポ蛋白増加	0	0	0
リパーゼ増加	0	0	0
リンパ球数減少	0	0	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
臨床検査 (Cont.)					
血中コレステロール増加	0	0	0	1 (1.0)	1 (0.3)
血中クレアチンホスホキナーゼ増加	2 (81.6)	5 (6.1)	13 (11.7)	16 (15.9)	42 (11.8)
血中クレアチニン増加	0	1 (1.2)	0	2 (2.0)	2 (0.6)
血中尿酸増加	0	1 (1.2)	0	0	1 (0.3)
尿中血陽性	0	0	0	1 (1.0)	1 (0.3)
γ-グルタミルトランスフェラーゼ増加	0	1 (1.2)	5 (4.5)	1 (1.0)	9 (2.5)
高比重リポ蛋白増加	0	0	3 (2.7)	0	3 (0.8)
リパーゼ増加	1 (40.8)	0	1 (0.9)	0	2 (0.6)
リンパ球数減少	0	2 (2.4)	1 (0.9)	5 (5.0)	9 (2.5)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
臨床検査 (Cont.)			
リンパ球数増加	0	0	0
リンパ球百分率減少	0	0	0
リンパ球百分率増加	0	0	0
好中球数減少	0	0	1 (1.3)
好中球数増加	0	0	1 (1.3)
前立腺特異性抗原増加	0	0	0
尿中蛋白陽性	1 (5.1)	0	0
尿中白血球エステラーゼ陽性	0	0	0
体重減少	1 (5.1)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
臨床検査 (Cont.)					
リンパ球数増加	1 (40.8)	1 (1.2)	0	1 (1.0)	2 (0.6)
リンパ球百分率減少	0	0	1 (0.9)	0	1 (0.3)
リンパ球百分率増加	0	0	2 (1.8)	0	2 (0.6)
好中球数減少	2 (81.6)	4 (4.9)	6 (5.4)	17 (16.8)	28 (7.9)
好中球数増加	0	0	0	1 (1.0)	2 (0.6)
前立腺特異性抗原増加	1 (40.8)	0	0	0	1 (0.3)
尿中蛋白陽性	0	0	0	0	0
尿中白血球エステラーゼ陽性	0	0	2 (1.8)	0	2 (0.6)
体重減少	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
臨床検査 (Cont.)			
体重増加	0	0	0
白血球数減少	0	0	3 (3.8)
白血球数増加	0	0	1 (1.3)
代謝および栄養障害	4 (20.3)	1 (11.7)	5 (6.4)
食欲減退	1 (5.1)	0	0
糖尿病	1 (5.1)	0	0
脂質異常症	0	0	1 (1.3)
高コレステロール血症	0	1 (11.7)	2 (2.5)
高リパーゼ血症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
臨床検査 (Cont.)					
体重増加	0	0	1 (0.9)	1 (1.0)	2 (0.6)
白血球数減少	1 (40.8)	3 (3.6)	5 (4.5)	7 (6.9)	18 (5.1)
白血球数増加	1 (40.8)	0	0	0	2 (0.6)
代謝および栄養障害	0	7 (8.5)	8 (7.2)	6 (5.9)	25 (7.0)
食欲減退	0	0	0	0	0
糖尿病	0	0	0	1 (1.0)	1 (0.3)
脂質異常症	0	1 (1.2)	3 (2.7)	0	5 (1.4)
高コレステロール血症	0	1 (1.2)	1 (0.9)	2 (2.0)	7 (2.0)
高リパーゼ血症	0	1 (1.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
高脂血症	0	0	2 (2.5)
高尿酸血症	1 (5.1)	0	0
低アルブミン血症	1 (5.1)	0	0
低ナトリウム血症	0	0	0
低蛋白血症	0	0	0
栄養障害	0	0	0
筋骨格系および結合組織障害	6 (30.5)	0	12 (15.3)
関節痛	1 (5.1)	0	2 (2.5)
関節炎	0	0	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
高脂血症	0	1 (1.2)	4 (3.6)	1 (1.0)	8 (2.3)
高尿酸血症	0	1 (1.2)	0	1 (1.0)	2 (0.6)
低アルブミン血症	0	0	0	0	0
低ナトリウム血症	0	1 (1.2)	0	0	0
低蛋白血症	0	1 (1.2)	0	0	1 (0.3)
栄養障害	0	0	0	1 (1.0)	1 (0.3)
筋骨格系および結合組織障害	3 (122.4)	36 (43.7)	23 (20.7)	19 (18.8)	78 (22.0)
関節痛	0	4 (4.9)	7 (6.3)	2 (2.0)	11 (3.1)
関節炎	1 (40.8)	1 (1.2)	1 (0.9)	0	4 (1.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
関節障害	2 (10.2)	0	0
背部痛	1 (5.1)	0	1 (1.3)
頚部脊柱管狭窄症	0	0	0
側腹部痛	0	0	0
椎間板突出	0	0	3 (3.8)
腰部脊柱管狭窄症	0	0	0
筋痙縮	0	0	1 (1.3)
筋骨格系胸痛	0	0	0
筋骨格痛	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
関節障害	1 (40.8)	2 (2.4)	0	0	2 (0.6)
背部痛	0	4 (4.9)	4 (3.6)	4 (4.0)	10 (2.8)
頚部脊柱管狭窄症	0	1 (1.2)	0	0	1 (0.3)
側腹部痛	0	2 (2.4)	0	0	2 (0.6)
椎間板突出	0	3 (3.6)	0	3 (3.0)	9 (2.5)
腰部脊柱管狭窄症	0	1 (1.2)	0	1 (1.0)	2 (0.6)
筋痙縮	0	0	1 (0.9)	2 (2.0)	4 (1.1)
筋骨格系胸痛	0	4 (4.9)	0	0	2 (0.6)
筋骨格痛	0	0	1 (0.9)	1 (1.0)	2 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
筋骨格硬直	1 (5.1)	0	0
筋肉痛	0	0	2 (2.5)
変形性関節症	1 (5.1)	0	0
骨端症	0	0	0
骨壊死	0	0	1 (1.3)
骨粗鬆症	0	0	0
四肢痛	0	0	0
関節周囲炎	0	0	0
横紋筋融解症	0	0	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
筋骨格硬直	0	0	2 (1.8)	0	2 (0.6)
筋肉痛	0	1 (1.2)	2 (1.8)	1 (1.0)	6 (1.7)
変形性関節症	0	3 (3.6)	1 (0.9)	0	3 (0.8)
骨端症	0	1 (1.2)	0	0	1 (0.3)
骨壊死	0	0	2 (1.8)	0	3 (0.8)
骨粗鬆症	0	0	1 (0.9)	0	1 (0.3)
四肢痛	0	4 (4.9)	0	4 (4.0)	6 (1.7)
関節周囲炎	0	2 (2.4)	0	1 (1.0)	3 (0.8)
横紋筋融解症	0	0	0	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
肩回旋筋腱板症候群	0	0	0
変形性脊椎症	0	0	0
腱鞘炎	0	0	0
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）	2 (10.2)	0	2 (2.5)
結腸腺癌	0	0	0
肛門性器疣贅	0	0	0
大腸腺腫	0	0	1 (1.3)
線維腫	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
肩回旋筋腱板症候群	0	1 (1.2)	0	0	0
変形性脊椎症	0	1 (1.2)	0	0	1 (0.3)
腱鞘炎	0	1 (1.2)	0	0	0
弾発指	1 (40.8)	0	1 (0.9)	0	2 (0.6)
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 (3.6)	3 (2.7)	4 (4.0)	11 (3.1)
結腸腺癌	0	0	0	1 (1.0)	1 (0.3)
肛門性器疣贅	0	1 (1.2)	0	0	1 (0.3)
大腸腺腫	0	1 (1.2)	1 (0.9)	0	2 (0.6)
線維腫	0	0	0	1 (1.0)	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
脂漏性角化症	2 (10.2)	0	0
皮膚乳頭腫	0	0	1 (1.3)
子宮平滑筋腫	0	0	0
神経系障害	3 (15.3)	0	8 (10.2)
手根管症候群	2 (10.2)	0	0
大脳障害	0	0	0
浮動性めまい	0	0	1 (1.3)
異常感覚	0	0	1 (1.3)
てんかん	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
脂漏性角化症	0	0	0	0	0
皮膚乳頭腫	0	1 (1.2)	0	2 (2.0)	4 (1.1)
子宮平滑筋腫	0	0	2 (1.8)	0	2 (0.6)
神経系障害	5 (204.1)	8 (9.7)	6 (5.4)	17 (16.8)	41 (11.5)
手根管症候群	0	0	0	0	0
大脳障害	0	1 (1.2)	0	0	1 (0.3)
浮動性めまい	0	0	1 (0.9)	4 (4.0)	6 (1.7)
異常感覚	0	0	0	0	1 (0.3)
てんかん	0	1 (1.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
神経系障害 (Cont.)			
頭痛	0	0	4 (5.1)
感覚鈍麻	0	0	1 (1.3)
頭蓋内動脈瘤	0	0	1 (1.3)
片頭痛	0	0	0
神経痛	0	0	0
末梢性ニューロパチー	0	0	0
後頭神経痛	0	0	0
ヘルペス後神経痛	0	0	0
失神寸前の状態	1 (5.1)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
神経系障害 (Cont.)					
頭痛	3 (122.4)	1 (1.2)	3 (2.7)	5 (5.0)	16 (4.5)
感覚鈍麻	0	0	1 (0.9)	3 (3.0)	5 (1.4)
頭蓋内動脈瘤	0	0	0	0	1 (0.3)
片頭痛	0	2 (2.4)	0	0	1 (0.3)
神経痛	0	1 (1.2)	0	0	1 (0.3)
末梢性ニューロパチー	1 (40.8)	1 (1.2)	0	0	1 (0.3)
後頭神経痛	0	0	1 (0.9)	0	1 (0.3)
ヘルペス後神経痛	1 (40.8)	0	0	1 (1.0)	2 (0.6)
失神寸前の状態	0	1 (1.2)	0	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
神経系障害 (Cont.)			
傾眠	0	0	0
くも膜下出血	0	0	0
失神	0	0	0
味覚障害	0	0	0
精神障害	2 (10.2)	0	3 (3.8)
不安	0	0	0
不安障害	0	0	0
抑うつ気分	0	0	0
不眠症	2 (10.2)	0	3 (3.8)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
神経系障害 (Cont.)					
傾眠	0	0	0	1 (1.0)	1 (0.3)
くも膜下出血	0	0	0	1 (1.0)	1 (0.3)
失神	0	0	0	1 (1.0)	1 (0.3)
味覚障害	0	0	0	1 (1.0)	1 (0.3)
精神障害	0	5 (6.1)	2 (1.8)	5 (5.0)	12 (3.4)
不安	0	0	1 (0.9)	1 (1.0)	2 (0.6)
不安障害	0	0	1 (0.9)	0	1 (0.3)
抑うつ気分	0	0	0	1 (1.0)	1 (0.3)
不眠症	0	5 (6.1)	0	3 (3.0)	8 (2.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
腎および尿路障害	0	2 (23.5)	6 (7.6)
急性腎障害	0	0	0
慢性腎臓病	0	0	0
排尿困難	0	0	1 (1.3)
腎結石症	0	2 (23.5)	0
蛋白尿	0	0	2 (2.5)
腎機能障害	0	0	1 (1.3)
尿管結石症	0	0	2 (2.5)
生殖系および乳房障害	0	0	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
腎および尿路障害	1 (40.8)	0	1 (0.9)	3 (3.0)	13 (3.7)
急性腎障害	0	0	0	1 (1.0)	1 (0.3)
慢性腎臓病	1 (40.8)	0	0	0	1 (0.3)
排尿困難	0	0	0	0	1 (0.3)
腎結石症	0	0	0	0	2 (0.6)
蛋白尿	0	0	0	1 (1.0)	3 (0.8)
腎機能障害	0	0	1 (0.9)	0	2 (0.6)
尿管結石症	0	0	0	1 (1.0)	3 (0.8)
生殖系および乳房障害	0	4 (4.9)	2 (1.8)	0	5 (1.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
無月経	0	0	0
子宮頚管ポリープ	0	0	1 (1.3)
機能不全性子宮出血	0	0	0
月経困難症	0	0	0
閉経期症状	0	0	0
不規則月経	0	0	0
前立腺炎	0	0	0
呼吸器、胸郭および縦隔障害	3 (15.3)	0	2 (2.5)
喘息	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
無月経	0	1 (1.2)	0	0	1 (0.3)
子宮頚管ポリープ	0	0	0	0	1 (0.3)
機能不全性子宮出血	0	1 (1.2)	0	0	0
月経困難症	0	0	1 (0.9)	0	1 (0.3)
閉経期症状	0	1 (1.2)	0	0	1 (0.3)
不規則月経	0	1 (1.2)	0	0	0
前立腺炎	0	0	1 (0.9)	0	1 (0.3)
呼吸器、胸郭および縦隔障害	3 (122.4)	12 (14.6)	7 (6.3)	8 (7.9)	29 (8.2)
喘息	0	1 (1.2)	0	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
咳嗽	0	0	0
発声障害	0	0	0
しゃっくり	0	0	0
過換気	0	0	0
口腔咽頭不快感	0	0	1 (1.3)
口腔咽頭痛	0	0	0
咽頭病変	0	0	1 (1.3)
気胸	1 (5.1)	0	0
アレルギー性鼻炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
咳嗽	1 (40.8)	0	3 (2.7)	0	4 (1.1)
発声障害	0	1 (1.2)	0	0	1 (0.3)
しゃっくり	0	1 (1.2)	0	1 (1.0)	1 (0.3)
過換気	0	0	0	1 (1.0)	1 (0.3)
口腔咽頭不快感	0	1 (1.2)	0	0	2 (0.6)
口腔咽頭痛	2 (81.6)	2 (2.4)	1 (0.9)	4 (4.0)	9 (2.5)
咽頭病変	0	0	0	0	1 (0.3)
気胸	0	0	0	0	0
アレルギー性鼻炎	0	2 (2.4)	2 (1.8)	0	4 (1.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
睡眠時無呼吸症候群	0	0	0
上気道の炎症	2 (10.2)	0	0
皮膚および皮下組織障害	9 (45.8)	1 (11.7)	12 (15.3)
ざ瘡	0	0	1 (1.3)
脱毛症	0	0	0
皮脂欠乏症	0	0	0
皮膚嚢腫	0	0	0
皮膚炎	1 (5.1)	0	0
ざ瘡様皮膚炎	0	0	2 (2.5)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
睡眠時無呼吸症候群	0	0	0	1 (1.0)	1 (0.3)
上気道の炎症	0	4 (4.9)	1 (0.9)	1 (1.0)	4 (1.1)
皮膚および皮下組織障害	3 (122.4)	32 (38.8)	28 (25.2)	42 (41.6)	101 (28.4)
ざ瘡	0	7 (8.5)	6 (5.4)	13 (12.9)	24 (6.8)
脱毛症	0	0	0	2 (2.0)	2 (0.6)
皮脂欠乏症	0	0	0	1 (1.0)	1 (0.3)
皮膚嚢腫	0	0	1 (0.9)	0	1 (0.3)
皮膚炎	0	0	1 (0.9)	0	1 (0.3)
ざ瘡様皮膚炎	0	0	1 (0.9)	1 (1.0)	4 (1.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
アトピー性皮膚炎	0	0	0
接触皮膚炎	0	0	0
薬疹	0	0	1 (1.3)
皮膚乾燥	1 (5.1)	0	1 (1.3)
異汗性湿疹	1 (5.1)	0	0
湿疹	3 (15.3)	0	2 (2.5)
皮脂欠乏性湿疹	0	0	0
紅斑	0	0	1 (1.3)
多形紅斑	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
アトピー性皮膚炎	0	0	2 (1.8)	0	2 (0.6)
接触皮膚炎	0	2 (2.4)	0	0	1 (0.3)
薬疹	0	0	0	0	1 (0.3)
皮膚乾燥	0	0	0	0	1 (0.3)
異汗性湿疹	0	0	0	1 (1.0)	1 (0.3)
湿疹	1 (40.8)	4 (4.9)	5 (4.5)	4 (4.0)	15 (4.2)
皮脂欠乏性湿疹	0	1 (1.2)	0	4 (4.0)	4 (1.1)
紅斑	0	0	0	0	1 (0.3)
多形紅斑	1 (40.8)	0	0	0	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
瘢痕そう痒感	0	0	0
毛孔性角化症	0	0	0
汗疹	0	0	0
皮膚疼痛	0	0	0
掌蹠膿疱症	0	0	0
脂肪織炎	0	0	0
丘疹	0	0	1 (1.3)
光線過敏性反応	0	0	0
そう痒症	2 (10.2)	0	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
瘢痕そう痒感	0	0	0	1 (1.0)	1 (0.3)
毛孔性角化症	0	1 (1.2)	0	0	1 (0.3)
汗疹	0	1 (1.2)	1 (0.9)	0	2 (0.6)
皮膚疼痛	1 (40.8)	0	0	1 (1.0)	2 (0.6)
掌蹠膿疱症	0	0	1 (0.9)	0	1 (0.3)
脂肪織炎	0	0	1 (0.9)	0	1 (0.3)
丘疹	0	0	0	0	1 (0.3)
光線過敏性反応	0	1 (1.2)	0	1 (1.0)	1 (0.3)
そう痒症	0	0	3 (2.7)	0	4 (1.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
壊疽性膿皮症	1 (5.1)	0	0
発疹	0	1 (11.7)	1 (1.3)
紅斑性皮疹	0	0	0
斑状丘疹状皮疹	0	0	0
脂漏性皮膚炎	0	0	0
皮膚潰瘍	0	0	0
蕁麻疹	0	0	1 (1.3)
乾皮症	0	0	0
血管障害	3 (15.3)	2 (23.5)	1 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
壊疽性膿皮症	0	1 (1.2)	0	0	0
発疹	0	5 (6.1)	3 (2.7)	2 (2.0)	8 (2.3)
紅斑性皮疹	0	1 (1.2)	0	0	0
斑状丘疹状皮疹	0	0	0	4 (4.0)	4 (1.1)
脂漏性皮膚炎	0	6 (7.3)	3 (2.7)	2 (2.0)	7 (2.0)
皮膚潰瘍	0	1 (1.2)	0	0	1 (0.3)
蕁麻疹	0	1 (1.2)	0	4 (4.0)	6 (1.7)
乾皮症	0	0	0	1 (1.0)	1 (0.3)
血管障害	0	5 (6.1)	3 (2.7)	9 (8.9)	18 (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 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
血管障害 (Cont.)			
大動脈瘤	0	0	0
深部静脈血栓症	0	1 (11.7)	0
本態性高血圧症	0	0	0
血腫	0	0	0
ほてり	0	0	0
高血圧	1 (5.1)	1 (11.7)	1 (1.3)
低血圧	1 (5.1)	0	0
末梢冷感	1 (5.1)	0	0
静脈炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
血管障害 (Cont.)					
大動脈瘤	0	0	1 (0.9)	0	1 (0.3)
深部静脈血栓症	0	0	0	0	1 (0.3)
本態性高血圧症	0	0	0	1 (1.0)	1 (0.3)
血腫	0	0	0	1 (1.0)	1 (0.3)
ほてり	0	0	0	1 (1.0)	1 (0.3)
高血圧	0	4 (4.9)	2 (1.8)	5 (5.0)	12 (3.4)
低血圧	0	0	0	0	0
末梢冷感	0	0	0	0	0
静脈炎	0	0	0	1 (1.0)	1 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=19.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=8.5) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=30) (PYs=78.6) Events (E/100 PYs)
血管障害 (Cont.)			
静脈血栓症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.1 J

Treatment-Emergent Adverse 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=82.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=110.9) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=100.9) Events (E/100 PYs)	 Any UPA (N=193) (PYs=355.3) Events (E/100 PYs)
血管障害 (Cont.)					
静脈血栓症	0	1 (1.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-103.

[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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	84 (34.3) [33.8]	86 (34.4) [34.5]	96 (38.2) [38.3]	117 (41.1) [41.1]	130 (44.7) [44.5]
血液およびリンパ系障害	14 (5.7) [5.6]	7 (2.8) [2.8]	9 (3.6) [3.6]	15 (5.3) [5.3]	13 (4.5) [4.4]
貧血	6 (2.4) [2.4]	1 (0.4) [0.4]	4 (1.6) [1.6]	2 (0.7) [0.7]	5 (1.7) [1.7]
好酸球増加症	1 (0.4) [0.4]	0	0	0	0
鉄欠乏性貧血	0	0	0	1 (0.4) [0.4]	0
白血球減少症	3 (1.2) [1.2]	3 (1.2) [1.2]	1 (0.4) [0.4]	6 (2.1) [2.1]	5 (1.7) [1.7]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
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]	1 (0.4) [0.4]	1 (0.4) [0.4]	3 (1.1) [1.1]	1 (0.3) [0.3]
小球性貧血	0	0	0	1 (0.4) [0.4]	0
好中球減少症	3 (1.2) [1.2]	3 (1.2) [1.2]	5 (2.0) [2.0]	3 (1.1) [1.1]	7 (2.4) [2.4]
汎血球減少症	0	0	0	1 (0.4) [0.4]	0
血小板減少症	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
第一度房室ブロック	0	0	0	0	1 (0.3) [0.3]
洞性徐脈	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
耳および迷路障害	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
耳部腫脹	1 (0.4) [0.4]	0	0	0	0
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).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	2 (0.8) [0.8]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	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
眼充血	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
眼窩周囲腫脹	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	30 (12.2) [12.0]	10 (4.0) [4.1]	13 (5.2) [5.2]	17 (6.0) [6.0]	19 (6.5) [6.5]
腹部膨満	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
腹痛	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
上腹部痛	1 (0.4) [0.4]	0	0	0	0
腹部圧痛	0	0	0	0	1 (0.3) [0.4]
肛門の炎症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
アフタ性潰瘍	0	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
大腸炎	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
潰瘍性大腸炎	23 (9.4) [9.2]	6 (2.4) [2.4]	3 (1.2) [1.2]	11 (3.9) [3.9]	4 (1.4) [1.4]
結腸異形成	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]
便秘	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
下痢	0	0	0	1 (0.4) [0.3]	0
消化不良	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
胃食道逆流性疾患	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
痔核	0	0	0	0	1 (0.3) [0.3]
悪心	2 (0.8) [0.8]	0	3 (1.2) [1.2]	0	4 (1.4) [1.4]
非感染性歯肉炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
嚥下痛	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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
直腸分泌物	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
直腸出血	1 (0.4) [0.4]	0	0	0	0
口内炎	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
歯痛	0	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	0	0	0	0	2 (0.7) [0.7]
一般・全身障害および投与部位の状態	6 (2.4) [2.4]	2 (0.8) [0.8]	8 (3.2) [3.2]	5 (1.8) [1.7]	9 (3.1) [3.1]
胸痛	0	0	0	0	1 (0.3) [0.3]
悪寒	0	0	0	0	1 (0.3) [0.4]
薬効欠如	1 (0.4) [0.4]	0	0	0	0
疲労	2 (0.8) [0.8]	2 (0.8) [0.8]	0	4 (1.4) [1.4]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
インフルエンザ様疾患	0	0	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]
倦怠感	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
腫瘤	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
小結節	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
疼痛	0	0	0	1 (0.4) [0.3]	0
末梢腫脹	0	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	2 (0.8) [0.8]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
異物感	1 (0.4) [0.4]	0	0	0	0
腫脹	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肝胆道系障害	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]
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]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
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
肝障害	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
肝損傷	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
感染症および寄生虫症	29 (11.8) [11.6]	34 (13.6) [13.6]	40 (15.9) [16.0]	51 (17.9) [17.9]	59 (20.3) [20.2]
腹壁膿瘍	0	0	0	1 (0.4) [0.3]	0
細菌性関節炎	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
細菌性膣症	1 (0.4) [0.4]	0	0	0	0
気管支炎	1 (0.4) [0.4]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0
感染性滑液包炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
カンジダ感染	0	0	0	1 (0.4) [0.3]	0
蜂巣炎	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	1 (0.4) [0.4]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
結膜炎	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]
COVID-19	2 (0.8) [0.9]	0	1 (0.4) [0.4]	1 (0.4) [0.3]	2 (0.7) [0.7]
COVID-19肺炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
耳感染	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
眼感染	0	0	0	1 (0.4) [0.4]	0
毛包炎	1 (0.4) [0.4]	0	4 (1.6) [1.6]	0	5 (1.7) [1.7]
皮膚真菌感染	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
せつ	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.4]
胃腸炎	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
陰部単純ヘルペス	0	0	0	0	1 (0.3) [0.3]
単径部膿瘍	0	0	0	1 (0.4) [0.3]	0
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	9 (3.6) [3.5]	12 (4.8) [4.8]	18 (6.3) [6.3]	21 (7.2) [7.2]
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
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	0	2 (0.8) [0.8]	2 (0.8) [0.8]	4 (1.4) [1.4]	2 (0.7) [0.7]
潜伏結核	0	0	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
下気道感染	0	0	0	1 (0.4) [0.3]	0
上咽頭炎	5 (2.0) [2.0]	9 (3.6) [3.7]	4 (1.6) [1.6]	9 (3.2) [3.2]	6 (2.1) [2.1]
爪真菌症	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]
口腔カンジダ症	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
口腔ヘルペス	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]
咽頭炎	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
レンサ球菌性咽頭炎	1 (0.4) [0.4]	0	0	0	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	2 (0.8) [0.8]	0	0	0	1 (0.3) [0.3]
クリプトコッカス性肺炎	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
歯髄炎	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
膿疱	0	0	0	1 (0.4) [0.4]	0
腎盂腎炎	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
ウイルス性気道感染	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0
鼻炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
セラチア感染	1 (0.4) [0.4]	0	0	0	0
副鼻腔炎	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	3 (1.1) [1.1]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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]
股部白癬	0	0	0	0	1 (0.3) [0.3]
白癬感染	1 (0.4) [0.4]	0	0	0	0
足部白癬	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
癜風	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
扁桃炎	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]
歯膿瘍	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
歯感染	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
上気道感染	4 (1.6) [1.6]	1 (0.4) [0.4]	4 (1.6) [1.6]	3 (1.1) [1.0]	4 (1.4) [1.4]
尿路感染	3 (1.2) [1.2]	2 (0.8) [0.8]	1 (0.4) [0.4]	3 (1.1) [1.1]	1 (0.3) [0.3]
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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
ウイルス感染	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
ウイルス性上気道感染	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
外陰部腟カンジダ症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
傷害、中毒および処置合併症	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
挫傷	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肋骨骨折	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	12 (4.9) [4.9]	29 (11.6) [11.7]	38 (15.1) [15.1]	38 (13.3) [13.4]	51 (17.5) [17.4]
アラニンアミノトランスフェラーゼ増加	1 (0.4) [0.4]	6 (2.4) [2.5]	5 (2.0) [2.0]	7 (2.5) [2.5]	7 (2.4) [2.4]
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]	7 (2.8) [2.9]	3 (1.2) [1.2]	8 (2.8) [2.8]	6 (2.1) [2.0]
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]
血中ビリルビン増加	0	2 (0.8) [0.8]	2 (0.8) [0.8]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
血中カルシウム増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	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
血中コレステロール増加	0	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.7) [0.7]	4 (1.4) [1.4]
血中クレアチンホスホキナーゼ増加	4 (1.6) [1.7]	10 (4.0) [4.1]	13 (5.2) [5.2]	15 (5.3) [5.3]	23 (7.9) [7.8]
血中クレアチニン増加	0	0	3 (1.2) [1.2]	0	3 (1.0) [1.0]
血中カリウム減少	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
血圧上昇	0	0	0	1 (0.4) [0.3]	1 (0.3) [0.3]
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	1 (0.4) [0.4]	0	2 (0.7) [0.7]
γ-グルタミルトランスフェラーゼ増加	1 (0.4) [0.4]	2 (0.8) [0.8]	0	2 (0.7) [0.7]	2 (0.7) [0.7]
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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
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
ヘモグロビン減少	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.4) [0.3]	3 (1.0) [1.0]
肝酵素上昇	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	2 (0.7) [0.7]
B型肝炎DNA測定陽性	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.
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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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
高比重リポ蛋白増加	0	2 (0.8) [0.8]	1 (0.4) [0.4]	3 (1.1) [1.0]	1 (0.3) [0.4]
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]	4 (1.6) [1.6]	1 (0.4) [0.3]	4 (1.4) [1.4]
リンパ球数減少	2 (0.8) [0.8]	4 (1.6) [1.6]	2 (0.8) [0.8]	6 (2.1) [2.1]	5 (1.7) [1.7]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
リンパ球百分率減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	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]	0
単球数増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
好中球数減少	2 (0.8) [0.8]	4 (1.6) [1.6]	7 (2.8) [2.8]	7 (2.5) [2.5]	9 (3.1) [3.1]
好中球数増加	2 (0.8) [0.8]	1 (0.4) [0.4]	1 (0.4) [0.4]	3 (1.1) [1.0]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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]
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]	1 (0.4) [0.4]	2 (0.7) [0.7]
赤血球数減少	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	2 (0.7) [0.7]
網状赤血球数減少	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
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
体重増加	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
白血球数減少	1 (0.4) [0.4]	4 (1.6) [1.6]	5 (2.0) [2.0]	6 (2.1) [2.1]	8 (2.7) [2.8]
白血球数増加	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
尿中白血球陽性	0	0	0	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	1 (0.4) [0.4]	7 (2.8) [2.9]	5 (2.0) [2.0]	8 (2.8) [2.8]	7 (2.4) [2.4]
脂質異常症	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]
高コレステロール血症	0	3 (1.2) [1.3]	2 (0.8) [0.8]	3 (1.1) [1.1]	3 (1.0) [1.0]
高血糖	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0
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]	1 (0.4) [0.4]	3 (1.1) [1.1]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
高尿酸血症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
筋骨格系および結合組織障害	9 (3.7) [3.6]	1 (0.4) [0.4]	5 (2.0) [2.0]	4 (1.4) [1.4]	8 (2.7) [2.8]
関節痛	3 (1.2) [1.3]	0	3 (1.2) [1.2]	1 (0.4) [0.4]	5 (1.7) [1.7]
関節障害	3 (1.2) [1.2]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
背部痛	2 (0.8) [0.8]	0	0	1 (0.4) [0.4]	0
骨痛	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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
筋拘縮	0	0	0	1 (0.4) [0.4]	0
筋骨格系胸痛	1 (0.4) [0.4]	0	0	0	0
筋骨格痛	1 (0.4) [0.4]	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
筋肉痛	2 (0.8) [0.8]	0	0	0	2 (0.7) [0.7]
頚部痛	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	0	0	1 (0.4) [0.4]	0	3 (1.0) [1.0]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4) [0.4]	0	3 (1.2) [1.2]	0	4 (1.4) [1.4]
基底細胞癌	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
ボーエン病	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]
浸潤性乳癌	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	6 (2.4) [2.4]	3 (1.2) [1.2]	2 (0.8) [0.8]	7 (2.5) [2.4]	7 (2.4) [2.4]
灼熱感	0	0	0	1 (0.4) [0.3]	0
頚髄圧迫	0	0	0	0	1 (0.3) [0.3]
注意力障害	0	0	0	1 (0.4) [0.4]	0
浮動性めまい	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]
頭痛	6 (2.4) [2.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
感覚鈍麻	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
片頭痛	0	0	0	1 (0.4) [0.3]	0
脊髄症	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]
会話障害	0	0	0	1 (0.4) [0.4]	0
視野欠損	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	0	0	4 (1.6) [1.6]	0	5 (1.7) [1.7]
うつ病	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
不眠症	0	0	3 (1.2) [1.2]	0	3 (1.0) [1.0]
腎および尿路障害	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]
急性腎障害	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
血尿	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
水腎症	1 (0.4) [0.4]	0	0	0	0
蛋白尿	1 (0.4) [0.4]	0	0	0	2 (0.7) [0.7]
腎仙痛	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
腎機能障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
生殖系および乳房障害	2 (0.8) [0.9]	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.7) [0.7]	2 (0.7) [0.7]
バルトリン嚢腫	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
良性前立腺肥大症	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
勃起不全	0	0	0	1 (0.4) [0.3]	0
前立腺腫瘤	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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]	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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	6 (2.4) [2.4]	2 (0.8) [0.8]	7 (2.8) [2.8]	5 (1.8) [1.8]	9 (3.1) [3.1]
気管支拡張症	1 (0.4) [0.4]	0	0	0	0
咳嗽	0	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]
労作性呼吸困難	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
鼻出血	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.4]
間質性肺疾患	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
鼻閉	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
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	3 (1.2) [1.2]	0	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]
湿性咳嗽	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.3]
肺塞栓症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]
副鼻腔うっ血	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
上気道の炎症	1 (0.4) [0.4]	0	0	0	0
上気道咳症候群	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
皮膚および皮下組織障害	20 (8.2) [8.0]	18 (7.2) [7.2]	16 (6.4) [6.4]	26 (9.1) [9.1]	27 (9.3) [9.2]
ざ瘡	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.8) [0.8]	5 (1.8) [1.7]	5 (1.7) [1.7]
嚢胞性ざ瘡	0	0	0	1 (0.4) [0.3]	0
光線角化症	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.
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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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
脱毛症	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]
皮膚炎	1 (0.4) [0.4]	0	0	0	0
ざ瘡様皮膚炎	0	0	0	1 (0.4) [0.4]	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	1 (0.4) [0.4]	0	0	0	0
接触皮膚炎	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.
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[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
皮膚乾燥	2 (0.8) [0.8]	0	0	1 (0.4) [0.3]	0
異汗性湿疹	1 (0.4) [0.4]	0	0	0	0
斑状出血	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
湿疹	2 (0.8) [0.8]	0	0	0	1 (0.3) [0.3]
紅斑	2 (0.8) [0.8]	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]	3 (1.0) [1.0]
結節性紅斑	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
間擦疹	0	0	0	1 (0.4) [0.3]	0
神経皮膚炎	1 (0.4) [0.4]	0	0	0	0
寝汗	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
爪破損	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
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
そう痒症	4 (1.6) [1.6]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	2 (0.7) [0.7]
発疹	3 (1.2) [1.2]	4 (1.6) [1.6]	9 (3.6) [3.6]	6 (2.1) [2.1]	12 (4.1) [4.1]
紅斑性皮疹	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0
毛孔性皮疹	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
斑状皮疹	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.3) [0.4]
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]
酒さ	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]	0
脂漏性皮膚炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
皮膚病変	0	0	0	1 (0.4) [0.4]	3 (1.0) [1.0]
皮膚潰瘍	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
蕁麻疹	1 (0.4) [0.4]	0	0	0	0
血管障害	2 (0.8) [0.9]	1 (0.4) [0.4]	1 (0.4) [0.4]	4 (1.4) [1.4]	2 (0.7) [0.7]
高血圧	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]
レイノー現象	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 3.3.10

Number and Percentage of Subjects with Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug 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.)					
静脈血栓症	1 (0.4) [0.4]	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]

表 2.7.4.7-104.

[redacted]20[redacted] 09:30 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY UPDATE (CUTOFF [redacted]20[redacted])
R&D/22/0029 - CLINICAL/STATISTICAL

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
Any adverse event	162 (123.2)	100 (79.9)	482 (68.9)
血液およびリンパ系障害	10 (7.6)	3 (2.4)	26 (3.7)
貧血	4 (3.0)	2 (1.6)	4 (0.6)
失血性貧血	0	0	0
周期性好中球減少症	0	0	0
好酸球増加症	1 (0.8)	0	0
内出血発生の増加傾向	0	0	0
鉄欠乏性貧血	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
Any adverse event	88 (365.5)	531 (111.0)	600 (96.4)	621 (104.9)	2182 (92.8)
血液およびリンパ系障害	5 (20.8)	47 (9.8)	54 (8.7)	39 (6.6)	151 (6.4)
貧血	2 (8.3)	12 (2.5)	4 (0.6)	7 (1.2)	22 (0.9)
失血性貧血	0	0	0	1 (0.2)	1 (<0.1)
周期性好中球減少症	0	1 (0.2)	0	0	1 (<0.1)
好酸球増加症	0	1 (0.2)	0	0	0
内出血発生の増加傾向	0	1 (0.2)	0	0	1 (<0.1)
鉄欠乏性貧血	0	0	2 (0.3)	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)			
白血球増加症	0	0	2 (0.3)
白血球減少症	0	0	4 (0.6)
リンパ節症	0	1 (0.8)	0
リンパ球増加症	0	0	0
リンパ球減少症	1 (0.8)	0	8 (1.1)
小球性貧血	0	0	0
好中球減少症	3 (2.3)	0	7 (1.0)
好中球増加症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)					
白血球増加症	0	0	0	1 (0.2)	3 (0.1)
白血球減少症	0	8 (1.7)	21 (3.4)	7 (1.2)	36 (1.5)
リンパ節症	0	0	0	0	0
リンパ球増加症	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
リンパ球減少症	2 (8.3)	8 (1.7)	8 (1.3)	5 (0.8)	28 (1.2)
小球性貧血	0	0	1 (0.2)	0	1 (<0.1)
好中球減少症	1 (4.2)	14 (2.9)	15 (2.4)	16 (2.7)	50 (2.1)
好中球増加症	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)			
汎血球減少症	0	0	0
網状赤血球増加症	0	0	1 (0.1)
血小板減少症	1 (0.8)	0	0
心臓障害	2 (1.5)	0	2 (0.3)
急性心筋梗塞	0	0	0
第一度房室ブロック	0	0	0
期外収縮	0	0	0
動悸	1 (0.8)	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)					
汎血球減少症	0	0	2 (0.3)	0	2 (<0.1)
網状赤血球増加症	0	0	0	0	1 (<0.1)
血小板減少症	0	1 (0.2)	0	0	0
心臓障害	0	2 (0.4)	2 (0.3)	2 (0.3)	8 (0.3)
急性心筋梗塞	0	0	1 (0.2)	0	1 (<0.1)
第一度房室ブロック	0	0	0	1 (0.2)	1 (<0.1)
期外収縮	0	0	1 (0.2)	0	1 (<0.1)
動悸	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
心臓障害 (Cont.)			
心嚢液貯留	0	0	0
心膜炎	0	0	0
洞性徐脈	0	0	0
頻脈	1 (0.8)	0	1 (0.1)
耳および迷路障害	1 (0.8)	0	2 (0.3)
耳痛	1 (0.8)	0	0
耳部腫脹	0	0	0
外耳の炎症	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)					
心嚢液貯留	0	1 (0.2)	0	0	1 (<0.1)
心膜炎	0	1 (0.2)	0	0	1 (<0.1)
洞性徐脈	0	0	0	1 (0.2)	1 (<0.1)
頻脈	0	0	0	0	1 (<0.1)
耳および迷路障害	2 (8.3)	3 (0.6)	3 (0.5)	2 (0.3)	11 (0.5)
耳痛	0	1 (0.2)	0	0	1 (<0.1)
耳部腫脹	0	1 (0.2)	0	0	0
外耳の炎症	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
耳および迷路障害 (Cont.)			
聴力低下	0	0	0
内耳障害	0	0	1 (0.1)
メニエール病	0	0	0
突発性難聴	0	0	0
耳鳴	0	0	1 (0.1)
回転性めまい	0	0	0
内分泌障害	0	0	1 (0.1)
クッシング様症状	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
耳および迷路障害 (Cont.)					
聴力低下	0	0	1 (0.2)	0	1 (<0.1)
内耳障害	0	0	0	0	1 (<0.1)
メニエール病	0	0	0	1 (0.2)	1 (<0.1)
突発性難聴	0	0	1 (0.2)	0	1 (<0.1)
耳鳴	2 (8.3)	0	1 (0.2)	0	4 (0.2)
回転性めまい	0	0	0	1 (0.2)	1 (<0.1)
内分泌障害	0	0	0	0	1 (<0.1)
クッシング様症状	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
眼障害	1 (0.8)	2 (1.6)	1 (0.1)
眼精疲労	0	0	0
眼瞼炎	0	0	0
霰粒腫	0	0	0
ドライアイ	0	0	0
上強膜炎	0	1 (0.8)	0
眼部腫脹	0	0	0
眼瞼障害	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害	2 (8.3)	6 (1.3)	5 (0.8)	2 (0.3)	13 (0.6)
眼精疲労	0	1 (0.2)	0	0	0
眼瞼炎	0	2 (0.4)	0	0	2 (<0.1)
霰粒腫	1 (4.2)	0	0	0	1 (<0.1)
ドライアイ	0	0	0	2 (0.3)	2 (<0.1)
上強膜炎	0	0	0	0	0
眼部腫脹	0	0	1 (0.2)	0	1 (<0.1)
眼瞼障害	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
眼障害 (Cont.)			
角膜炎	0	0	0
眼部不快感	1 (0.8)	0	0
眼充血	0	0	0
眼窩周囲腫脹	0	0	0
ぶどう膜炎	0	0	0
霧視	0	0	0
視力障害	0	0	1 (0.1)
硝子体浮遊物	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
眼障害 (Cont.)					
角膜炎	0	0	2 (0.3)	0	2 (<0.1)
眼部不快感	0	0	0	0	0
眼充血	0	0	1 (0.2)	0	1 (<0.1)
眼窩周囲腫脹	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
ぶどう膜炎	0	1 (0.2)	0	0	0
霧視	1 (4.2)	0	0	0	1 (<0.1)
視力障害	0	0	0	0	1 (<0.1)
硝子体浮遊物	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害	37 (28.1)	11 (8.8)	49 (7.0)
腹部不快感	0	2 (1.6)	0
腹部膨満	1 (0.8)	1 (0.8)	1 (0.1)
腹痛	2 (1.5)	0	3 (0.4)
下腹部痛	1 (0.8)	0	1 (0.1)
上腹部痛	2 (1.5)	0	1 (0.1)
腹部圧痛	0	0	0
肛門の炎症	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害	16 (66.4)	73 (15.3)	38 (6.1)	52 (8.8)	195 (8.3)
腹部不快感	0	0	0	0	1 (<0.1)
腹部膨満	0	1 (0.2)	0	4 (0.7)	5 (0.2)
腹痛	3 (12.5)	2 (0.4)	1 (0.2)	2 (0.3)	11 (0.5)
下腹部痛	0	1 (0.2)	1 (0.2)	0	3 (0.1)
上腹部痛	0	2 (0.4)	1 (0.2)	0	3 (0.1)
腹部圧痛	0	0	0	1 (0.2)	1 (<0.1)
肛門の炎症	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
肛門潰瘍	0	0	0
口角口唇炎	0	0	1 (0.1)
肛門直腸不快感	0	0	0
アフタ性潰瘍	0	0	1 (0.1)
大腸炎	1 (0.8)	0	2 (0.3)
潰瘍性大腸炎	20 (15.2)	2 (1.6)	14 (2.0)
結腸異形成	0	0	1 (0.1)
便秘	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
肛門潰瘍	1 (4.2)	0	0	0	1 (<0.1)
口角口唇炎	0	0	0	0	1 (<0.1)
肛門直腸不快感	1 (4.2)	0	0	0	1 (<0.1)
アフタ性潰瘍	0	1 (0.2)	0	5 (0.8)	7 (0.3)
大腸炎	0	1 (0.2)	2 (0.3)	0	4 (0.2)
潰瘍性大腸炎	5 (20.8)	37 (7.7)	21 (3.4)	7 (1.2)	57 (2.4)
結腸異形成	0	0	2 (0.3)	1 (0.2)	4 (0.2)
便秘	2 (8.3)	6 (1.3)	2 (0.3)	4 (0.7)	15 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
便意切迫	1 (0.8)	0	1 (0.1)
下痢	1 (0.8)	1 (0.8)	1 (0.1)
血性下痢	0	0	0
口内乾燥	0	1 (0.8)	0
消化不良	1 (0.8)	0	0
おくび	0	0	0
大腿ヘルニア	0	0	0
鼓腸	2 (1.5)	1 (0.8)	5 (0.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
便意切迫	0	0	0	0	1 (<0.1)
下痢	1 (4.2)	1 (0.2)	2 (0.3)	0	6 (0.3)
血性下痢	1 (4.2)	0	0	0	1 (<0.1)
口内乾燥	0	0	0	0	1 (<0.1)
消化不良	0	1 (0.2)	1 (0.2)	1 (0.2)	2 (<0.1)
おくび	0	0	0	1 (0.2)	1 (<0.1)
大腿ヘルニア	0	1 (0.2)	0	0	1 (<0.1)
鼓腸	0	0	0	5 (0.8)	11 (0.5)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
排便回数増加	0	0	1 (0.1)
胃炎	0	0	0
胃食道逆流性疾患	0	0	0
歯肉痛	0	0	0
血便排泄	0	0	0
痔核	0	0	2 (0.3)
回腸潰瘍	1 (0.8)	0	0
腸閉塞	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
排便回数増加	0	0	0	0	1 (<0.1)
胃炎	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
胃食道逆流性疾患	0	2 (0.4)	2 (0.3)	1 (0.2)	5 (0.2)
歯肉痛	0	0	0	1 (0.2)	1 (<0.1)
血便排泄	0	2 (0.4)	0	0	0
痔核	0	1 (0.2)	0	1 (0.2)	4 (0.2)
回腸潰瘍	0	0	0	0	0
腸閉塞	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
大腸ポリープ	0	0	1 (0.1)
口唇水疱	0	0	0
口腔内潰瘍形成	0	1 (0.8)	1 (0.1)
悪心	2 (1.5)	0	7 (1.0)
非感染性歯肉炎	0	0	0
嚥下痛	0	0	0
口腔障害	0	0	0
口腔内痛	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
大腸ポリープ	0	0	0	0	1 (<0.1)
口唇水疱	0	0	0	1 (0.2)	1 (<0.1)
口腔内潰瘍形成	0	0	0	0	1 (<0.1)
悪心	0	8 (1.7)	0	6 (1.0)	19 (0.8)
非感染性歯肉炎	0	0	0	1 (0.2)	1 (<0.1)
嚥下痛	0	0	0	1 (0.2)	1 (<0.1)
口腔障害	0	0	0	1 (0.2)	1 (<0.1)
口腔内痛	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
膵炎	0	0	0
肛門周囲痛	0	0	0
直腸分泌物	1 (0.8)	0	0
直腸出血	0	1 (0.8)	0
直腸しぶり	0	0	0
口内炎	0	0	1 (0.1)
歯痛	0	0	0
嘔吐	1 (0.8)	1 (0.8)	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
膵炎	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
肛門周囲痛	1 (4.2)	0	0	0	1 (<0.1)
直腸分泌物	0	0	0	1 (0.2)	1 (<0.1)
直腸出血	0	2 (0.4)	0	0	2 (<0.1)
直腸しぶり	1 (4.2)	0	0	0	1 (<0.1)
口内炎	0	1 (0.2)	0	2 (0.3)	3 (0.1)
歯痛	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
嘔吐	0	1 (0.2)	0	2 (0.3)	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態	5 (3.8)	3 (2.4)	26 (3.7)
無力症	1 (0.8)	0	2 (0.3)
胸部不快感	0	0	0
胸痛	1 (0.8)	0	0
悪寒	1 (0.8)	1 (0.8)	3 (0.4)
不快感	0	0	0
薬効欠如	0	0	1 (0.1)
疲労	1 (0.8)	1 (0.8)	3 (0.4)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態	6 (24.9)	12 (2.5)	22 (3.5)	23 (3.9)	82 (3.5)
無力症	0	0	1 (0.2)	2 (0.3)	5 (0.2)
胸部不快感	1 (4.2)	0	1 (0.2)	0	2 (<0.1)
胸痛	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
悪寒	0	2 (0.4)	0	2 (0.3)	7 (0.3)
不快感	0	0	0	1 (0.2)	1 (<0.1)
薬効欠如	0	1 (0.2)	0	0	1 (<0.1)
疲労	1 (4.2)	3 (0.6)	7 (1.1)	3 (0.5)	15 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
異常感	0	0	0
びくびく感	0	0	0
全身性浮腫	0	0	1 (0.1)
過形成	0	0	0
治癒不良	0	0	1 (0.1)
インフルエンザ様疾患	0	0	4 (0.6)
注射部位疼痛	0	0	0
倦怠感	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
異常感	0	0	0	1 (0.2)	1 (<0.1)
びくびく感	0	0	1 (0.2)	0	1 (<0.1)
全身性浮腫	0	0	0	0	1 (<0.1)
過形成	0	1 (0.2)	0	0	1 (<0.1)
治癒不良	0	0	0	0	1 (<0.1)
インフルエンザ様疾患	0	0	2 (0.3)	1 (0.2)	7 (0.3)
注射部位疼痛	0	0	1 (0.2)	0	1 (<0.1)
倦怠感	1 (4.2)	0	2 (0.3)	1 (0.2)	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
腫瘤	0	0	0
小結節	0	0	0
末梢性浮腫	0	0	0
疼痛	0	0	0
末梢腫脹	0	0	0
発熱	1 (0.8)	1 (0.8)	10 (1.4)
異物感	0	0	0
腫脹	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
腫瘤	0	0	0	2 (0.3)	2 (<0.1)
小結節	0	0	0	1 (0.2)	1 (<0.1)
末梢性浮腫	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
疼痛	0	0	2 (0.3)	0	2 (<0.1)
末梢腫脹	0	0	0	2 (0.3)	2 (<0.1)
発熱	3 (12.5)	4 (0.8)	2 (0.3)	4 (0.7)	20 (0.9)
異物感	0	1 (0.2)	0	0	0
腫脹	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
評価不能の事象	0	0	0
肝胆道系障害	1 (0.8)	1 (0.8)	1 (0.1)
硬化性胆管炎	0	0	0
胆石症	0	0	0
薬物性肝障害	0	0	0
肝機能異常	0	0	0
脂肪肝	0	1 (0.8)	0
肝炎	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
評価不能の事象	0	0	1 (0.2)	0	1 (<0.1)
肝胆道系障害	1 (4.2)	5 (1.0)	3 (0.5)	4 (0.7)	12 (0.5)
硬化性胆管炎	0	0	0	1 (0.2)	1 (<0.1)
胆石症	0	0	0	1 (0.2)	1 (<0.1)
薬物性肝障害	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
肝機能異常	0	3 (0.6)	0	0	0
脂肪肝	0	0	0	0	1 (<0.1)
肝炎	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
高トランスアミナーゼ血症	0	0	0
肝障害	0	0	0
肝損傷	1 (0.8)	0	0
非アルコール性脂肪性肝疾患	0	0	0
免疫系障害	0	0	2 (0.3)
薬物過敏症	0	0	1 (0.1)
過敏症	0	0	1 (0.1)
感染症および寄生虫症	30 (22.8)	31 (24.8)	155 (22.2)

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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
肝胆道系障害 (Cont.)					
高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 (0.2)	0	1 (0.2)	2 (<0.1)
肝損傷	0	0	1 (0.2)	0	1 (<0.1)
非アルコール性脂肪性肝疾患	0	1 (0.2)	0	0	1 (<0.1)
免疫系障害	0	0	0	0	2 (<0.1)
薬物過敏症	0	0	0	0	1 (<0.1)
過敏症	0	0	0	0	1 (<0.1)
感染症および寄生虫症	13 (54.0)	118 (24.7)	152 (24.4)	137 (23.2)	560 (23.8)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
腹部膿瘍	0	0	0
腹壁膿瘍	0	0	0
膿瘍	1 (0.8)	0	0
急性副鼻腔炎	0	0	1 (0.1)
肛門膿瘍	1 (0.8)	0	1 (0.1)
虫垂炎	0	0	0
細菌性関節炎	0	0	0
無症候性COVID-19	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
腹部膿瘍	0	0	1 (0.2)	0	1 (<0.1)
腹壁膿瘍	0	0	1 (0.2)	0	1 (<0.1)
膿瘍	0	1 (0.2)	0	0	1 (<0.1)
急性副鼻腔炎	0	0	0	0	1 (<0.1)
肛門膿瘍	0	1 (0.2)	0	0	2 (<0.1)
虫垂炎	0	0	1 (0.2)	0	1 (<0.1)
細菌性関節炎	0	0	1 (0.2)	0	1 (<0.1)
無症候性COVID-19	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
無症候性細菌尿	0	0	0
細菌感染	0	0	0
細菌性膣症	0	0	1 (0.1)
気管支炎	0	0	7 (1.0)
感染性滑液包炎	0	0	0
COVID-19	1 (0.8)	0	2 (0.3)
COVID-19肺炎	0	0	0
カンジダ感染	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
無症候性細菌尿	0	0	1 (0.2)	0	1 (<0.1)
細菌感染	0	1 (0.2)	0	0	1 (<0.1)
細菌性膣症	0	1 (0.2)	0	0	1 (<0.1)
気管支炎	1 (4.2)	4 (0.8)	3 (0.5)	0	14 (0.6)
感染性滑液包炎	0	0	0	1 (0.2)	1 (<0.1)
COVID-19	0	2 (0.4)	2 (0.3)	4 (0.7)	8 (0.3)
COVID-19肺炎	0	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.2)
カンジダ感染	0	0	1 (0.2)	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
蜂巣炎	4 (3.0)	0	1 (0.1)
条虫感染	0	0	0
感染性胆嚢炎	0	0	0
クロストリジウム・ディフィシレ感染	3 (2.3)	1 (0.8)	2 (0.3)
結膜炎	0	0	0
ウイルス性結膜炎	0	0	0
膀胱炎	0	0	0
サイトメガロウイルス感染	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
蜂巣炎	0	1 (0.2)	4 (0.6)	0	6 (0.3)
条虫感染	1 (4.2)	0	0	0	1 (<0.1)
感染性胆嚢炎	0	0	1 (0.2)	0	1 (<0.1)
クロストリジウム・ディフィシレ感染	0	1 (0.2)	1 (0.2)	4 (0.7)	8 (0.3)
結膜炎	0	0	1 (0.2)	2 (0.3)	3 (0.1)
ウイルス性結膜炎	0	1 (0.2)	0	0	1 (<0.1)
膀胱炎	0	1 (0.2)	0	0	1 (<0.1)
サイトメガロウイルス感染	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
毛嚢虫症	0	1 (0.8)	2 (0.3)
皮膚糸状菌症	0	0	1 (0.1)
爪の皮膚糸状菌症	0	0	1 (0.1)
感染性下痢	0	0	0
耳感染	0	0	1 (0.1)
丹毒	0	0	1 (0.1)
眼感染	0	0	0
毛包炎	0	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
毛嚢虫症	0	0	4 (0.6)	4 (0.7)	11 (0.5)
皮膚糸状菌症	0	1 (0.2)	0	0	1 (<0.1)
爪の皮膚糸状菌症	0	0	0	2 (0.3)	3 (0.1)
感染性下痢	0	0	0	1 (0.2)	1 (<0.1)
耳感染	0	0	2 (0.3)	0	3 (0.1)
丹毒	0	0	0	0	1 (<0.1)
眼感染	0	0	1 (0.2)	0	1 (<0.1)
毛包炎	1 (4.2)	3 (0.6)	2 (0.3)	14 (2.4)	21 (0.9)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
真菌感染	1 (0.8)	0	0
皮膚真菌感染	0	0	0
せつ	0	0	0
胃腸炎	1 (0.8)	0	1 (0.1)
ウイルス性胃腸炎	0	0	1 (0.1)
性器カンジダ症	0	0	1 (0.1)
陰部ヘルペス	0	0	1 (0.1)
陰部単純ヘルペス	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
真菌感染	0	0	0	0	0
皮膚真菌感染	0	2 (0.4)	0	1 (0.2)	3 (0.1)
せつ	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
胃腸炎	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
ウイルス性胃腸炎	0	0	0	0	1 (<0.1)
性器カンジダ症	0	0	0	0	1 (<0.1)
陰部ヘルペス	0	0	1 (0.2)	1 (0.2)	3 (0.1)
陰部単純ヘルペス	0	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
真菌性性器感染	0	0	0
歯肉炎	1 (0.8)	0	0
肛径部膿瘍	0	0	0
ヘモフィルス感染	0	0	0
手足口病	0	0	0
ヘルペス性皮膚炎	0	0	0
ヘルペス眼感染	0	0	0
単純ヘルペス	0	5 (4.0)	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
真菌性性器感染	0	1 (0.2)	0	0	1 (<0.1)
歯肉炎	0	3 (0.6)	0	0	3 (0.1)
肛径部膿瘍	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
ヘモフィルス感染	0	1 (0.2)	0	0	0
手足口病	0	0	0	1 (0.2)	1 (<0.1)
ヘルペス性皮膚炎	0	0	1 (0.2)	0	1 (<0.1)
ヘルペス眼感染	0	0	0	1 (0.2)	1 (<0.1)
単純ヘルペス	0	2 (0.4)	1 (0.2)	1 (0.2)	11 (0.5)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
単純ヘルペス性咽頭炎	0	1 (0.8)	0
帯状疱疹	0	4 (3.2)	21 (3.0)
播種性帯状疱疹	0	0	0
帯状疱疹性髄膜炎	0	0	0
耳帯状疱疹	0	0	0
麦粒腫	0	0	0
膿痂疹	0	0	1 (0.1)
感染性皮膚嚢腫	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
単純ヘルペス性咽頭炎	0	0	0	0	1 (<0.1)
帯状疱疹	6 (24.9)	8 (1.7)	28 (4.5)	24 (4.1)	89 (3.8)
播種性帯状疱疹	0	1 (0.2)	0	0	1 (<0.1)
帯状疱疹性髄膜炎	0	0	0	1 (0.2)	1 (<0.1)
耳帯状疱疹	0	0	1 (0.2)	0	1 (<0.1)
麦粒腫	0	0	0	1 (0.2)	1 (<0.1)
膿痂疹	0	0	0	0	1 (<0.1)
感染性皮膚嚢腫	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
伝染性単核症	0	0	1 (0.1)
インフルエンザ	0	0	2 (0.3)
潜伏結核	0	1 (0.8)	2 (0.3)
限局性感染	0	0	1 (0.1)
下気道感染	0	0	0
上咽頭炎	2 (1.5)	2 (1.6)	8 (1.1)
爪真菌症	0	0	0
口腔カンジダ症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
伝染性単核症	0	0	0	0	1 (<0.1)
インフルエンザ	0	2 (0.4)	6 (1.0)	6 (1.0)	15 (0.6)
潜伏結核	0	1 (0.2)	2 (0.3)	2 (0.3)	8 (0.3)
限局性感染	0	0	0	0	1 (<0.1)
下気道感染	0	0	1 (0.2)	0	1 (<0.1)
上咽頭炎	0	14 (2.9)	23 (3.7)	16 (2.7)	57 (2.4)
爪真菌症	0	4 (0.8)	2 (0.3)	1 (0.2)	6 (0.3)
口腔カンジダ症	0	1 (0.2)	0	2 (0.3)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
口腔ヘルペス	1 (0.8)	5 (4.0)	13 (1.9)
精巣炎	0	0	1 (0.1)
真菌性外耳炎	0	0	0
中耳炎	0	0	0
急性中耳炎	0	0	0
爪囲炎	0	0	0
直腸周囲膿瘍	0	0	0
咽頭炎	2 (1.5)	0	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	0	5 (1.0)	2 (0.3)	4 (0.7)	26 (1.1)
精巣炎	0	0	0	0	1 (<0.1)
真菌性外耳炎	0	1 (0.2)	0	0	1 (<0.1)
中耳炎	0	0	1 (0.2)	0	1 (<0.1)
急性中耳炎	0	1 (0.2)	0	0	1 (<0.1)
爪囲炎	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
直腸周囲膿瘍	0	1 (0.2)	0	0	1 (<0.1)
咽頭炎	1 (4.2)	1 (0.2)	3 (0.5)	1 (0.2)	8 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
レンサ球菌性咽頭炎	0	0	0
胸膜感染	0	0	0
ニューモシスチス・イロベチイ肺炎	0	0	0
肺炎	0	2 (1.6)	7 (1.0)
クリプトコッカス性肺炎	0	0	0
肺炎球菌性肺炎	0	0	1 (0.1)
処置後感染	1 (0.8)	0	0
歯髄炎	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
レンサ球菌性咽頭炎	0	1 (0.2)	0	0	0
胸膜感染	0	0	0	1 (0.2)	1 (<0.1)
ニューモシスチス・イロベチイ肺炎	0	1 (0.2)	0	0	0
肺炎	1 (4.2)	3 (0.6)	0	2 (0.3)	13 (0.6)
クリプトコッカス性肺炎	0	0	0	2 (0.3)	2 (<0.1)
肺炎球菌性肺炎	0	0	0	0	1 (<0.1)
処置後感染	0	0	0	0	0
歯髄炎	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
膿疱	0	0	0
腎盂腎炎	0	0	1 (0.1)
膿疱性皮疹	0	0	0
直腸膿瘍	0	0	0
RSウイルス感染	0	0	0
気道感染	0	0	2 (0.3)
ウイルス性気道感染	0	0	1 (0.1)
鼻炎	1 (0.8)	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
膿疱	0	0	2 (0.3)	0	2 (<0.1)
腎盂腎炎	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
膿疱性皮疹	0	1 (0.2)	0	0	1 (<0.1)
直腸膿瘍	0	0	1 (0.2)	0	1 (<0.1)
RSウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
気道感染	0	0	1 (0.2)	0	3 (0.1)
ウイルス性気道感染	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
鼻炎	0	1 (0.2)	0	1 (0.2)	3 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
根管感染	0	0	1 (0.1)
敗血症	0	0	1 (0.1)
セラチア感染	0	0	0
副鼻腔炎	1 (0.8)	1 (0.8)	8 (1.1)
皮膚カンジダ	0	0	1 (0.1)
皮膚感染	0	0	0
ブドウ球菌感染	0	0	0
皮下組織膿瘍	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
根管感染	0	0	0	0	1 (<0.1)
敗血症	0	0	1 (0.2)	0	2 (<0.1)
セラチア感染	0	1 (0.2)	0	0	0
副鼻腔炎	0	2 (0.4)	6 (1.0)	2 (0.3)	18 (0.8)
皮膚カンジダ	0	0	0	0	1 (<0.1)
皮膚感染	0	0	0	2 (0.3)	2 (<0.1)
ブドウ球菌感染	0	1 (0.2)	0	0	0
皮下組織膿瘍	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
股部白癬	0	0	0
白癬感染	0	0	0
足部白癬	0	0	0
癜風	0	0	0
扁桃炎	0	0	1 (0.1)
歯膿瘍	0	0	0
歯感染	0	0	1 (0.1)
結核	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
股部白癬	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
白癬感染	0	2 (0.4)	0	0	0
足部白癬	0	2 (0.4)	0	2 (0.3)	3 (0.1)
癜風	0	0	2 (0.3)	0	2 (<0.1)
扁桃炎	0	0	2 (0.3)	1 (0.2)	4 (0.2)
歯膿瘍	0	0	3 (0.5)	0	3 (0.1)
歯感染	0	0	0	2 (0.3)	3 (0.1)
結核	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
上気道感染	4 (3.0)	5 (4.0)	25 (3.6)
尿路感染	4 (3.0)	1 (0.8)	11 (1.6)
尿路性敗血症	0	0	1 (0.1)
膣感染	0	0	1 (0.1)
水痘	0	0	1 (0.1)
水痘帯状疱疹ウイルス感染	0	0	0
ウイルス感染	0	0	0
ウイルス性心膜炎	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
上気道感染	1 (4.2)	17 (3.6)	13 (2.1)	14 (2.4)	70 (3.0)
尿路感染	0	5 (1.0)	8 (1.3)	2 (0.3)	24 (1.0)
尿路性敗血症	0	0	0	0	1 (<0.1)
腟感染	0	0	0	0	1 (<0.1)
水痘	0	0	0	0	1 (<0.1)
水痘帯状疱疹ウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
ウイルス感染	1 (4.2)	2 (0.4)	0	2 (0.3)	5 (0.2)
ウイルス性心膜炎	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ウイルス性上気道感染	0	1 (0.8)	2 (0.3)
女性外陰部蜂巣炎	0	0	1 (0.1)
外陰部腟カンジダ症	0	0	3 (0.4)
外陰腟真菌感染	0	0	1 (0.1)
創傷感染	1 (0.8)	0	0
傷害、中毒および処置合併症	4 (3.0)	2 (1.6)	11 (1.6)
偶発的過量投与	3 (2.3)	2 (1.6)	5 (0.7)
挫傷	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ウイルス性上気道感染	0	2 (0.4)	1 (0.2)	1 (0.2)	6 (0.3)
女性外陰部蜂巣炎	0	0	0	0	1 (<0.1)
外陰部腟カンジダ症	0	1 (0.2)	2 (0.3)	0	6 (0.3)
外陰腟真菌感染	0	0	0	0	1 (<0.1)
創傷感染	0	0	0	0	0
傷害、中毒および処置合併症	0	5 (1.0)	1 (0.2)	3 (0.5)	21 (0.9)
偶発的過量投与	0	0	1 (0.2)	2 (0.3)	10 (0.4)
挫傷	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
筋断裂	0	0	3 (0.4)
過量投与	0	0	2 (0.3)
肋骨骨折	0	0	0
皮膚裂傷	0	0	0
皮下血腫	0	0	1 (0.1)
創傷	0	0	0
臨床検査	21 (16.0)	19 (15.2)	84 (12.0)
アラニンアミノトランスフェラーゼ増加	3 (2.3)	2 (1.6)	7 (1.0)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
筋断裂	0	0	0	0	3 (0.1)
過量投与	0	0	0	0	2 (<0.1)
肋骨骨折	0	1 (0.2)	0	0	0
皮膚裂傷	0	1 (0.2)	0	0	1 (<0.1)
皮下血腫	0	0	0	0	1 (<0.1)
創傷	0	3 (0.6)	0	0	3 (0.1)
臨床検査	17 (70.6)	97 (20.3)	166 (26.7)	175 (29.6)	529 (22.5)
アラニンアミノトランスフェラーゼ増加	0	5 (1.0)	11 (1.8)	12 (2.0)	35 (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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
αヒドロキシ酪酸脱水素酵素増加	0	0	0
アミラーゼ増加	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	3 (2.3)	1 (0.8)	7 (1.0)
細菌検査陽性	0	0	0
血中アルブミン増加	0	0	0
血中アルカリホスファターゼ増加	1 (0.8)	0	0
血中ビリルビン増加	0	0	1 (0.1)
血中カルシウム増加	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.2)	0	0	1 (<0.1)
アミラーゼ増加	1 (4.2)	0	0	0	1 (<0.1)
アスパラギン酸アミノトランスフェラーゼ増加	0	7 (1.5)	13 (2.1)	10 (1.7)	36 (1.5)
細菌検査陽性	0	1 (0.2)	0	0	0
血中アルブミン増加	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
血中アルカリホスファターゼ増加	0	0	0	1 (0.2)	1 (<0.1)
血中ビリルビン増加	0	0	8 (1.3)	2 (0.3)	11 (0.5)
血中カルシウム増加	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血中クロール減少	0	0	0
血中コレステロール減少	0	0	0
血中コレステロール増加	0	1 (0.8)	3 (0.4)
血中クレアチンホスホキナーゼ増加	1 (0.8)	9 (7.2)	27 (3.9)
血中クレアチニン増加	1 (0.8)	0	1 (0.1)
血中葉酸減少	0	1 (0.8)	0
血中乳酸脱水素酵素増加	0	0	0
血中カリウム減少	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血中クロール減少	0	1 (0.2)	0	0	1 (<0.1)
血中コレステロール減少	0	0	1 (0.2)	0	1 (<0.1)
血中コレステロール増加	0	1 (0.2)	2 (0.3)	5 (0.8)	12 (0.5)
血中クレアチンホスホキナーゼ増加	5 (20.8)	26 (5.4)	38 (6.1)	47 (7.9)	146 (6.2)
血中クレアチニン増加	0	0	1 (0.2)	5 (0.8)	7 (0.3)
血中葉酸減少	0	0	0	0	1 (<0.1)
血中乳酸脱水素酵素増加	0	1 (0.2)	0	0	1 (<0.1)
血中カリウム減少	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血圧上昇	0	0	0
血中トリグリセリド異常	0	0	0
血中トリグリセリド増加	0	2 (1.6)	1 (0.1)
血中尿素増加	0	0	0
尿中血陽性	0	0	0
クロストリジウム検査陽性	0	0	0
凝固時間延長	0	0	1 (0.1)
尿中結晶陽性	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血圧上昇	0	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.1)
血中トリグリセリド異常	0	0	1 (0.2)	0	1 (<0.1)
血中トリグリセリド増加	0	0	1 (0.2)	1 (0.2)	5 (0.2)
血中尿素増加	0	0	1 (0.2)	0	1 (<0.1)
尿中血陽性	0	0	0	2 (0.3)	2 (<0.1)
クロストリジウム検査陽性	0	0	1 (0.2)	0	1 (<0.1)
凝固時間延長	0	0	0	0	1 (<0.1)
尿中結晶陽性	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
心電図再分極異常	0	0	1 (0.1)
γ-グルタミルトランスフェラーゼ増加	2 (1.5)	1 (0.8)	1 (0.1)
糸球体濾過率減少	0	0	0
顆粒球数減少	0	0	0
握力低下	0	0	0
ヘマトクリット減少	0	0	0
ヘモグロビン減少	0	0	2 (0.3)
肝酵素上昇	0	0	5 (0.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
心電図再分極異常	0	0	0	0	1 (<0.1)
γ-グルタミルトランスフェラーゼ増加	0	4 (0.8)	2 (0.3)	3 (0.5)	9 (0.4)
糸球体濾過率減少	1 (4.2)	1 (0.2)	1 (0.2)	0	2 (<0.1)
顆粒球数減少	0	0	0	1 (0.2)	1 (<0.1)
握力低下	0	0	1 (0.2)	0	1 (<0.1)
ヘマトクリット減少	0	0	1 (0.2)	0	1 (<0.1)
ヘモグロビン減少	0	2 (0.4)	1 (0.2)	4 (0.7)	8 (0.3)
肝酵素上昇	4 (16.6)	1 (0.2)	3 (0.5)	3 (0.5)	16 (0.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
B型肝炎DNA測定陽性	1 (0.8)	0	0
高比重リポ蛋白増加	0	0	0
臨床検査異常	0	0	1 (0.1)
肝機能検査異常	0	1 (0.8)	0
肝機能検査値上昇	1 (0.8)	0	1 (0.1)
低比重リポ蛋白減少	0	0	0
低比重リポ蛋白増加	0	1 (0.8)	0
リンパ球数減少	1 (0.8)	0	6 (0.9)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
B型肝炎DNA測定陽性	0	0	0	1 (0.2)	1 (<0.1)
高比重リポ蛋白増加	0	0	3 (0.5)	3 (0.5)	6 (0.3)
臨床検査異常	0	0	0	0	1 (<0.1)
肝機能検査異常	0	0	0	0	1 (<0.1)
肝機能検査値上昇	0	0	0	2 (0.3)	3 (0.1)
低比重リポ蛋白減少	0	0	1 (0.2)	0	1 (<0.1)
低比重リポ蛋白増加	0	0	1 (0.2)	5 (0.8)	7 (0.3)
リンパ球数減少	0	4 (0.8)	15 (2.4)	8 (1.4)	31 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
リンパ球数増加	0	0	0
リンパ球百分率減少	0	0	0
平均赤血球容積異常	0	0	0
平均赤血球容積増加	0	0	0
単球数増加	0	0	0
好中球数減少	0	0	5 (0.7)
好中球数増加	1 (0.8)	0	2 (0.3)
好中球百分率増加	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
リンパ球数増加	0	2 (0.4)	1 (0.2)	4 (0.7)	6 (0.3)
リンパ球百分率減少	0	0	6 (1.0)	1 (0.2)	7 (0.3)
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)	0	1 (<0.1)
単球数増加	0	0	1 (0.2)	0	1 (<0.1)
好中球数減少	4 (16.6)	17 (3.6)	19 (3.1)	21 (3.5)	63 (2.7)
好中球数増加	0	2 (0.4)	3 (0.5)	3 (0.5)	8 (0.3)
好中球百分率増加	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血小板数減少	0	0	1 (0.1)
血小板数増加	0	0	0
総蛋白増加	0	0	0
尿蛋白	0	0	0
尿中蛋白陽性	1 (0.8)	0	0
赤血球数減少	0	0	0
網状赤血球数減少	0	0	0
網状赤血球数増加	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血小板数減少	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
血小板数増加	0	0	0	3 (0.5)	3 (0.1)
総蛋白増加	0	0	0	1 (0.2)	1 (<0.1)
尿蛋白	0	1 (0.2)	0	0	1 (<0.1)
尿中蛋白陽性	0	1 (0.2)	1 (0.2)	2 (0.3)	3 (0.1)
赤血球数減少	0	0	2 (0.3)	3 (0.5)	5 (0.2)
網状赤血球数減少	0	0	1 (0.2)	0	1 (<0.1)
網状赤血球数増加	0	0	1 (0.2)	0	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
トランスアミナーゼ上昇	0	0	0
尿中ケトン体陽性	0	0	0
尿中白血球エステラーゼ陽性	0	0	1 (0.1)
体重増加	0	0	2 (0.3)
白血球数減少	3 (2.3)	0	5 (0.7)
白血球数増加	1 (0.8)	0	0
尿中白血球陽性	0	0	2 (0.3)
代謝および栄養障害	4 (3.0)	1 (0.8)	9 (1.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
トランスアミナーゼ上昇	0	0	3 (0.5)	0	3 (0.1)
尿中ケトン体陽性	0	0	0	1 (0.2)	1 (<0.1)
尿中白血球エステラーゼ陽性	0	0	2 (0.3)	0	3 (0.1)
体重増加	0	1 (0.2)	0	2 (0.3)	4 (0.2)
白血球数減少	2 (8.3)	15 (3.1)	13 (2.1)	13 (2.2)	45 (1.9)
白血球数増加	0	0	1 (0.2)	0	1 (<0.1)
尿中白血球陽性	0	1 (0.2)	0	1 (0.2)	4 (0.2)
代謝および栄養障害	0	12 (2.5)	17 (2.7)	10 (1.7)	48 (2.0)

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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
食欲減退	0	1 (0.8)	0
脂質異常症	0	0	1 (0.1)
痛風	0	0	0
高コレステロール血症	0	0	4 (0.6)
高血糖	3 (2.3)	0	1 (0.1)
高リパーゼ血症	0	0	0
高脂血症	0	0	2 (0.3)
高尿酸血症	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
食欲減退	0	1 (0.2)	0	0	2 (<0.1)
脂質異常症	0	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.2)
痛風	0	1 (0.2)	0	0	1 (<0.1)
高コレステロール血症	0	4 (0.8)	4 (0.6)	3 (0.5)	15 (0.6)
高血糖	0	0	6 (1.0)	1 (0.2)	8 (0.3)
高リパーゼ血症	0	1 (0.2)	0	0	0
高脂血症	0	0	5 (0.8)	2 (0.3)	9 (0.4)
高尿酸血症	0	0	0	1 (0.2)	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
低ナトリウム血症	0	0	0
低リン酸血症	1 (0.8)	0	1 (0.1)
低蛋白血症	0	0	0
食欲亢進	0	0	0
肥満	0	0	0
筋骨格系および結合組織障害	12 (9.1)	4 (3.2)	20 (2.9)
関節痛	2 (1.5)	1 (0.8)	9 (1.3)
関節炎	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
低ナトリウム血症	0	1 (0.2)	0	0	1 (<0.1)
低リン酸血症	0	1 (0.2)	0	2 (0.3)	4 (0.2)
低蛋白血症	0	1 (0.2)	0	0	1 (<0.1)
食欲亢進	0	1 (0.2)	0	0	1 (<0.1)
肥満	0	0	1 (0.2)	0	1 (<0.1)
筋骨格系および結合組織障害	3 (12.5)	30 (6.3)	15 (2.4)	29 (4.9)	86 (3.7)
関節痛	1 (4.2)	7 (1.5)	3 (0.5)	12 (2.0)	29 (1.2)
関節炎	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
関節障害	0	0	2 (0.3)
背部痛	1 (0.8)	1 (0.8)	1 (0.1)
骨痛	0	0	0
指炎	0	0	0
四肢拘縮	0	0	0
関節弛緩	0	0	0
関節ロック	0	0	0
筋拘縮	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
関節障害	0	3 (0.6)	1 (0.2)	1 (0.2)	5 (0.2)
背部痛	0	3 (0.6)	2 (0.3)	1 (0.2)	6 (0.3)
骨痛	0	0	0	1 (0.2)	1 (<0.1)
指炎	0	1 (0.2)	0	0	1 (<0.1)
四肢拘縮	0	0	1 (0.2)	0	1 (<0.1)
関節弛緩	0	0	0	1 (0.2)	1 (<0.1)
関節ロック	0	0	0	2 (0.3)	2 (<0.1)
筋拘縮	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
筋痙縮	4 (3.0)	0	1 (0.1)
筋緊張	0	0	0
筋骨格系胸痛	0	0	0
筋骨格痛	0	0	0
筋骨格硬直	0	0	1 (0.1)
筋肉痛	2 (1.5)	0	4 (0.6)
頚部痛	0	0	0
四肢痛	2 (1.5)	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
筋痙縮	1 (4.2)	2 (0.4)	1 (0.2)	1 (0.2)	6 (0.3)
筋緊張	1 (4.2)	0	0	0	1 (<0.1)
筋骨格系胸痛	0	4 (0.8)	0	0	2 (<0.1)
筋骨格痛	0	2 (0.4)	1 (0.2)	0	2 (<0.1)
筋骨格硬直	0	0	0	1 (0.2)	2 (<0.1)
筋肉痛	0	3 (0.6)	2 (0.3)	4 (0.7)	11 (0.5)
頚部痛	0	0	1 (0.2)	0	1 (<0.1)
四肢痛	0	2 (0.4)	1 (0.2)	3 (0.5)	7 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
顎痛	0	0	1 (0.1)
関節周囲炎	0	0	0
足底筋膜炎	0	0	0
横紋筋融解症	0	0	0
関節リウマチ	0	1 (0.8)	0
仙腸骨炎	1 (0.8)	0	0
顎関節症候群	0	0	0
腱炎	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
顎痛	0	0	0	0	1 (<0.1)
関節周囲炎	0	2 (0.4)	0	0	2 (<0.1)
足底筋膜炎	0	0	0	1 (0.2)	1 (<0.1)
横紋筋融解症	0	0	1 (0.2)	0	1 (<0.1)
関節リウマチ	0	0	0	0	0
仙腸骨炎	0	0	0	0	0
顎関節症候群	0	0	0	1 (0.2)	1 (<0.1)
腱炎	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	3 (2.4)	3 (0.4)
血管肉腫	0	0	0
基底細胞癌	0	2 (1.6)	1 (0.1)
ボーエン病	0	1 (0.8)	0
線維性組織球腫	0	0	0
浸潤性乳癌	0	0	0
皮膚乳頭腫	0	0	1 (0.1)
皮膚有棘細胞癌	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	3 (0.6)	4 (0.6)	5 (0.8)	17 (0.7)
血管肉腫	0	1 (0.2)	0	0	1 (<0.1)
基底細胞癌	0	0	0	3 (0.5)	6 (0.3)
ボーエン病	0	0	0	1 (0.2)	2 (<0.1)
線維性組織球腫	0	0	0	1 (0.2)	1 (<0.1)
浸潤性乳癌	0	1 (0.2)	0	0	0
皮膚乳頭腫	0	0	4 (0.6)	0	5 (0.2)
皮膚有棘細胞癌	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
舌扁平上皮癌	0	0	1 (0.1)
神経系障害	10 (7.6)	3 (2.4)	14 (2.0)
灼熱感	0	0	0
脳虚血	0	0	0
頚髄圧迫	0	0	0
注意力障害	0	0	0
浮動性めまい	0	0	1 (0.1)
構語障害	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
舌扁平上皮癌	0	0	0	0	1 (<0.1)
神経系障害	6 (24.9)	12 (2.5)	26 (4.2)	22 (3.7)	74 (3.1)
灼熱感	1 (4.2)	0	1 (0.2)	0	2 (<0.1)
脳虚血	0	0	2 (0.3)	0	2 (<0.1)
頚髄圧迫	0	0	0	1 (0.2)	1 (<0.1)
注意力障害	0	0	1 (0.2)	0	1 (<0.1)
浮動性めまい	0	2 (0.4)	4 (0.6)	6 (1.0)	12 (0.5)
構語障害	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
頭痛	8 (6.1)	3 (2.4)	10 (1.4)
知覚過敏	0	0	1 (0.1)
感覚鈍麻	0	0	0
記憶障害	0	0	0
片頭痛	2 (1.5)	0	1 (0.1)
脊髄症	0	0	0
末梢性ニューロパチー	0	0	0
錯感覚	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
頭痛	3 (12.5)	8 (1.7)	14 (2.2)	7 (1.2)	37 (1.6)
知覚過敏	0	0	0	0	1 (<0.1)
感覚鈍麻	0	0	1 (0.2)	2 (0.3)	3 (0.1)
記憶障害	0	0	0	1 (0.2)	1 (<0.1)
片頭痛	0	0	2 (0.3)	1 (0.2)	4 (0.2)
脊髄症	0	0	0	1 (0.2)	1 (<0.1)
末梢性ニューロパチー	1 (4.2)	0	0	0	1 (<0.1)
錯感覚	0	1 (0.2)	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
ヘルペス後神経痛	0	0	0
会話障害	0	0	0
失神	0	0	0
視野欠損	0	0	0
精神障害	3 (2.3)	2 (1.6)	3 (0.4)
不安	0	1 (0.8)	0
抑うつ気分	0	0	1 (0.1)
うつ病	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
ヘルペス後神経痛	1 (4.2)	0	0	1 (0.2)	2 (<0.1)
会話障害	0	0	1 (0.2)	0	1 (<0.1)
失神	0	1 (0.2)	0	0	1 (<0.1)
視野欠損	0	0	0	1 (0.2)	1 (<0.1)
精神障害	1 (4.2)	5 (1.0)	1 (0.2)	6 (1.0)	15 (0.6)
不安	0	2 (0.4)	1 (0.2)	0	3 (0.1)
抑うつ気分	0	0	0	0	1 (<0.1)
うつ病	0	0	0	2 (0.3)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
精神障害 (Cont.)			
不眠症	1 (0.8)	0	1 (0.1)
易刺激性	0	1 (0.8)	1 (0.1)
リビドー減退	0	0	0
睡眠障害	1 (0.8)	0	0
腎および尿路障害	2 (1.5)	0	11 (1.6)
急性腎障害	0	0	0
慢性腎臓病	0	0	0
出血性膀胱炎	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)					
不眠症	1 (4.2)	1 (0.2)	0	4 (0.7)	7 (0.3)
易刺激性	0	0	0	0	1 (<0.1)
リビドー減退	0	1 (0.2)	0	0	1 (<0.1)
睡眠障害	0	1 (0.2)	0	0	0
腎および尿路障害	2 (8.3)	11 (2.3)	5 (0.8)	8 (1.4)	33 (1.4)
急性腎障害	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
慢性腎臓病	1 (4.2)	0	0	1 (0.2)	2 (<0.1)
出血性膀胱炎	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
排尿困難	0	0	1 (0.1)
血尿	0	0	1 (0.1)
水腎症	0	0	0
ケトン尿	0	0	0
白血球尿	0	0	0
尿意切迫	0	0	1 (0.1)
腎結石症	0	0	1 (0.1)
頻尿	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
排尿困難	0	4 (0.8)	0	2 (0.3)	7 (0.3)
血尿	0	0	1 (0.2)	0	2 (<0.1)
水腎症	0	1 (0.2)	0	0	0
ケトン尿	0	1 (0.2)	0	0	0
白血球尿	1 (4.2)	0	0	0	1 (<0.1)
尿意切迫	0	0	0	0	1 (<0.1)
腎結石症	0	0	0	0	1 (<0.1)
頻尿	0	1 (0.2)	0	0	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
蛋白尿	2 (1.5)	0	2 (0.3)
腎仙痛	0	0	1 (0.1)
腎機能障害	0	0	1 (0.1)
腎臓痛	0	0	1 (0.1)
生殖系および乳房障害	0	1 (0.8)	4 (0.6)
バルトリン嚢腫	0	0	0
良性前立腺肥大症	0	0	1 (0.1)
勃起不全	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
蛋白尿	0	4 (0.8)	1 (0.2)	3 (0.5)	8 (0.3)
腎仙痛	0	0	0	1 (0.2)	2 (<0.1)
腎機能障害	0	0	2 (0.3)	0	3 (0.1)
腎臓痛	0	0	0	0	1 (<0.1)
生殖系および乳房障害	0	5 (1.0)	2 (0.3)	6 (1.0)	16 (0.7)
バルトリン嚢腫	0	1 (0.2)	0	0	0
良性前立腺肥大症	0	0	0	1 (0.2)	2 (<0.1)
勃起不全	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
性器びらん	0	0	1 (0.1)
不規則月経	0	0	1 (0.1)
月経前頭痛	0	0	0
前立腺腫瘤	0	0	0
前立腺炎	0	1 (0.8)	1 (0.1)
精液変色	0	0	0
腟分泌物	0	0	0
外陰腟そう痒症	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
性器びらん	0	0	0	0	1 (<0.1)
不規則月経	0	0	0	1 (0.2)	2 (<0.1)
月経前頭痛	0	0	0	1 (0.2)	1 (<0.1)
前立腺腫瘤	0	0	0	1 (0.2)	1 (<0.1)
前立腺炎	0	1 (0.2)	0	0	3 (0.1)
精液変色	0	1 (0.2)	0	2 (0.3)	3 (0.1)
腟分泌物	0	0	1 (0.2)	0	1 (<0.1)
外陰腟そう痒症	0	2 (0.4)	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害	4 (3.0)	1 (0.8)	17 (2.4)
気管支拡張症	0	0	0
咳嗽	0	0	4 (0.6)
横隔膜痛	1 (0.8)	0	0
呼吸困難	0	0	0
労作性呼吸困難	0	0	0
鼻出血	0	0	0
上気道分泌増加	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害	3 (12.5)	15 (3.1)	12 (1.9)	18 (3.0)	59 (2.5)
気管支拡張症	0	1 (0.2)	0	0	0
咳嗽	1 (4.2)	2 (0.4)	4 (0.6)	2 (0.3)	13 (0.6)
横隔膜痛	0	0	0	0	0
呼吸困難	1 (4.2)	0	0	0	1 (<0.1)
労作性呼吸困難	0	0	0	1 (0.2)	1 (<0.1)
鼻出血	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
上気道分泌増加	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
間質性肺疾患	0	0	0
鼻閉	1 (0.8)	0	3 (0.4)
鼻中隔穿孔	0	0	1 (0.1)
非感染性気管支炎	0	0	0
口腔咽頭痛	0	1 (0.8)	6 (0.9)
胸水	0	0	0
肺臓炎	1 (0.8)	0	0
湿性咳嗽	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
間質性肺疾患	0	1 (0.2)	0	0	0
鼻閉	0	1 (0.2)	0	2 (0.3)	5 (0.2)
鼻中隔穿孔	0	0	0	0	1 (<0.1)
非感染性気管支炎	0	0	0	1 (0.2)	1 (<0.1)
口腔咽頭痛	0	4 (0.8)	3 (0.5)	2 (0.3)	13 (0.6)
胸水	0	1 (0.2)	0	0	1 (<0.1)
肺臓炎	0	0	0	0	0
湿性咳嗽	0	0	1 (0.2)	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
肺塞栓症	1 (0.8)	0	1 (0.1)
肺腫瘤	0	0	0
気道うっ血	0	0	0
アレルギー性鼻炎	0	0	1 (0.1)
鼻漏	0	0	0
副鼻腔うっ血	0	0	0
副鼻腔障害	0	0	0
上気道の炎症	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
肺塞栓症	1 (4.2)	0	1 (0.2)	1 (0.2)	4 (0.2)
肺腫瘤	0	1 (0.2)	0	0	1 (<0.1)
気道うっ血	0	1 (0.2)	0	0	1 (<0.1)
アレルギー性鼻炎	0	0	0	0	1 (<0.1)
鼻漏	0	0	0	1 (0.2)	1 (<0.1)
副鼻腔うっ血	0	0	2 (0.3)	4 (0.7)	6 (0.3)
副鼻腔障害	0	0	0	1 (0.2)	1 (<0.1)
上気道の炎症	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
上気道咳症候群	0	0	1 (0.1)
皮膚および皮下組織障害	12 (9.1)	12 (9.6)	37 (5.3)
ざ瘡	2 (1.5)	1 (0.8)	7 (1.0)
嚢胞性ざ瘡	0	0	0
光線角化症	0	0	0
脱毛症	0	1 (0.8)	6 (0.9)
水疱	0	0	0
皮膚炎	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
上気道咳症候群	0	1 (0.2)	0	1 (0.2)	3 (0.1)
皮膚および皮下組織障害	10 (41.5)	64 (13.4)	64 (10.3)	72 (12.2)	225 (9.6)
ざ瘡	3 (12.5)	7 (1.5)	17 (2.7)	20 (3.4)	53 (2.3)
嚢胞性ざ瘡	0	0	1 (0.2)	0	1 (<0.1)
光線角化症	0	1 (0.2)	0	1 (0.2)	2 (<0.1)
脱毛症	1 (4.2)	2 (0.4)	4 (0.6)	5 (0.8)	19 (0.8)
水疱	0	0	0	1 (0.2)	1 (<0.1)
皮膚炎	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
ざ瘡様皮膚炎	0	0	2 (0.3)
アレルギー性皮膚炎	0	0	0
アトピー性皮膚炎	0	0	1 (0.1)
接触皮膚炎	0	0	0
剥脱性皮膚炎	0	0	0
皮膚症	0	0	0
皮膚乾燥	0	2 (1.6)	1 (0.1)
異汗性湿疹	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
ざ瘡様皮膚炎	0	0	1 (0.2)	2 (0.3)	5 (0.2)
アレルギー性皮膚炎	0	0	0	1 (0.2)	1 (<0.1)
アトピー性皮膚炎	0	2 (0.4)	0	0	2 (<0.1)
接触皮膚炎	0	0	1 (0.2)	0	1 (<0.1)
剥脱性皮膚炎	0	0	1 (0.2)	0	1 (<0.1)
皮膚症	0	1 (0.2)	0	0	1 (<0.1)
皮膚乾燥	0	2 (0.4)	1 (0.2)	0	3 (0.1)
異汗性湿疹	0	2 (0.4)	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
斑状出血	0	0	0
湿疹	0	0	0
紅斑	1 (0.8)	0	1 (0.1)
環状紅斑	0	0	1 (0.1)
結節性紅斑	0	0	0
多汗症	0	0	0
過角化	0	0	0
多毛症	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
斑状出血	0	0	0	1 (0.2)	1 (<0.1)
湿疹	1 (4.2)	3 (0.6)	0	1 (0.2)	3 (0.1)
紅斑	0	3 (0.6)	2 (0.3)	4 (0.7)	7 (0.3)
環状紅斑	0	0	0	0	1 (<0.1)
結節性紅斑	0	1 (0.2)	0	0	0
多汗症	0	1 (0.2)	0	0	1 (<0.1)
過角化	0	1 (0.2)	0	0	1 (<0.1)
多毛症	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
間擦疹	0	0	0
毛孔性角化症	0	0	0
神経皮膚炎	0	0	0
寝汗	0	0	0
爪破損	0	0	0
皮膚疼痛	0	0	0
脂肪織炎	0	0	0
丘疹	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
間擦疹	0	0	1 (0.2)	0	1 (<0.1)
毛孔性角化症	0	1 (0.2)	0	0	1 (<0.1)
神経皮膚炎	0	1 (0.2)	0	0	0
寝汗	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
爪破損	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
皮膚疼痛	1 (4.2)	0	0	1 (0.2)	2 (<0.1)
脂肪織炎	0	0	1 (0.2)	0	1 (<0.1)
丘疹	0	1 (0.2)	2 (0.3)	3 (0.5)	7 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
口囲皮膚炎	0	0	0
光線性皮膚症	0	0	0
光線過敏性反応	0	0	0
そう痒症	4 (3.0)	2 (1.6)	0
壊疽性膿皮症	0	0	0
発疹	3 (2.3)	2 (1.6)	11 (1.6)
紅斑性皮疹	1 (0.8)	0	2 (0.3)
毛孔性皮疹	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
口囲皮膚炎	0	0	1 (0.2)	0	1 (<0.1)
光線性皮膚症	0	1 (0.2)	0	0	0
光線過敏性反応	0	1 (0.2)	1 (0.2)	0	2 (<0.1)
そう痒症	0	5 (1.0)	3 (0.5)	3 (0.5)	8 (0.3)
壊疽性膿皮症	1 (4.2)	0	0	0	1 (<0.1)
発疹	2 (8.3)	11 (2.3)	9 (1.4)	14 (2.4)	46 (2.0)
紅斑性皮疹	0	0	2 (0.3)	0	4 (0.2)
毛孔性皮疹	1 (4.2)	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
斑状皮疹	0	0	0
斑状丘疹状皮疹	0	2 (1.6)	0
丘疹性皮疹	0	0	1 (0.1)
そう痒性皮疹	0	0	1 (0.1)
酒さ	1 (0.8)	0	0
脂漏性皮膚炎	0	0	1 (0.1)
皮膚変色	0	0	0
皮膚びらん	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
斑状皮疹	0	0	2 (0.3)	1 (0.2)	3 (0.1)
斑状丘疹状皮疹	0	1 (0.2)	2 (0.3)	4 (0.7)	6 (0.3)
丘疹性皮疹	0	3 (0.6)	1 (0.2)	0	5 (0.2)
そう痒性皮疹	0	0	0	0	1 (<0.1)
酒さ	0	2 (0.4)	3 (0.5)	0	5 (0.2)
脂漏性皮膚炎	0	1 (0.2)	0	2 (0.3)	4 (0.2)
皮膚変色	0	0	1 (0.2)	0	1 (<0.1)
皮膚びらん	0	1 (0.2)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
皮膚剥脱	0	0	0
皮膚病変	0	0	1 (0.1)
皮膚線条	0	0	0
皮膚潰瘍	0	0	0
日光皮膚炎	0	1 (0.8)	0
毛細血管拡張症	0	0	0
蕁麻疹	0	0	0
血管障害	3 (2.3)	1 (0.8)	4 (0.6)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
皮膚剥脱	0	2 (0.4)	1 (0.2)	1 (0.2)	3 (0.1)
皮膚病変	0	2 (0.4)	2 (0.3)	3 (0.5)	8 (0.3)
皮膚線条	0	0	1 (0.2)	0	1 (<0.1)
皮膚潰瘍	0	0	0	3 (0.5)	3 (0.1)
日光皮膚炎	0	0	0	0	0
毛細血管拡張症	0	0	1 (0.2)	0	1 (<0.1)
蕁麻疹	0	2 (0.4)	0	0	0
血管障害	1 (4.2)	6 (1.3)	8 (1.3)	6 (1.0)	24 (1.0)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血管障害 (Cont.)			
深部静脈血栓症	0	1 (0.8)	1 (0.1)
潮紅	0	0	0
血腫	0	0	1 (0.1)
ほてり	0	0	0
高血圧	2 (1.5)	0	1 (0.1)
高血圧クリーゼ	0	0	1 (0.1)
蒼白	0	0	0
骨盤静脈血栓症	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害 (Cont.)					
深部静脈血栓症	1 (4.2)	0	0	0	3 (0.1)
潮紅	0	0	1 (0.2)	0	1 (<0.1)
血腫	0	0	0	0	1 (<0.1)
ほてり	0	1 (0.2)	0	0	1 (<0.1)
高血圧	0	3 (0.6)	4 (0.6)	6 (1.0)	13 (0.6)
高血圧クリーゼ	0	0	0	0	1 (<0.1)
蒼白	0	0	1 (0.2)	0	1 (<0.1)
骨盤静脈血栓症	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
血管障害 (Cont.)			
レイノー現象	0	0	0
血栓性静脈炎	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 4.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to 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=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
血管障害 (Cont.)					
レイノー現象	0	0	1 (0.2)	0	1 (<0.1)
血栓性静脈炎	0	1 (0.2)	0	0	1 (<0.1)
静脈血栓症	0	1 (0.2)	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

表 2.7.4.7-105.

[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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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	23 (9.4) [9.3]	14 (5.6) [5.6]	20 (8.0) [8.0]	27 (9.5) [9.5]	35 (12.0) [12.0]
血液およびリンパ系障害	2 (0.8) [0.8]	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]
貧血	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
鉄欠乏性貧血	1 (0.4) [0.4]	0	0	0	0
リンパ球減少症	0	0	0	0	1 (0.3) [0.3]
好中球減少症	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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	1 (0.4) [0.4]	0	2 (0.8) [0.8]	1 (0.4) [0.4]	2 (0.7) [0.7]
急性心筋梗塞	1 (0.4) [0.4]	0	0	0	0
完全房室ブロック	0	0	0	1 (0.4) [0.4]	0
慢性左室不全	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
上室性頻脈	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
眼障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
白内障	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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	11 (4.5) [4.5]	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.1) [1.1]	4 (1.4) [1.4]
腹部腫瘤	1 (0.4) [0.4]	0	0	0	0
痔瘻	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
潰瘍性大腸炎	9 (3.7) [3.6]	1 (0.4) [0.4]	1 (0.4) [0.4]	3 (1.1) [1.1]	2 (0.7) [0.7]
大腸穿孔	1 (0.4) [0.4]	0	0	0	0
膵炎	1 (0.4) [0.4]	0	0	0	0
埋伏歯	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0
発熱	1 (0.4) [0.4]	0	0	1 (0.4) [0.4]	0
肝胆道系障害	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
肝障害	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
感染症および寄生虫症	4 (1.6) [1.6]	7 (2.8) [2.8]	7 (2.8) [2.8]	12 (4.2) [4.2]	13 (4.5) [4.5]
腹部膿瘍	1 (0.4) [0.4]	0	0	0	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	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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.)					
虫垂炎	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]
乳房膿瘍	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
感染性滑液包炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
蜂巣炎	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	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
COVID-19	0	0	0	2 (0.7) [0.7]	2 (0.7) [0.7]
COVID-19肺炎	0	0	2 (0.8) [0.8]	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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.)					
単純ヘルペス	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
帯状疱疹	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.3]
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
インフルエンザ	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
大腸感染	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
レンサ球菌性咽頭炎	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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.)					
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	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
クリプトコッカス性肺炎	0	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
傷害、中毒および処置合併症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
肺挫傷	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	3 (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	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
血中クレアチンホスホキナーゼ増加	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肝機能検査値上昇	0	0	0	0	1 (0.3) [0.3]
リンパ球数減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
リンパ球百分率減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
好中球数減少	1 (0.4) [0.4]	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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	0	0	0	1 (0.4) [0.3]	0
過少体重	0	0	0	1 (0.4) [0.3]	0
筋骨格系および結合組織障害	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	1 (0.3) [0.4]
関節炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
滑液包炎	0	0	0	0	1 (0.3) [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）	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.4]	3 (1.0) [1.0]
結腸腺癌	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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.)					
小細胞癌	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
子宮頚部扁平上皮癌	0	0	0	0	1 (0.3) [0.4]
神経系障害	1 (0.4) [0.4]	0	1 (0.4) [0.4]	1 (0.4) [0.3]	3 (1.0) [1.0]
脳損傷	0	0	0	1 (0.4) [0.3]	0
脳血管発作	0	0	0	0	1 (0.3) [0.3]
頭痛	1 (0.4) [0.4]	0	0	0	0
片頭痛	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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.)					
坐骨神経痛	0	0	0	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]
精神障害	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
不安	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
うつ病	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
精神障害	1 (0.4) [0.4]	0	0	0	0
自殺念慮	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
子宮頚部上皮異形成	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.4]
呼吸器、胸郭および縦隔障害	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	2 (0.7) [0.7]
急性呼吸不全	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
肺塞栓症	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	2 (0.7) [0.7]
皮膚および皮下組織障害	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
脱毛症	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 3.3.8

Number and Percentage of Subjects with Treatment-Emergent Severe 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.)					
結節性紅斑	1 (0.4) [0.4]	0	0	0	0
外科および内科処置	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
人工流産	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
血管障害	0	0	0	1 (0.4) [0.4]	1 (0.3) [0.3]
深部静脈血栓症	0	0	0	0	1 (0.3) [0.3]
静脈血栓症	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]

表 2.7.4.7-106.

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TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
Any adverse event	51 (38.8)	5 (4.0)	82 (11.7)
血液およびリンパ系障害	1 (0.8)	0	1 (0.1)
貧血	1 (0.8)	0	1 (0.1)
鉄欠乏性貧血	0	0	0
リンパ球減少症	0	0	0
好中球減少症	0	0	0
心臓障害	0	0	0
急性心筋梗塞	0	0	0
心房細動	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
Any adverse event	20 (83.1)	66 (13.8)	61 (9.8)	64 (10.8)	265 (11.3)
血液およびリンパ系障害	1 (4.2)	6 (1.3)	0	4 (0.7)	10 (0.4)
貧血	1 (4.2)	0	0	1 (0.2)	3 (0.1)
鉄欠乏性貧血	0	1 (0.2)	0	0	0
リンパ球減少症	0	2 (0.4)	0	2 (0.3)	4 (0.2)
好中球減少症	0	3 (0.6)	0	1 (0.2)	3 (0.1)
心臓障害	0	4 (0.8)	2 (0.3)	2 (0.3)	7 (0.3)
急性心筋梗塞	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
心房細動	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
心臓障害 (Cont.)			
完全房室ブロック	0	0	0
慢性左室不全	0	0	0
心嚢液貯留	0	0	0
心膜炎	0	0	0
上室性頻脈	0	0	0
耳および迷路障害	0	0	1 (0.1)
突発性難聴	0	0	1 (0.1)
眼障害	0	0	0
白内障	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
心臓障害 (Cont.)					
完全房室ブロック	0	0	1 (0.2)	0	1 (<0.1)
慢性左室不全	0	0	0	1 (0.2)	1 (<0.1)
心嚢液貯留	0	1 (0.2)	0	0	1 (<0.1)
心膜炎	0	1 (0.2)	0	0	1 (<0.1)
上室性頻脈	0	0	0	1 (0.2)	1 (<0.1)
耳および迷路障害	0	0	0	0	1 (<0.1)
突発性難聴	0	0	0	0	1 (<0.1)
眼障害	0	0	1 (0.2)	0	1 (<0.1)
白内障	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害	39 (29.7)	3 (2.4)	22 (3.1)
腹部腫瘤	0	0	0
腹痛	0	0	1 (0.1)
裂肛	0	0	1 (0.1)
痔瘻	0	0	0
肛門潰瘍	0	0	0
大腸炎	6 (4.6)	0	0
潰瘍性大腸炎	26 (19.8)	2 (1.6)	15 (2.1)
結腸異形成	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害	13 (54.0)	21 (4.4)	9 (1.4)	11 (1.9)	64 (2.7)
腹部腫瘤	0	1 (0.2)	0	0	0
腹痛	0	0	0	1 (0.2)	2 (<0.1)
裂肛	0	0	0	0	1 (<0.1)
痔瘻	0	0	0	2 (0.3)	2 (<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	10 (41.5)	17 (3.6)	8 (1.3)	6 (1.0)	47 (2.0)
結腸異形成	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
下痢	0	0	0
血性下痢	0	0	0
排便困難	1 (0.8)	0	0
大腿ヘルニア	0	0	0
鼓腸	1 (0.8)	0	0
食中毒	1 (0.8)	0	0
胃食道逆流性疾患	0	0	0
イレウス	0	0	1 (0.1)
腸閉塞	1 (0.8)	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
下痢	1 (4.2)	0	0	0	1 (<0.1)
血性下痢	1 (4.2)	0	0	0	1 (<0.1)
排便困難	0	0	0	0	0
大腿ヘルニア	0	1 (0.2)	0	0	1 (<0.1)
鼓腸	0	0	0	0	0
食中毒	0	0	0	0	0
胃食道逆流性疾患	0	0	1 (0.2)	0	1 (<0.1)
イレウス	0	0	0	0	1 (<0.1)
腸閉塞	0	0	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
大腸穿孔	1 (0.8)	0	1 (0.1)
大腸ポリープ	0	0	1 (0.1)
口腔内潰瘍形成	0	1 (0.8)	0
悪心	1 (0.8)	0	0
膵炎	0	0	0
直腸出血	0	0	1 (0.1)
埋伏歯	0	0	0
嘔吐	1 (0.8)	0	0
一般・全身障害および投与部位の状態	0	0	5 (0.7)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
胃腸障害 (Cont.)					
大腸穿孔	0	1 (0.2)	0	0	1 (<0.1)
大腸ポリープ	0	0	0	0	1 (<0.1)
口腔内潰瘍形成	0	0	0	0	0
悪心	0	0	0	0	0
膵炎	0	1 (0.2)	0	1 (0.2)	1 (<0.1)
直腸出血	0	0	0	0	1 (<0.1)
埋伏歯	0	0	0	1 (0.2)	1 (<0.1)
嘔吐	0	0	0	0	0
一般・全身障害および投与部位の状態	0	1 (0.2)	1 (0.2)	0	6 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
悪寒	0	0	1 (0.1)
疲労	0	0	1 (0.1)
疼痛	0	0	1 (0.1)
発熱	0	0	2 (0.3)
肝胆道系障害	0	0	0
胆嚢炎	0	0	0
肝障害	0	0	0
感染症および寄生虫症	5 (3.8)	1 (0.8)	19 (2.7)
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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
悪寒	0	0	0	0	1 (<0.1)
疲労	0	0	0	0	1 (<0.1)
疼痛	0	0	0	0	1 (<0.1)
発熱	0	1 (0.2)	1 (0.2)	0	3 (0.1)
肝胆道系障害	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
胆嚢炎	0	0	1 (0.2)	0	1 (<0.1)
肝障害	0	0	0	1 (0.2)	1 (<0.1)
感染症および寄生虫症	2 (8.3)	6 (1.3)	23 (3.7)	18 (3.0)	64 (2.7)
腹部膿瘍	0	1 (0.2)	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
急性心内膜炎	0	0	0
肛門膿瘍	0	0	0
虫垂炎	0	0	0
乳房膿瘍	0	0	0
感染性滑液包炎	0	0	0
COVID-19	0	0	0
COVID-19肺炎	0	0	2 (0.3)
蜂巣炎	3 (2.3)	0	0
感染性胆嚢炎	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
急性心内膜炎	0	1 (0.2)	0	0	0
肛門膿瘍	0	0	1 (0.2)	0	1 (<0.1)
虫垂炎	0	0	2 (0.3)	1 (0.2)	3 (0.1)
乳房膿瘍	0	0	1 (0.2)	0	1 (<0.1)
感染性滑液包炎	0	0	0	1 (0.2)	1 (<0.1)
COVID-19	0	0	3 (0.5)	2 (0.3)	5 (0.2)
COVID-19肺炎	0	1 (0.2)	2 (0.3)	6 (1.0)	11 (0.5)
蜂巣炎	0	0	1 (0.2)	0	1 (<0.1)
感染性胆嚢炎	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
クロストリジウム・ディフィシレ感染	0	0	2 (0.3)
サイトメガロウイルス感染	0	0	0
医療機器関連敗血症	0	0	0
大腸菌感染	0	0	1 (0.1)
大腸菌性敗血症	0	0	1 (0.1)
ノロウイルス性胃腸炎	0	0	0
消化管感染	0	0	0
単純ヘルペス	0	0	0
帯状疱疹	0	1 (0.8)	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
クロストリジウム・ディフィシレ感染	0	0	1 (0.2)	0	3 (0.1)
サイトメガロウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
医療機器関連敗血症	0	0	0	1 (0.2)	1 (<0.1)
大腸菌感染	0	0	0	0	1 (<0.1)
大腸菌性敗血症	0	0	0	0	1 (<0.1)
ノロウイルス性胃腸炎	1 (4.2)	0	0	0	1 (<0.1)
消化管感染	0	0	0	1 (0.2)	1 (<0.1)
単純ヘルペス	0	0	1 (0.2)	0	1 (<0.1)
帯状疱疹	1 (4.2)	1 (0.2)	2 (0.3)	1 (0.2)	5 (0.2)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
帯状疱疹性髄膜炎	0	0	0
耳帯状疱疹	0	0	0
インフルエンザ	0	0	0
大腸感染	0	0	0
レンサ球菌性咽頭炎	0	0	0
毛巣嚢胞	0	0	4 (0.6)
ニューモシスチス・イロベチイ肺炎	0	0	0
肺炎	0	0	2 (0.3)
細菌性肺炎	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
帯状疱疹性髄膜炎	0	0	0	1 (0.2)	1 (<0.1)
耳帯状疱疹	0	0	1 (0.2)	0	1 (<0.1)
インフルエンザ	0	0	1 (0.2)	0	1 (<0.1)
大腸感染	0	0	1 (0.2)	0	1 (<0.1)
レンサ球菌性咽頭炎	0	0	0	1 (0.2)	1 (<0.1)
毛巣嚢胞	0	0	0	0	4 (0.2)
ニューモシスチス・イロベチイ肺炎	0	1 (0.2)	0	0	0
肺炎	0	1 (0.2)	0	1 (0.2)	3 (0.1)
細菌性肺炎	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
クリプトコッカス性肺炎	0	0	0
肺炎球菌性肺炎	0	0	1 (0.1)
ウイルス性肺炎	0	0	1 (0.1)
処置後感染	1 (0.8)	0	0
直腸膿瘍	0	0	0
RSウイルス感染	0	0	0
敗血症	0	0	1 (0.1)
副鼻腔炎	1 (0.8)	0	0
上気道感染	0	0	1 (0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
クリプトコッカス性肺炎	0	0	0	2 (0.3)	2 (<0.1)
肺炎球菌性肺炎	0	0	0	0	1 (<0.1)
ウイルス性肺炎	0	0	0	0	1 (<0.1)
処置後感染	0	0	0	0	0
直腸膿瘍	0	0	1 (0.2)	0	1 (<0.1)
RSウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
敗血症	0	0	1 (0.2)	0	2 (<0.1)
副鼻腔炎	0	0	0	0	0
上気道感染	0	0	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
尿路性敗血症	0	0	2 (0.3)
傷害、中毒および処置合併症	1 (0.8)	0	5 (0.7)
腓骨骨折	0	0	0
股関節部骨折	1 (0.8)	0	0
企図的過量投与	0	0	0
靭帯捻挫	0	0	1 (0.1)
処置による腸管穿孔	0	0	1 (0.1)
肺挫傷	0	0	0
橈骨骨折	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
尿路性敗血症	0	0	0	0	2 (<0.1)
傷害、中毒および処置合併症	0	4 (0.8)	2 (0.3)	0	11 (0.5)
腓骨骨折	0	1 (0.2)	0	0	1 (<0.1)
股関節部骨折	0	0	0	0	0
企図的過量投与	0	1 (0.2)	0	0	1 (<0.1)
靭帯捻挫	0	0	0	0	1 (<0.1)
処置による腸管穿孔	0	0	0	0	1 (<0.1)
肺挫傷	0	0	1 (0.2)	0	1 (<0.1)
橈骨骨折	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
肋骨骨折	0	0	1 (0.1)
胸椎骨折	0	0	0
脛骨骨折	0	0	0
子宮穿孔	0	0	1 (0.1)
創傷	0	0	1 (0.1)
臨床検査	2 (1.5)	1 (0.8)	7 (1.0)
アミラーゼ増加	0	0	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
血中クレアチンホスホキナーゼ増加	1 (0.8)	1 (0.8)	2 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
肋骨骨折	0	0	0	0	1 (<0.1)
胸椎骨折	0	0	1 (0.2)	0	1 (<0.1)
脛骨骨折	0	1 (0.2)	0	0	1 (<0.1)
子宮穿孔	0	0	0	0	1 (<0.1)
創傷	0	0	0	0	1 (<0.1)
臨床検査	2 (8.3)	5 (1.0)	6 (1.0)	5 (0.8)	25 (1.1)
アミラーゼ増加	1 (4.2)	0	0	0	1 (<0.1)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	1 (0.2)	1 (<0.1)
血中クレアチンホスホキナーゼ増加	0	0	1 (0.2)	2 (0.3)	6 (0.3)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
臨床検査 (Cont.)			
血中リン減少	0	0	0
血中トリグリセリド増加	0	0	1 (0.1)
ヘモグロビン減少	1 (0.8)	0	2 (0.3)
肝酵素上昇	0	0	1 (0.1)
肝機能検査値上昇	0	0	0
リンパ球数減少	0	0	1 (0.1)
リンパ球百分率減少	0	0	0
好中球数減少	0	0	0
白血球数増加	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
臨床検査 (Cont.)					
血中リン減少	0	1 (0.2)	0	0	1 (<0.1)
血中トリグリセリド増加	0	0	0	0	1 (<0.1)
ヘモグロビン減少	0	0	1 (0.2)	0	3 (0.1)
肝酵素上昇	0	0	0	0	1 (<0.1)
肝機能検査値上昇	0	0	0	1 (0.2)	1 (<0.1)
リンパ球数減少	0	0	1 (0.2)	0	2 (<0.1)
リンパ球百分率減少	0	0	1 (0.2)	0	1 (<0.1)
好中球数減少	0	4 (0.8)	2 (0.3)	1 (0.2)	6 (0.3)
白血球数増加	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
代謝および栄養障害	2 (1.5)	0	1 (0.1)
脱水	0	0	0
高血糖	0	0	1 (0.1)
低アルブミン血症	1 (0.8)	0	0
低リン酸血症	1 (0.8)	0	0
過少体重	0	0	0
筋骨格系および結合組織障害	0	0	3 (0.4)
関節痛	0	0	1 (0.1)
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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
代謝および栄養障害	0	0	1 (0.2)	4 (0.7)	6 (0.3)
脱水	0	0	0	1 (0.2)	1 (<0.1)
高血糖	0	0	0	0	1 (<0.1)
低アルブミン血症	0	0	0	0	0
低リン酸血症	0	0	0	3 (0.5)	3 (0.1)
過少体重	0	0	1 (0.2)	0	1 (<0.1)
筋骨格系および結合組織障害	0	1 (0.2)	1 (0.2)	1 (0.2)	6 (0.3)
関節痛	0	0	0	0	1 (<0.1)
関節炎	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
滑液包炎	0	0	0
骨壊死	0	0	0
四肢痛	0	0	1 (0.1)
肩回旋筋腱板症候群	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	0	3 (0.4)
結腸腺癌	0	0	0
膵腺癌	0	0	1 (0.1)
血管肉腫	0	0	0
基底細胞癌	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
滑液包炎	0	0	0	1 (0.2)	1 (<0.1)
骨壊死	0	1 (0.2)	0	0	1 (<0.1)
四肢痛	0	0	0	0	1 (<0.1)
肩回旋筋腱板症候群	0	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	3 (0.6)	2 (0.3)	4 (0.7)	11 (0.5)
結腸腺癌	0	0	0	1 (0.2)	1 (<0.1)
膵腺癌	0	0	0	0	1 (<0.1)
血管肉腫	0	1 (0.2)	0	0	1 (<0.1)
基底細胞癌	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
乳癌	0	0	1 (0.1)
浸潤性乳癌	0	0	0
悪性黒色腫	0	0	1 (0.1)
小細胞癌	0	0	0
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
神経系障害	1 (0.8)	0	0
脳損傷	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
乳癌	0	0	0	0	1 (<0.1)
浸潤性乳癌	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
悪性黒色腫	0	0	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)
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	0	4 (0.8)	2 (0.3)	5 (0.8)	9 (0.4)
脳損傷	0	0	1 (0.2)	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
神経系障害 (Cont.)			
脳血管発作	0	0	0
頭痛	1 (0.8)	0	0
片頭痛	0	0	0
神経炎	0	0	0
坐骨神経痛	0	0	0
くも膜下出血	0	0	0
失神	0	0	0
精神障害	0	0	5 (0.7)
不安	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
神経系障害 (Cont.)					
脳血管発作	0	0	0	1 (0.2)	1 (<0.1)
頭痛	0	2 (0.4)	0	0	1 (<0.1)
片頭痛	0	1 (0.2)	1 (0.2)	0	1 (<0.1)
神経炎	0	0	0	1 (0.2)	1 (<0.1)
坐骨神経痛	0	0	0	2 (0.3)	2 (<0.1)
くも膜下出血	0	0	0	1 (0.2)	1 (<0.1)
失神	0	1 (0.2)	0	0	1 (<0.1)
精神障害	0	7 (1.5)	2 (0.3)	2 (0.3)	12 (0.5)
不安	0	2 (0.4)	0	1 (0.2)	2 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
精神障害 (Cont.)			
双極I型障害	0	0	0
うつ病	0	0	4 (0.6)
精神障害	0	0	0
自殺念慮	0	0	0
自殺企図	0	0	1 (0.1)
腎および尿路障害	0	0	5 (0.7)
出血性膀胱炎	0	0	1 (0.1)
排尿困難	0	0	0
腎結石症	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
精神障害 (Cont.)					
双極I型障害	0	0	1 (0.2)	0	1 (<0.1)
うつ病	0	2 (0.4)	1 (0.2)	1 (0.2)	7 (0.3)
精神障害	0	1 (0.2)	0	0	0
自殺念慮	0	2 (0.4)	0	0	1 (<0.1)
自殺企図	0	0	0	0	1 (<0.1)
腎および尿路障害	0	2 (0.4)	0	0	7 (0.3)
出血性膀胱炎	0	0	0	0	1 (<0.1)
排尿困難	0	1 (0.2)	0	0	1 (<0.1)
腎結石症	0	1 (0.2)	0	0	1 (<0.1)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
腎仙痛	0	0	1 (0.1)
尿管閉塞	0	0	1 (0.1)
尿管結石症	0	0	2 (0.3)
生殖系および乳房障害	0	0	0
子宮頚部上皮異形成	0	0	0
子宮頚部の炎症	0	0	0
呼吸器、胸郭および縦隔障害	0	0	2 (0.3)
急性呼吸不全	0	0	0
喘息	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
腎仙痛	0	0	0	0	1 (<0.1)
尿管閉塞	0	0	0	0	1 (<0.1)
尿管結石症	0	0	0	0	2 (<0.1)
生殖系および乳房障害	0	0	1 (0.2)	1 (0.2)	2 (<0.1)
子宮頚部上皮異形成	0	0	0	1 (0.2)	1 (<0.1)
子宮頚部の炎症	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 (0.2)	4 (0.6)	4 (0.7)	12 (0.5)
急性呼吸不全	0	0	0	1 (0.2)	1 (<0.1)
喘息	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
慢性閉塞性肺疾患	0	0	0
胸水	0	0	0
肺塞栓症	0	0	1 (0.1)
睡眠時無呼吸症候群	0	0	0
皮膚および皮下組織障害	0	0	1 (0.1)
ざ瘡	0	0	1 (0.1)
脱毛症	0	0	0
湿疹	0	0	0
多形紅斑	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
慢性閉塞性肺疾患	0	0	1 (0.2)	0	1 (<0.1)
胸水	0	1 (0.2)	0	0	1 (<0.1)
肺塞栓症	1 (4.2)	0	3 (0.5)	2 (0.3)	7 (0.3)
睡眠時無呼吸症候群	0	0	0	1 (0.2)	1 (<0.1)
皮膚および皮下組織障害	1 (4.2)	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.2)
ざ瘡	0	0	0	0	1 (<0.1)
脱毛症	0	0	0	1 (0.2)	1 (<0.1)
湿疹	0	0	1 (0.2)	0	1 (<0.1)
多形紅斑	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 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=131.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=125.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=285) (PYs=699.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
結節性紅斑	0	0	0
外科および内科処置	0	0	1 (0.1)
人工流産	0	0	1 (0.1)
血管障害	0	0	1 (0.1)
深部静脈血栓症	0	0	1 (0.1)
静脈血栓症	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part of induction. Subjects are further categorized by primary dose received during maintenance (or LTE).

Program Source Code: [redacted]

TABLE 2.4 4.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(All Treated [SUBJ] Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=478.5) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=622.4) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=591.7) Events (E/100 PYs)	 Any UPA (N=1308) (PYs=2350.2) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
結節性紅斑	0	1 (0.2)	0	0	0
外科および内科処置	0	0	1 (0.2)	0	2 (<0.1)
人工流産	0	0	1 (0.2)	0	2 (<0.1)
血管障害	0	0	1 (0.2)	1 (0.2)	3 (0.1)
深部静脈血栓症	0	0	0	1 (0.2)	2 (<0.1)
静脈血栓症	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]

表 2.7.4.7-107.

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

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=53.4)	(PYs=59.1)	(PYs=60.7)	(PYs=70.6)	(PYs=70.1)
	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 adverse event (AE)	382 (714.7) [644.8, 790.1]	275 (465.1) [411.7, 523.4]	318 (524.0) [468.0, 584.9]	323 (457.8) [409.2, 510.6]	362 (516.6) [464.8, 572.7]
COVID-19 infection related AE	4 (7.5) [2.0, 19.2]	4 (6.8) [1.8, 17.3]	0	5 (7.1) [2.3, 16.5]	1 (1.4) [0.0, 8.0]
Any serious AE	11 (20.6) [10.3, 36.8]	10 (16.9) [8.1, 31.1]	5 (8.2) [2.7, 19.2]	10 (14.2) [6.8, 26.1]	8 (11.4) [4.9, 22.5]
Any AE leading to discontinuation of study drug	13 (24.3) [13.0, 41.6]	0	5 (8.2) [2.7, 19.2]	0	7 (10.0) [4.0, 20.6]
Any severe AE	11 (20.6) [10.3, 36.8]	7 (11.8) [4.8, 24.4]	7 (11.5) [4.6, 23.8]	8 (11.3) [4.9, 22.3]	9 (12.8) [5.9, 24.4]
Any AE with reasonable possibility of being related to study drug$	113 (211.4) [174.2, 254.2]	85 (143.8) [114.8, 177.8]	117 (192.8) [159.5, 231.1]	96 (136.1) [110.2, 166.2]	134 (191.2) [160.2, 226.5]
Any AE leading to death	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. 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.

$ As assessed by investigator.

Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/53.4	0/59.1	0/60.7	0/70.6	0/70.1
Deaths occurring <= 30 days after last dose of study drug	0/53.4	0/59.1	0/60.7	0/70.6	0/70.1
Deaths occurring > 30 days after last dose of study drug	0/53.4	0/59.1	0/60.7	0/70.6	0/70.1
COVID-19 infection related deaths	0/53.4	0/59.1	0/60.7	0/70.6	0/70.1

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

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=35.0)	(PYs=52.2)	(PYs=55.6)	(PYs=66.2)	(PYs=63.8)
	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 adverse event (AE)	117 (334.0) [276.2, 400.3]	131 (250.9) [209.7, 297.7]	142 (255.5) [215.2, 301.2]	177 (267.5) [229.5, 309.9]	170 (266.4) [227.8, 309.6]
COVID-19 infection related AE	2 (5.7) [0.7, 20.6]	0	5 (9.0) [2.9, 21.0]	1 (1.5) [0.0, 8.4]	6 (9.4) [3.5, 20.5]
Any serious AE	9 (25.7) [11.7, 48.8]	9 (17.2) [7.9, 32.7]	7 (12.6) [5.1, 26.0]	11 (16.6) [8.3, 29.7]	9 (14.1) [6.4, 26.8]
Any AE leading to discontinuation of study drug	7 (20.0) [8.0, 41.2]	4 (7.7) [2.1, 19.6]	6 (10.8) [4.0, 23.5]	6 (9.1) [3.3, 19.7]	6 (9.4) [3.5, 20.5]
Any severe AE	7 (20.0) [8.0, 41.2]	5 (9.6) [3.1, 22.3]	7 (12.6) [5.1, 26.0]	9 (13.6) [6.2, 25.8]	7 (11.0) [4.4, 22.6]
Any AE with reasonable possibility of being related to study drug$	35 (99.9) [69.6, 139.0]	40 (76.6) [54.7, 104.3]	51 (91.8) [68.3, 120.7]	55 (83.1) [62.6, 108.2]	58 (90.9) [69.0, 117.5]
Any AE leading to death	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. 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.

$ As assessed by investigator.

Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/35.0	0/52.2	0/55.6	0/66.2	0/63.8
Deaths occurring <= 30 days after last dose of study drug	0/35.0	0/52.2	0/55.6	0/66.2	0/63.8
Deaths occurring > 30 days after last dose of study drug	0/35.0	0/52.2	0/55.6	0/66.2	0/63.8
COVID-19 infection related deaths	0/35.0	0/52.2	0/55.6	0/66.2	0/63.8

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. 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.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=119)	UPA 15 mg QD (N=196)	UPA 30 mg QD (N=216)	UPA 15 mg QD (N=253)	UPA 30 mg QD (N=249)
Subgroup: >= 6 - < 9 Month					
Exposure-adjusted event rate:	(PYs=26.1)	(PYs=46.5)	(PYs=52.8)	(PYs=60.3)	(PYs=60.9)
	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 adverse event (AE)	109 (417.5) [342.8, 503.6]	150 (322.5) [273.0, 378.4]	132 (249.8) [209.0, 296.3]	191 (316.7) [273.4, 364.9]	156 (256.2) [217.5, 299.7]
COVID-19 infection related AE	2 (7.7) [0.9, 27.7]	0	4 (7.6) [2.1, 19.4]	2 (3.3) [0.4, 12.0]	5 (8.2) [2.7, 19.2]
Any serious AE	4 (15.3) [4.2, 39.2]	4 (8.6) [2.3, 22.0]	7 (13.2) [5.3, 27.3]	6 (9.9) [3.7, 21.7]	8 (13.1) [5.7, 25.9]
Any AE leading to discontinuation of study drug	5 (19.2) [6.2, 44.7]	1 (2.2) [0.1, 12.0]	4 (7.6) [2.1, 19.4]	2 (3.3) [0.4, 12.0]	4 (6.6) [1.8, 16.8]
Any severe AE	7 (26.8) [10.8, 55.2]	6 (12.9) [4.7, 28.1]	5 (9.5) [3.1, 22.1]	6 (9.9) [3.7, 21.7]	5 (8.2) [2.7, 19.2]
Any AE with reasonable possibility of being related to study drug$	31 (118.7) [80.7, 168.5]	36 (77.4) [54.2, 107.2]	38 (71.9) [50.9, 98.7]	53 (87.9) [65.8, 114.9]	41 (67.3) [48.3, 91.3]
Any AE leading to death	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. 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.

$ As assessed by investigator.

Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=119)	UPA 15 mg QD (N=196)	UPA 30 mg QD (N=216)	UPA 15 mg QD (N=253)	UPA 30 mg QD (N=249)
Subgroup: >= 6 - < 9 Month (Cont.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/26.1	0/46.5	0/52.8	0/60.3	0/60.9
Deaths occurring <= 30 days after last dose of study drug	0/26.1	0/46.5	0/52.8	0/60.3	0/60.9
Deaths occurring > 30 days after last dose of study drug	0/26.1	0/46.5	0/52.8	0/60.3	0/60.9
COVID-19 infection related deaths	0/26.1	0/46.5	0/52.8	0/60.3	0/60.9

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. 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.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=89)	UPA 15 mg QD (N=178)	UPA 30 mg QD (N=206)	UPA 15 mg QD (N=232)	UPA 30 mg QD (N=237)
Subgroup: >= 9 - < 12 Month Exposure-adjusted event rate:	(PYs=19.9) Events (E/100PYs) [95% CI]	(PYs=40.8) Events (E/100PYs) [95% CI]	(PYs=47.8) Events (E/100PYs) [95% CI]	(PYs=55.6) Events (E/100PYs) [95% CI]	(PYs=56.1) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any adverse event (AE)	64 (322.3) [248.2, 411.6]	73 (179.1) [140.4, 225.2]	91 (190.6) [153.4, 234.0]	107 (192.3) [157.6, 232.3]	130 (231.7) [193.6, 275.1]
COVID-19 infection related AE	1 (5.0) [0.1, 28.1]	2 (4.9) [0.6, 17.7]	4 (8.4) [2.3, 21.4]	3 (5.4) [1.1, 15.8]	4 (7.1) [1.9, 18.3]
Any serious AE	4 (20.1) [5.5, 51.6]	1 (2.5) [0.1, 13.7]	3 (6.3) [1.3, 18.4]	2 (3.6) [0.4, 13.0]	4 (7.1) [1.9, 18.3]
Any AE leading to discontinuation of study drug	1 (5.0) [0.1, 28.1]	1 (2.5) [0.1, 13.7]	3 (6.3) [1.3, 18.4]	2 (3.6) [0.4, 13.0]	3 (5.3) [1.1, 15.6]
Any severe AE	4 (20.1) [5.5, 51.6]	0	4 (8.4) [2.3, 21.4]	0	4 (7.1) [1.9, 18.3]
Any AE with reasonable possibility of being related to study drug$	13 (65.5) [34.9, 112.0]	17 (41.7) [24.3, 66.8]	20 (41.9) [25.6, 64.7]	32 (57.5) [39.3, 81.2]	32 (57.0) [39.0, 80.5]
Any AE leading to death	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. 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.

$ As assessed by investigator.

Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=89)	UPA 15 mg QD (N=178)	UPA 30 mg QD (N=206)	UPA 15 mg QD (N=232)	UPA 30 mg QD (N=237)
Subgroup: >= 9 - < 12 Month (Cont.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/19.9	0/40.8	0/47.8	0/55.6	0/56.1
Deaths occurring <= 30 days after last dose of study drug	0/19.9	0/40.8	0/47.8	0/55.6	0/56.1
Deaths occurring > 30 days after last dose of study drug	0/19.9	0/40.8	0/47.8	0/55.6	0/56.1
COVID-19 infection related deaths	0/19.9	0/40.8	0/47.8	0/55.6	0/56.1

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

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=30)	UPA 15 mg QD (N=65)	UPA 30 mg QD (N=82)	UPA 15 mg QD (N=178)	UPA 30 mg QD (N=212)
Subgroup: >= 12 - < 15 Month					
Exposure-adjusted event rate:	(PYs=0.5)	(PYs=0.8)	(PYs=1.7)	(PYs=36.1)	(PYs=48.2)
	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 adverse event (AE)	2 (392.7) [47.6, 1418.7]	0	12 (726.9) [375.6, 1269.7]	90 (249.2) [200.4, 306.3]	161 (334.2) [284.6, 390.0]
COVID-19 infection related AE	0	0	0	3 (8.3) [1.7, 24.3]	6 (12.5) [4.6, 27.1]
Any serious AE	0	0	0	3 (8.3) [1.7, 24.3]	2 (4.2) [0.5, 15.0]
Any AE leading to discontinuation of study drug	0	0	0	4 (11.1) [3.0, 28.4]	2 (4.2) [0.5, 15.0]
Any severe AE	0	0	0	2 (5.5) [0.7, 20.0]	5 (10.4) [3.4, 24.2]
Any AE with reasonable possibility of being related to study drug$	0	0	3 (181.7) [37.5, 531.1]	19 (52.6) [31.7, 82.1]	66 (137.0) [106.0, 174.3]
Any AE leading to death	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. 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.

$ As assessed by investigator.

Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=30)	UPA 15 mg QD (N=65)	UPA 30 mg QD (N=82)	UPA 15 mg QD (N=178)	UPA 30 mg QD (N=212)
Subgroup: >= 12 - < 15 Month (Cont.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/0.5	0/0.8	0/1.7	0/36.1	0/48.2
Deaths occurring <= 30 days after last dose of study drug	0/0.5	0/0.8	0/1.7	0/36.1	0/48.2
Deaths occurring > 30 days after last dose of study drug	0/0.5	0/0.8	0/1.7	0/36.1	0/48.2
COVID-19 infection related deaths	0/0.5	0/0.8	0/1.7	0/36.1	0/48.2

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

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=128)	UPA 30 mg QD (N=172)
Subgroup: >= 15 - < 18 Month					
Exposure-adjusted event rate:	(PYs=0.0)	(PYs=0.0)	(PYs=0.0)	(PYs=29.4)	(PYs=39.1)
	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 adverse event (AE)	0	0	0	68 (231.6) [179.8, 293.6]	73 (186.9) [146.5, 235.0]
COVID-19 infection related AE	0	0	0	2 (6.8) [0.8, 24.6]	5 (12.8) [4.2, 29.9]
Any serious AE	0	0	0	3 (10.2) [2.1, 29.9]	9 (23.0) [10.5, 43.7]
Any AE leading to discontinuation of study drug	0	0	0	0	7 (17.9) [7.2, 36.9]
Any severe AE	0	0	0	2 (6.8) [0.8, 24.6]	5 (12.8) [4.2, 29.9]
Any AE with reasonable possibility of being related to study drug$	0	0	0	12 (40.9) [21.1, 71.4]	21 (53.8) [33.3, 82.2]
Any AE leading to death	0	0	0	0	1 (2.6) [0.1, 14.3]

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. 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.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=128)	UPA 30 mg QD (N=172)
Subgroup: >= 15 - < 18 Month (Cont.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/0.0	0/0.0	0/0.0	0/29.4	0/39.1
Deaths occurring <= 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/29.4	0/39.1
Deaths occurring > 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/29.4	0/39.1
COVID-19 infection related deaths	0/0.0	0/0.0	0/0.0	0/29.4	0/39.1

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

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=109)	UPA 30 mg QD (N=140)
Subgroup: >= 18 - < 21 Month					
Exposure-adjusted event rate:	(PYs=0.0)	(PYs=0.0)	(PYs=0.0)	(PYs=25.0)	(PYs=30.6)
	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 adverse event (AE)	0	0	0	43 (171.7) [124.2, 231.2]	56 (183.1) [138.3, 237.8]
COVID-19 infection related AE	0	0	0	2 (8.0) [1.0, 28.8]	6 (19.6) [7.2, 42.7]
Any serious AE	0	0	0	3 (12.0) [2.5, 35.0]	6 (19.6) [7.2, 42.7]
Any AE leading to discontinuation of study drug	0	0	0	1 (4.0) [0.1, 22.2]	3 (9.8) [2.0, 28.7]
Any severe AE	0	0	0	3 (12.0) [2.5, 35.0]	4 (13.1) [3.6, 33.5]
Any AE with reasonable possibility of being related to study drug$	0	0	0	8 (31.9) [13.8, 62.9]	15 (49.1) [27.5, 80.9]
Any AE leading to death	0	0	0	0	1 (3.3) [0.1, 18.2]

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

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=109)	UPA 30 mg QD (N=140)
Subgroup: >= 18 - < 21 Month (Cont.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/0.0	0/0.0	0/0.0	0/25.0	0/30.6
Deaths occurring <= 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/25.0	0/30.6
Deaths occurring > 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/25.0	0/30.6
COVID-19 infection related deaths	0/0.0	0/0.0	0/0.0	0/25.0	0/30.6

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. 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.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=90)	UPA 30 mg QD (N=109)
Subgroup: >= 21 - < 24 Month					
Exposure-adjusted event rate:	(PYs=0.0)	(PYs=0.0)	(PYs=0.0)	(PYs=19.4)	(PYs=23.4)
	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 adverse event (AE)	0	0	0	31 (159.7) [108.5, 226.7]	44 (188.0) [136.6, 252.4]
COVID-19 infection related AE	0	0	0	1 (5.2) [0.1, 28.7]	2 (8.5) [1.0, 30.9]
Any serious AE	0	0	0	1 (5.2) [0.1, 28.7]	6 (25.6) [9.4, 55.8]
Any AE leading to discontinuation of study drug	0	0	0	0	1 (4.3) [0.1, 23.8]
Any severe AE	0	0	0	1 (5.2) [0.1, 28.7]	2 (8.5) [1.0, 30.9]
Any AE with reasonable possibility of being related to study drug$	0	0	0	8 (41.2) [17.8, 81.2]	5 (21.4) [6.9, 49.9]
Any AE leading to death	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. 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.

$ As assessed by investigator.

Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=90)	UPA 30 mg QD (N=109)
Subgroup: >= 21 - < 24 Month (Cont.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/0.0	0/0.0	0/0.0	0/19.4	0/23.4
Deaths occurring <= 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/19.4	0/23.4
Deaths occurring > 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/19.4	0/23.4
COVID-19 infection related deaths	0/0.0	0/0.0	0/0.0	0/19.4	0/23.4

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. 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.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=67)	UPA 30 mg QD (N=77)
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=51.2) Events (E/100PYs) [95% CI]	(PYs=33.1) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any adverse event (AE)	0	0	0	103 (201.2) [164.2, 244.0]	60 (181.5) [138.5, 233.6]
COVID-19 infection related AE	0	0	0	4 (7.8) [2.1, 20.0]	3 (9.1) [1.9, 26.5]
Any serious AE	0	0	0	3 (5.9) [1.2, 17.1]	4 (12.1) [3.3, 31.0]
Any AE leading to discontinuation of study drug	0	0	0	2 (3.9) [0.5, 14.1]	2 (6.0) [0.7, 21.8]
Any severe AE	0	0	0	2 (3.9) [0.5, 14.1]	2 (6.0) [0.7, 21.8]
Any AE with reasonable possibility of being related to study drug$	0	0	0	26 (50.8) [33.2, 74.4]	8 (24.2) [10.4, 47.7]
Any AE leading to death	0	0	0	1 (2.0) [0.0, 10.9]	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. 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.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment emergent deaths.

Program Source Code: [redacted]

TABLE 2.4 6.1.1

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted 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=67)	UPA 30 mg QD (N=77)
Subgroup: >= 24 Month (Cont.)					
Exposure-adjusted event rate:	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]	n/PYs (n/100PYs) [95% CI]
Deaths#	0/0.0	0/0.0	0/0.0	1/51.2 (2.0) [0.0, 10.9]	0/33.1
Deaths occurring <= 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	1/51.2 (2.0) [0.0, 10.9]	0/33.1
Deaths occurring > 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/51.2	0/33.1
COVID-19 infection related deaths	0/0.0	0/0.0	0/0.0	0/51.2	0/33.1

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month					
Any adverse event	382 (714.7)	275 (465.1)	318 (524.0)	323 (457.8)	362 (516.6)
血液およびリンパ系障害	18 (33.7)	20 (33.8)	13 (21.4)	23 (32.6)	16 (22.8)
貧血	7 (13.1)	7 (11.8)	5 (8.2)	10 (14.2)	6 (8.6)
好酸球増加症	1 (1.9)	0	0	0	0
内出血発生の増加傾向	0	0	1 (1.6)	0	1 (1.4)
鉄欠乏性貧血	2 (3.7)	0	0	0	0
白血球減少症	1 (1.9)	6 (10.1)	1 (1.6)	6 (8.5)	2 (2.9)
リンパ節症	0	0	1 (1.6)	0	1 (1.4)
リンパ球増加症	1 (1.9)	0	0	0	0
リンパ球減少症	3 (5.6)	2 (3.4)	0	2 (2.8)	0
好中球減少症	2 (3.7)	5 (8.5)	4 (6.6)	5 (7.1)	5 (7.1)
血小板減少症	1 (1.9)	0	0	0	0
血小板増加症	0	0	1 (1.6)	0	1 (1.4)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
心臓障害	4 (7.5)	2 (3.4)	3 (4.9)	3 (4.3)	3 (4.3)
心房細動	1 (1.9)	0	0	0	0
うっ血性心不全	1 (1.9)	1 (1.7)	0	1 (1.4)	0
動悸	2 (3.7)	0	0	0	0
洞性徐脈	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
頻脈	0	0	0	1 (1.4)	0
心室性期外収縮	0	0	1 (1.6)	0	1 (1.4)
ウォルフ・パーキンソン・ホワイト症候群	0	0	1 (1.6)	0	1 (1.4)
耳および迷路障害	1 (1.9)	0	0	0	0
耳部腫脹	1 (1.9)	0	0	0	0
内分泌障害	1 (1.9)	1 (1.7)	0	1 (1.4)	0
クッシング症候群	1 (1.9)	0	0	0	0
甲状腺腫	0	1 (1.7)	0	1 (1.4)	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

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
眼障害	8 (15.0)	5 (8.5)	5 (8.2)	5 (7.1)	5 (7.1)
眼瞼炎	1 (1.9)	0	1 (1.6)	0	1 (1.4)
白内障	1 (1.9)	2 (3.4)	0	2 (2.8)	0
霰粒腫	0	0	2 (3.3)	0	2 (2.9)
上強膜炎	1 (1.9)	0	0	0	0
眼部腫脹	0	1 (1.7)	0	1 (1.4)	0
眼瞼障害	1 (1.9)	0	0	0	0
角膜炎	1 (1.9)	0	1 (1.6)	0	1 (1.4)
流涙増加	0	1 (1.7)	0	1 (1.4)	0
眼充血	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
眼窩周囲腫脹	1 (1.9)	0	0	0	0
潰瘍性角膜炎	1 (1.9)	0	0	0	0
ぶどう膜炎	1 (1.9)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
胃腸障害	69 (129.1)	39 (66.0)	42 (69.2)	51 (72.3)	49 (69.9)
腹部膨満	0	0	4 (6.6)	0	4 (5.7)
腹痛	2 (3.7)	3 (5.1)	1 (1.6)	4 (5.7)	1 (1.4)
上腹部痛	2 (3.7)	1 (1.7)	0	1 (1.4)	0
腹部圧痛	0	0	1 (1.6)	0	1 (1.4)
裂肛	1 (1.9)	0	0	0	0
痔瘻	0	0	1 (1.6)	0	1 (1.4)
肛門そう痒症	1 (1.9)	0	0	0	0
アフタ性潰瘍	2 (3.7)	1 (1.7)	2 (3.3)	1 (1.4)	3 (4.3)
大腸炎	1 (1.9)	1 (1.7)	0	1 (1.4)	0
潰瘍性大腸炎	37 (69.2)	18 (30.4)	9 (14.8)	24 (34.0)	11 (15.7)
結腸異形成	0	0	0	0	1 (1.4)
便秘	0	2 (3.4)	2 (3.3)	2 (2.8)	2 (2.9)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
胃腸障害 (Cont.)					
便意切迫	0	0	1 (1.6)	0	1 (1.4)
下痢	1 (1.9)	1 (1.7)	2 (3.3)	1 (1.4)	2 (2.9)
口内乾燥	0	0	1 (1.6)	0	1 (1.4)
消化不良	0	0	1 (1.6)	0	2 (2.9)
嚥下障害	0	0	1 (1.6)	0	1 (1.4)
小腸炎	0	1 (1.7)	0	1 (1.4)	0
鼓腸	1 (1.9)	0	2 (3.3)	0	2 (2.9)
胃炎	0	1 (1.7)	0	1 (1.4)	0
胃食道逆流性疾患	0	0	1 (1.6)	0	1 (1.4)
血便排泄	1 (1.9)	0	0	0	0
痔出血	1 (1.9)	0	0	0	0
痔核	0	1 (1.7)	1 (1.6)	2 (2.8)	1 (1.4)
大腸ポリープ	2 (3.7)	0	0	0	1 (1.4)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
胃腸障害 (Cont.)					
口唇腫脹	0	0	1 (1.6)	0	1 (1.4)
口腔嚢胞	1 (1.9)	0	0	0	0
口腔内潰瘍形成	2 (3.7)	0	0	0	0
粘液便	1 (1.9)	0	0	0	0
悪心	5 (9.4)	3 (5.1)	2 (3.3)	4 (5.7)	2 (2.9)
嚥下痛	0	0	0	0	1 (1.4)
膵炎	1 (1.9)	0	0	0	0
歯周病	0	0	1 (1.6)	0	1 (1.4)
直腸分泌物	0	0	1 (1.6)	0	1 (1.4)
直腸出血	1 (1.9)	0	2 (3.3)	1 (1.4)	2 (2.9)
直腸攣縮	1 (1.9)	0	0	0	0
直腸しぶり	1 (1.9)	0	0	0	0
口内炎	3 (5.6)	1 (1.7)	3 (4.9)	1 (1.4)	3 (4.3)

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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
胃腸障害 (Cont.)					
埋伏歯	0	1 (1.7)	0	1 (1.4)	0
歯痛	0	3 (5.1)	2 (3.3)	5 (7.1)	2 (2.9)
嘔吐	1 (1.9)	1 (1.7)	0	1 (1.4)	0
一般・全身障害および投与部位の状態	16 (29.9)	10 (16.9)	14 (23.1)	13 (18.4)	14 (20.0)
胸痛	0	1 (1.7)	0	1 (1.4)	0
悪寒	2 (3.7)	2 (3.4)	0	2 (2.8)	0
薬効欠如	1 (1.9)	0	0	0	0
疲労	4 (7.5)	2 (3.4)	3 (4.9)	2 (2.8)	3 (4.3)
全身性浮腫	0	1 (1.7)	0	1 (1.4)	0
高体温症	1 (1.9)	0	0	0	0
インフルエンザ様疾患	1 (1.9)	0	2 (3.3)	0	2 (2.9)
倦怠感	1 (1.9)	0	1 (1.6)	0	1 (1.4)
小結節	0	0	1 (1.6)	0	1 (1.4)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
一般・全身障害および投与部位の状態 (Cont.)					
末梢性浮腫	2 (3.7)	0	1 (1.6)	1 (1.4)	1 (1.4)
末梢腫脹	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
発熱	4 (7.5)	3 (5.1)	3 (4.9)	5 (7.1)	3 (4.3)
腫脹	0	0	1 (1.6)	0	1 (1.4)
顔面腫脹	0	0	1 (1.6)	0	1 (1.4)
肝胆道系障害	2 (3.7)	3 (5.1)	0	3 (4.3)	0
薬物性肝障害	0	1 (1.7)	0	1 (1.4)	0
肝機能異常	1 (1.9)	0	0	0	0
脂肪肝	0	1 (1.7)	0	1 (1.4)	0
高トランスアミナーゼ血症	0	1 (1.7)	0	1 (1.4)	0
肝損傷	1 (1.9)	0	0	0	0
免疫系障害	1 (1.9)	0	0	0	0
薬物過敏症	1 (1.9)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
感染症および寄生虫症	72 (134.7)	67 (113.3)	69 (113.7)	76 (107.7)	78 (111.3)
ダニ皮膚炎	0	1 (1.7)	0	1 (1.4)	0
急性心内膜炎	1 (1.9)	0	0	0	0
肛門直腸感染	1 (1.9)	0	0	0	0
無症候性COVID-19	0	0	0	1 (1.4)	1 (1.4)
細菌感染	0	0	1 (1.6)	0	1 (1.4)
ブラストシスティス感染	0	0	0	1 (1.4)	0
乳房膿瘍	0	1 (1.7)	0	1 (1.4)	0
気管支炎	2 (3.7)	2 (3.4)	0	2 (2.8)	0
感染性滑液包炎	0	0	1 (1.6)	0	1 (1.4)
COVID-19	4 (7.5)	4 (6.8)	0	4 (5.7)	0
カンピロバクター感染	0	1 (1.7)	0	1 (1.4)	0
蜂巣炎	0	0	0	0	1 (1.4)

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
クロストリジウム・ディフィシレ感染	2 (3.7)	0	2 (3.3)	0	2 (2.9)
膀胱炎	0	1 (1.7)	0	1 (1.4)	0
サイトメガロウイルス感染	1 (1.9)	1 (1.7)	0	1 (1.4)	0
毛嚢虫症	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
皮膚糸状菌症	1 (1.9)	0	0	0	0
耳感染	0	0	1 (1.6)	1 (1.4)	1 (1.4)
エンテロウイルス感染	0	0	1 (1.6)	0	1 (1.4)
大腸菌性尿路感染	0	1 (1.7)	0	1 (1.4)	0
毛包炎	3 (5.6)	3 (5.1)	4 (6.6)	3 (4.3)	5 (7.1)
真菌感染	0	0	1 (1.6)	0	1 (1.4)
胃腸炎	3 (5.6)	3 (5.1)	1 (1.6)	3 (4.3)	1 (1.4)
ウイルス性胃腸炎	0	0	1 (1.6)	1 (1.4)	2 (2.9)
歯肉炎	0	1 (1.7)	0	1 (1.4)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
単純ヘルペス	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
帯状疱疹	0	2 (3.4)	4 (6.6)	2 (2.8)	4 (5.7)
麦粒腫	3 (5.6)	0	0	0	0
膿痂疹	1 (1.9)	0	0	0	0
インフルエンザ	1 (1.9)	3 (5.1)	3 (4.9)	3 (4.3)	3 (4.3)
大腸感染	0	1 (1.7)	0	1 (1.4)	0
潜伏結核	0	0	2 (3.3)	0	2 (2.9)
乳腺炎	0	1 (1.7)	0	1 (1.4)	0
上咽頭炎	12 (22.5)	15 (25.4)	19 (31.3)	18 (25.5)	21 (30.0)
食道カンジダ症	0	1 (1.7)	0	1 (1.4)	0
爪真菌症	2 (3.7)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
口腔カンジダ症	2 (3.7)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
口腔ヘルペス	3 (5.6)	1 (1.7)	3 (4.9)	1 (1.4)	4 (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

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
外耳炎	1 (1.9)	0	0	0	0
爪囲炎	0	1 (1.7)	0	1 (1.4)	0
咽頭炎	1 (1.9)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
レンサ球菌性咽頭炎	1 (1.9)	2 (3.4)	0	2 (2.8)	0
胸膜感染	0	0	1 (1.6)	0	1 (1.4)
ニューモシスチス・イロベチイ肺炎	1 (1.9)	0	0	0	0
肺炎	2 (3.7)	0	1 (1.6)	0	2 (2.9)
歯髄炎	0	1 (1.7)	0	1 (1.4)	0
膿疱	1 (1.9)	0	1 (1.6)	0	1 (1.4)
ウイルス性気道感染	0	1 (1.7)	0	1 (1.4)	0
鼻炎	2 (3.7)	0	0	0	0
副鼻腔炎	2 (3.7)	0	0	2 (2.8)	0
股部白癬	0	0	0	0	1 (1.4)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
白癬感染	2 (3.7)	0	0	0	0
足部白癬	1 (1.9)	2 (3.4)	1 (1.6)	2 (2.8)	1 (1.4)
癜風	0	0	1 (1.6)	0	1 (1.4)
扁桃炎	0	2 (3.4)	0	2 (2.8)	0
歯膿瘍	0	0	1 (1.6)	0	1 (1.4)
歯感染	3 (5.6)	0	2 (3.3)	0	2 (2.9)
上気道感染	5 (9.4)	5 (8.5)	6 (9.9)	5 (7.1)	6 (8.6)
尿路感染	5 (9.4)	3 (5.1)	1 (1.6)	3 (4.3)	1 (1.4)
ウイルス感染	0	1 (1.7)	2 (3.3)	1 (1.4)	2 (2.9)
ウイルス性上気道感染	3 (5.6)	0	1 (1.6)	0	1 (1.4)
外陰部腟カンジダ症	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
外陰腟真菌感染	0	0	1 (1.6)	0	1 (1.4)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
傷害、中毒および処置合併症	9 (16.8)	5 (8.5)	5 (8.2)	7 (9.9)	5 (7.1)
動物による引っかき傷	1 (1.9)	0	0	0	0
骨挫傷	1 (1.9)	0	0	0	0
挫傷	0	0	1 (1.6)	0	1 (1.4)
眼外傷	0	0	1 (1.6)	0	1 (1.4)
損傷	1 (1.9)	0	0	0	0
四肢損傷	1 (1.9)	0	0	0	0
四肢外傷性切断	0	0	1 (1.6)	0	1 (1.4)
腰椎骨折	0	0	1 (1.6)	0	1 (1.4)
筋断裂	0	0	1 (1.6)	1 (1.4)	1 (1.4)
肉離れ	1 (1.9)	0	0	0	0
外傷後疼痛	0	1 (1.7)	0	1 (1.4)	0
肺挫傷	0	1 (1.7)	0	1 (1.4)	0
皮膚裂傷	1 (1.9)	1 (1.7)	0	1 (1.4)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
傷害、中毒および処置合併症 (Cont.)					
脊椎圧迫骨折	1 (1.9)	0	0	0	0
スポーツ損傷	0	0	0	1 (1.4)	0
皮下血腫	1 (1.9)	0	0	0	0
胸椎骨折	0	1 (1.7)	0	1 (1.4)	0
歯牙破折	1 (1.9)	0	0	0	0
創傷	0	1 (1.7)	0	1 (1.4)	0
臨床検査	17 (31.8)	42 (71.0)	59 (97.2)	45 (63.8)	70 (99.9)
アラニンアミノトランスフェラーゼ増加	0	3 (5.1)	3 (4.9)	3 (4.3)	5 (7.1)
大動脈雑音	0	0	0	0	1 (1.4)
アスパラギン酸アミノトランスフェラーゼ増加	1 (1.9)	4 (6.8)	2 (3.3)	4 (5.7)	3 (4.3)
血中アルブミン増加	0	0	1 (1.6)	0	1 (1.4)
血中ビリルビン増加	0	1 (1.7)	3 (4.9)	1 (1.4)	3 (4.3)
血中カルシウム増加	0	1 (1.7)	0	1 (1.4)	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

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
臨床検査 (Cont.)					
血中コレステロール増加	0	2 (3.4)	3 (4.9)	2 (2.8)	3 (4.3)
血中クレアチンホスホキナーゼ増加	2 (3.7)	10 (16.9)	10 (16.5)	11 (15.6)	11 (15.7)
血中クレアチニン増加	2 (3.7)	0	4 (6.6)	0	4 (5.7)
血中カリウム減少	0	1 (1.7)	0	1 (1.4)	0
体温上昇	0	0	1 (1.6)	0	1 (1.4)
γ-グルタミルトランスフェラーゼ増加	1 (1.9)	2 (3.4)	1 (1.6)	2 (2.8)	2 (2.9)
糸球体濾過率減少	1 (1.9)	0	0	0	0
顆粒球数減少	0	0	1 (1.6)	0	1 (1.4)
ヘモグロビン減少	1 (1.9)	1 (1.7)	1 (1.6)	1 (1.4)	2 (2.9)
尿中ヘモグロビン陽性	0	0	1 (1.6)	0	1 (1.4)
B型肝炎DNA測定陽性	0	0	1 (1.6)	0	1 (1.4)
高比重リポ蛋白増加	0	3 (5.1)	1 (1.6)	3 (4.3)	1 (1.4)
低比重リポ蛋白増加	0	1 (1.7)	4 (6.6)	1 (1.4)	4 (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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
臨床検査 (Cont.)					
リンパ球数減少	2 (3.7)	3 (5.1)	2 (3.3)	3 (4.3)	2 (2.9)
リンパ球数増加	1 (1.9)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
リンパ球百分率減少	0	0	1 (1.6)	0	1 (1.4)
平均赤血球容積異常	0	0	0	0	1 (1.4)
単球数増加	0	1 (1.7)	0	1 (1.4)	0
好中球数減少	2 (3.7)	2 (3.4)	7 (11.5)	2 (2.8)	8 (11.4)
好中球数増加	2 (3.7)	1 (1.7)	0	1 (1.4)	0
好中球百分率増加	0	0	1 (1.6)	0	1 (1.4)
血小板数増加	0	0	2 (3.3)	0	2 (2.9)
総蛋白増加	0	0	1 (1.6)	0	1 (1.4)
尿中蛋白陽性	1 (1.9)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
赤血球数減少	0	1 (1.7)	2 (3.3)	1 (1.4)	2 (2.9)
トランスアミナーゼ上昇	0	0	0	1 (1.4)	1 (1.4)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
臨床検査 (Cont.)					
体重増加	0	0	1 (1.6)	1 (1.4)	2 (2.9)
白血球数減少	1 (1.9)	3 (5.1)	3 (4.9)	3 (4.3)	3 (4.3)
代謝および栄養障害	9 (16.8)	10 (16.9)	9 (14.8)	10 (14.2)	10 (14.3)
脂質異常症	0	1 (1.7)	0	1 (1.4)	0
葉酸欠乏	0	0	1 (1.6)	0	1 (1.4)
高カルシウム血症	0	0	1 (1.6)	0	1 (1.4)
高コレステロール血症	2 (3.7)	2 (3.4)	3 (4.9)	2 (2.8)	3 (4.3)
高血糖	1 (1.9)	2 (3.4)	0	2 (2.8)	1 (1.4)
高リパーゼ血症	1 (1.9)	0	0	0	0
高脂血症	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
高尿酸血症	0	0	1 (1.6)	0	1 (1.4)
低カリウム血症	1 (1.9)	1 (1.7)	0	1 (1.4)	0
低ナトリウム血症	2 (3.7)	0	0	0	0

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
代謝および栄養障害 (Cont.)					
低リン酸血症	1 (1.9)	0	0	0	0
鉄欠乏	0	0	1 (1.6)	0	1 (1.4)
代謝症候群	0	0	1 (1.6)	0	1 (1.4)
ビタミンD欠乏	1 (1.9)	3 (5.1)	0	3 (4.3)	0
筋骨格系および結合組織障害	38 (71.1)	16 (27.1)	20 (33.0)	22 (31.2)	21 (30.0)
関節痛	16 (29.9)	4 (6.8)	3 (4.9)	6 (8.5)	3 (4.3)
関節炎	0	1 (1.7)	0	1 (1.4)	0
関節障害	5 (9.4)	1 (1.7)	2 (3.3)	1 (1.4)	2 (2.9)
背部痛	3 (5.6)	1 (1.7)	1 (1.6)	4 (5.7)	2 (2.9)
骨痛	0	0	1 (1.6)	0	1 (1.4)
滑液包炎	0	0	1 (1.6)	0	1 (1.4)
頚部脊柱管狭窄症	0	0	1 (1.6)	0	1 (1.4)
軟骨軟化症	0	0	1 (1.6)	0	1 (1.4)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
肋軟骨炎	1 (1.9)	0	0	0	0
線維筋痛	0	1 (1.7)	0	1 (1.4)	0
出血性関節症	1 (1.9)	0	0	0	0
椎間板変性症	1 (1.9)	0	0	0	0
関節硬直	0	1 (1.7)	0	1 (1.4)	0
関節腫脹	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
筋骨格系胸痛	1 (1.9)	0	0	0	0
筋骨格痛	2 (3.7)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
筋肉痛	1 (1.9)	1 (1.7)	0	2 (2.8)	0
筋炎	1 (1.9)	0	0	0	0
頚部痛	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
骨炎	0	0	1 (1.6)	0	1 (1.4)
変形性関節症	2 (3.7)	0	0	0	0

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
骨減少症	0	0	2 (3.3)	0	2 (2.9)
骨粗鬆症	1 (1.9)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
四肢痛	1 (1.9)	0	2 (3.3)	0	2 (2.9)
足底筋膜炎	0	0	1 (1.6)	0	1 (1.4)
肩回旋筋腱板症候群	0	1 (1.7)	0	1 (1.4)	0
脊椎関節障害	1 (1.9)	1 (1.7)	0	1 (1.4)	0
腱炎	1 (1.9)	0	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）	1 (1.9)	2 (3.4)	4 (6.6)	2 (2.8)	4 (5.7)
結腸腺癌	0	0	1 (1.6)	0	1 (1.4)
良性脾腫瘍	0	0	1 (1.6)	0	1 (1.4)
メラノサイト性母斑	0	1 (1.7)	0	1 (1.4)	0
脂漏性角化症	1 (1.9)	1 (1.7)	0	1 (1.4)	0
皮膚乳頭腫	0	0	2 (3.3)	0	2 (2.9)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
神経系障害	21 (39.3)	8 (13.5)	11 (18.1)	8 (11.3)	14 (20.0)
手根管症候群	0	0	1 (1.6)	0	1 (1.4)
脳血管発作	0	0	0	0	1 (1.4)
頚髄神経根障害	1 (1.9)	0	0	0	0
浮動性めまい	3 (5.6)	1 (1.7)	0	1 (1.4)	1 (1.4)
味覚不全	1 (1.9)	0	0	0	0
てんかん	1 (1.9)	0	0	0	0
頭痛	8 (15.0)	3 (5.1)	5 (8.2)	3 (4.3)	5 (7.1)
知覚過敏	1 (1.9)	0	0	0	0
感覚鈍麻	1 (1.9)	0	1 (1.6)	0	1 (1.4)
片頭痛	1 (1.9)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
神経圧迫	0	0	1 (1.6)	0	1 (1.4)
末梢性ニューロパチー	1 (1.9)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
神経系障害 (Cont.)					
錯感覚	2 (3.7)	1 (1.7)	0	1 (1.4)	0
坐骨神経痛	0	1 (1.7)	0	1 (1.4)	0
脊椎炎性脊髄症	0	0	1 (1.6)	0	1 (1.4)
くも膜下出血	0	0	1 (1.6)	0	1 (1.4)
硬膜下滲出液	0	1 (1.7)	0	1 (1.4)	0
失神	1 (1.9)	0	0	0	0
緊張性頭痛	0	0	0	0	1 (1.4)
精神障害	9 (16.8)	3 (5.1)	7 (11.5)	4 (5.7)	7 (10.0)
不安	2 (3.7)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
不安障害	0	1 (1.7)	0	1 (1.4)	0
うつ病	1 (1.9)	0	2 (3.3)	0	2 (2.9)
不眠症	5 (9.4)	1 (1.7)	4 (6.6)	1 (1.4)	4 (5.7)
易刺激性	1 (1.9)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
精神障害 (Cont.)					
睡眠障害	0	0	0	1 (1.4)	0
腎および尿路障害	5 (9.4)	2 (3.4)	7 (11.5)	2 (2.8)	7 (10.0)
急性腎障害	1 (1.9)	0	0	0	0
排尿困難	1 (1.9)	0	0	0	0
糖尿	1 (1.9)	0	0	0	0
血尿	0	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
白血球尿	1 (1.9)	0	0	0	0
排尿異常	0	0	1 (1.6)	0	1 (1.4)
腎結石症	0	1 (1.7)	2 (3.3)	1 (1.4)	2 (2.9)
頻尿	0	0	1 (1.6)	0	1 (1.4)
蛋白尿	1 (1.9)	0	0	0	0
腎仙痛	0	0	2 (3.3)	0	2 (2.9)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
生殖系および乳房障害	5 (9.4)	3 (5.1)	4 (6.6)	4 (5.7)	6 (8.6)
無月経	0	0	1 (1.6)	0	1 (1.4)
バルトリン嚢腫	1 (1.9)	0	0	0	0
良性前立腺肥大症	0	0	1 (1.6)	1 (1.4)	1 (1.4)
乳房嚢胞	1 (1.9)	0	0	0	0
子宮頚部上皮異形成	0	0	1 (1.6)	0	1 (1.4)
月経困難症	0	0	0	0	1 (1.4)
勃起不全	0	0	0	0	1 (1.4)
不正子宮出血	0	1 (1.7)	0	1 (1.4)	0
卵巣静脈血栓症	1 (1.9)	0	0	0	0
多嚢胞性卵巣	0	1 (1.7)	0	1 (1.4)	0
精液変色	0	0	1 (1.6)	0	1 (1.4)
腟分泌物	0	1 (1.7)	0	1 (1.4)	0
腟出血	1 (1.9)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
生殖系および乳房障害 (Cont.)					
外陰腟そう痒症	1 (1.9)	0	0	0	0
呼吸器、胸郭および縦隔障害	16 (29.9)	8 (13.5)	9 (14.8)	9 (12.8)	10 (14.3)
急性呼吸不全	1 (1.9)	0	0	0	0
失声症	0	0	0	0	1 (1.4)
慢性閉塞性肺疾患	0	1 (1.7)	0	1 (1.4)	0
咳嗽	1 (1.9)	2 (3.4)	2 (3.3)	2 (2.8)	2 (2.9)
呼吸困難	0	1 (1.7)	0	1 (1.4)	0
鼻出血	0	0	0	1 (1.4)	0
喀血	1 (1.9)	0	0	0	0
しゃっくり	1 (1.9)	0	1 (1.6)	0	1 (1.4)
間質性肺疾患	1 (1.9)	0	0	0	0
鼻閉	2 (3.7)	0	0	0	0
口腔咽頭痛	3 (5.6)	1 (1.7)	2 (3.3)	1 (1.4)	2 (2.9)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
湿性咳嗽	1 (1.9)	1 (1.7)	0	1 (1.4)	0
肺塞栓症	0	1 (1.7)	0	1 (1.4)	0
肺出血	1 (1.9)	0	0	0	0
アレルギー性鼻炎	2 (3.7)	0	1 (1.6)	0	1 (1.4)
鼻漏	0	0	1 (1.6)	0	1 (1.4)
副鼻腔うっ血	1 (1.9)	0	1 (1.6)	0	1 (1.4)
咽喉刺激感	0	0	1 (1.6)	0	1 (1.4)
上気道の炎症	1 (1.9)	1 (1.7)	0	1 (1.4)	0
皮膚および皮下組織障害	57 (106.6)	23 (38.9)	32 (52.7)	28 (39.7)	34 (48.5)
ざ瘡	6 (11.2)	3 (5.1)	6 (9.9)	3 (4.3)	6 (8.6)
嚢胞性ざ瘡	0	0	0	1 (1.4)	0
脱毛症	0	1 (1.7)	3 (4.9)	1 (1.4)	3 (4.3)
皮脂欠乏症	0	0	1 (1.6)	0	1 (1.4)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
皮膚炎	2 (3.7)	2 (3.4)	0	2 (2.8)	0
アトピー性皮膚炎	3 (5.6)	1 (1.7)	0	1 (1.4)	0
接触皮膚炎	2 (3.7)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
びまん性脱毛症	0	1 (1.7)	0	1 (1.4)	0
皮膚乾燥	5 (9.4)	0	1 (1.6)	0	1 (1.4)
異汗性湿疹	2 (3.7)	0	0	0	0
斑状出血	1 (1.9)	0	1 (1.6)	0	1 (1.4)
湿疹	5 (9.4)	1 (1.7)	3 (4.9)	1 (1.4)	3 (4.3)
皮脂欠乏性湿疹	1 (1.9)	0	0	0	0
紅斑	3 (5.6)	1 (1.7)	1 (1.6)	1 (1.4)	2 (2.9)
結節性紅斑	1 (1.9)	0	0	0	0
機械性蕁麻疹	0	0	1 (1.6)	0	1 (1.4)
寝汗	1 (1.9)	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

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=245) (PYs=53.4) Events (E/100PYs)	 UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	 UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	 UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
爪破損	1 (1.9)	0	1 (1.6)	0	1 (1.4)
丘疹	0	0	1 (1.6)	0	1 (1.4)
口囲皮膚炎	0	0	0	1 (1.4)	0
光線過敏性反応	1 (1.9)	0	0	0	0
そう痒症	7 (13.1)	1 (1.7)	1 (1.6)	1 (1.4)	2 (2.9)
壊疽性膿皮症	1 (1.9)	0	0	0	0
発疹	4 (7.5)	4 (6.8)	6 (9.9)	5 (7.1)	6 (8.6)
紅斑性皮疹	0	1 (1.7)	0	1 (1.4)	0
斑状丘疹状皮疹	1 (1.9)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
丘疹性皮疹	0	1 (1.7)	0	1 (1.4)	0
酒さ	1 (1.9)	2 (3.4)	1 (1.6)	2 (2.8)	1 (1.4)
脂漏性皮膚炎	4 (7.5)	1 (1.7)	1 (1.6)	1 (1.4)	1 (1.4)
皮膚灼熱感	1 (1.9)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
皮膚剥脱	1 (1.9)	0	0	0	0
皮膚亀裂	1 (1.9)	0	0	1 (1.4)	0
皮膚病変	0	0	0	1 (1.4)	0
皮膚腫瘤	0	1 (1.7)	0	1 (1.4)	0
皮膚潰瘍	0	0	1 (1.6)	0	1 (1.4)
蕁麻疹	2 (3.7)	0	1 (1.6)	0	1 (1.4)
血管障害	3 (5.6)	6 (10.1)	5 (8.2)	7 (9.9)	9 (12.8)
大動脈瘤	0	1 (1.7)	0	1 (1.4)	0
大動脈硬化症	0	0	1 (1.6)	0	1 (1.4)
出血性静脈瘤	0	1 (1.7)	0	1 (1.4)	0
高血圧	1 (1.9)	4 (6.8)	4 (6.6)	5 (7.1)	6 (8.6)
低血圧	1 (1.9)	0	0	0	1 (1.4)
静脈血栓症	1 (1.9)	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

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=245) (PYs=53.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=250) (PYs=59.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=251) (PYs=60.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=285) (PYs=70.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=291) (PYs=70.1) Events (E/100PYs)
Subgroup:0 - < 3 Month (Cont.)					
血管障害 (Cont.)					
白衣性高血圧	0	0	0	0	1 (1.4)

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month					
Any adverse event	117 (334.0)	131 (250.9)	142 (255.5)	177 (267.5)	170 (266.4)
血液およびリンパ系障害	2 (5.7)	4 (7.7)	2 (3.6)	5 (7.6)	2 (3.1)
貧血	1 (2.9)	1 (1.9)	0	1 (1.5)	0
白血球減少症	1 (2.9)	1 (1.9)	0	1 (1.5)	0
リンパ球減少症	0	1 (1.9)	1 (1.8)	2 (3.0)	1 (1.6)
好中球減少症	0	1 (1.9)	1 (1.8)	1 (1.5)	1 (1.6)
心臓障害	0	1 (1.9)	1 (1.8)	1 (1.5)	2 (3.1)
心房細動	0	0	0	0	1 (1.6)
慢性左室不全	0	0	1 (1.8)	0	1 (1.6)
動悸	0	1 (1.9)	0	1 (1.5)	0
耳および迷路障害	1 (2.9)	0	0	0	0
外耳道の外骨腫	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
内分泌障害	0	0	0	0	1 (1.6)
続発性副腎皮質機能不全	0	0	0	0	1 (1.6)
眼障害	1 (2.9)	3 (5.7)	3 (5.4)	3 (4.5)	3 (4.7)
白内障	0	1 (1.9)	1 (1.8)	1 (1.5)	1 (1.6)
霰粒腫	0	0	1 (1.8)	0	1 (1.6)
アレルギー性結膜炎	1 (2.9)	0	1 (1.8)	0	1 (1.6)
ドライアイ	0	1 (1.9)	0	1 (1.5)	0
眼刺激	0	1 (1.9)	0	1 (1.5)	0
胃腸障害	36 (102.8)	21 (40.2)	16 (28.8)	30 (45.3)	17 (26.6)
腹部膨満	1 (2.9)	0	1 (1.8)	0	1 (1.6)
腹痛	1 (2.9)	2 (3.8)	1 (1.8)	2 (3.0)	1 (1.6)
下腹部痛	2 (5.7)	0	0	0	0
上腹部痛	0	2 (3.8)	0	2 (3.0)	0
裂肛	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
胃腸障害 (Cont.)					
大腸炎	1 (2.9)	1 (1.9)	0	1 (1.5)	0
虚血性大腸炎	0	1 (1.9)	0	1 (1.5)	0
潰瘍性大腸炎	25 (71.4)	8 (15.3)	6 (10.8)	13 (19.6)	6 (9.4)
便秘	1 (2.9)	0	2 (3.6)	1 (1.5)	2 (3.1)
齲歯	1 (2.9)	0	0	0	0
下痢	0	1 (1.9)	0	1 (1.5)	0
嚥下障害	0	1 (1.9)	0	1 (1.5)	0
小腸炎	0	0	1 (1.8)	0	1 (1.6)
変色便	0	0	1 (1.8)	0	1 (1.6)
鼓腸	1 (2.9)	0	0	0	0
胃炎	0	1 (1.9)	0	1 (1.5)	0
胃食道逆流性疾患	0	1 (1.9)	1 (1.8)	1 (1.5)	1 (1.6)
歯肉腫脹	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
胃腸障害 (Cont.)					
痔出血	0	1 (1.9)	0	1 (1.5)	0
血栓性痔核	1 (2.9)	0	0	0	0
悪心	0	1 (1.9)	1 (1.8)	3 (4.5)	1 (1.6)
非感染性歯肉炎	0	0	1 (1.8)	0	1 (1.6)
嚥下痛	0	0	0	0	1 (1.6)
食道炎	0	1 (1.9)	0	1 (1.5)	0
直腸炎	1 (2.9)	0	0	0	0
口内炎	0	0	1 (1.8)	0	1 (1.6)
一般・全身障害および投与部位の状態	2 (5.7)	6 (11.5)	4 (7.2)	10 (15.1)	8 (12.5)
胸痛	0	1 (1.9)	1 (1.8)	1 (1.5)	2 (3.1)
疲労	0	0	0	2 (3.0)	1 (1.6)
インフルエンザ様疾患	0	0	0	1 (1.5)	0
腫瘤	0	0	2 (3.6)	0	2 (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.
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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
一般・全身障害および投与部位の状態 (Cont.)					
浮腫	0	1 (1.9)	0	1 (1.5)	0
疼痛	0	1 (1.9)	0	1 (1.5)	1 (1.6)
発熱	2 (5.7)	3 (5.7)	1 (1.8)	4 (6.0)	2 (3.1)
肝胆道系障害	0	1 (1.9)	0	2 (3.0)	0
硬化性胆管炎	0	0	0	1 (1.5)	0
肝機能異常	0	1 (1.9)	0	1 (1.5)	0
免疫系障害	0	0	1 (1.8)	0	1 (1.6)
季節性アレルギー	0	0	1 (1.8)	0	1 (1.6)
感染症および寄生虫症	26 (74.2)	33 (63.2)	48 (86.4)	41 (62.0)	57 (89.3)
肛門膿瘍	0	1 (1.9)	0	1 (1.5)	0
肛門直腸感染	1 (2.9)	0	0	0	0
細菌性関節炎	0	1 (1.9)	0	1 (1.5)	0
無症候性COVID-19	0	0	0	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
細菌性膣症	1 (2.9)	0	0	0	0
気管支炎	0	3 (5.7)	0	4 (6.0)	0
COVID-19	1 (2.9)	0	3 (5.4)	1 (1.5)	3 (4.7)
COVID-19肺炎	1 (2.9)	0	2 (3.6)	0	2 (3.1)
カンジダ感染	1 (2.9)	0	0	0	0
クロストリジウム・ディフィシレ感染	0	0	0	1 (1.5)	0
結膜炎	0	1 (1.9)	1 (1.8)	1 (1.5)	1 (1.6)
膀胱炎	0	0	1 (1.8)	0	1 (1.6)
毛嚢虫症	0	0	1 (1.8)	0	2 (3.1)
爪の皮膚糸状菌症	0	0	0	0	1 (1.6)
毛包炎	1 (2.9)	0	3 (5.4)	0	4 (6.3)
皮膚真菌感染	0	0	1 (1.8)	0	1 (1.6)
胃腸炎	1 (2.9)	1 (1.9)	2 (3.6)	1 (1.5)	2 (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.
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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
歯肉膿瘍	0	0	1 (1.8)	0	1 (1.6)
帯状疱疹	0	4 (7.7)	3 (5.4)	5 (7.6)	4 (6.3)
帯状疱疹性髄膜炎	0	0	1 (1.8)	0	1 (1.6)
咬傷感染	0	0	0	0	1 (1.6)
感染性皮膚嚢腫	0	1 (1.9)	0	1 (1.5)	0
インフルエンザ	1 (2.9)	1 (1.9)	3 (5.4)	1 (1.5)	3 (4.7)
喉頭炎	1 (2.9)	0	0	0	1 (1.6)
上咽頭炎	5 (14.3)	5 (9.6)	9 (16.2)	5 (7.6)	9 (14.1)
口腔ヘルペス	1 (2.9)	3 (5.7)	1 (1.8)	3 (4.5)	2 (3.1)
乳頭腫ウイルス感染	0	0	1 (1.8)	0	1 (1.6)
歯周炎	0	0	2 (3.6)	0	2 (3.1)
レンサ球菌性咽頭炎	0	0	1 (1.8)	0	1 (1.6)
毛巣嚢胞	0	1 (1.9)	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
肺炎	1 (2.9)	1 (1.9)	0	1 (1.5)	0
クリプトコッカス性肺炎	0	0	1 (1.8)	0	1 (1.6)
歯髄炎	0	0	1 (1.8)	0	1 (1.6)
膿疱	0	0	0	1 (1.5)	0
腎盂腎炎	0	1 (1.9)	0	1 (1.5)	0
ウイルス性気道感染	0	2 (3.8)	0	2 (3.0)	0
副鼻腔炎	2 (5.7)	0	1 (1.8)	0	1 (1.6)
足部白癬	1 (2.9)	0	0	0	1 (1.6)
癜風	0	1 (1.9)	0	1 (1.5)	0
扁桃炎	1 (2.9)	0	2 (3.6)	0	2 (3.1)
歯膿瘍	0	1 (1.9)	0	2 (3.0)	0
トリコモナス症	1 (2.9)	0	0	0	0
上気道感染	2 (5.7)	1 (1.9)	3 (5.4)	1 (1.5)	3 (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

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=35.0) Events (E/100PYs)	 UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	 UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	 UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
尿路感染	1 (2.9)	2 (3.8)	1 (1.8)	4 (6.0)	1 (1.6)
水痘帯状疱疹ウイルス感染	0	1 (1.9)	0	1 (1.5)	0
ウイルス性上気道感染	0	1 (1.9)	2 (3.6)	1 (1.5)	2 (3.1)
外陰部腟カンジダ症	1 (2.9)	0	1 (1.8)	0	1 (1.6)
外陰腟真菌感染	1 (2.9)	0	0	0	0
傷害、中毒および処置合併症	2 (5.7)	3 (5.7)	3 (5.4)	3 (4.5)	3 (4.7)
骨挫傷	0	0	1 (1.8)	0	1 (1.6)
毒性物質曝露	0	1 (1.9)	0	1 (1.5)	0
関節損傷	0	2 (3.8)	0	2 (3.0)	0
肋骨骨折	1 (2.9)	0	0	0	0
交通事故	1 (2.9)	0	0	0	0
歯牙破折	0	0	2 (3.6)	0	2 (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.
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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
臨床検査	5 (14.3)	18 (34.5)	16 (28.8)	22 (33.2)	18 (28.2)
アラニンアミノトランスフェラーゼ増加	0	2 (3.8)	1 (1.8)	2 (3.0)	1 (1.6)
アミラーゼ増加	1 (2.9)	0	0	0	0
抗核抗体増加	1 (2.9)	0	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (3.8)	1 (1.8)	2 (3.0)	1 (1.6)
血中アルブミン増加	0	1 (1.9)	0	1 (1.5)	0
血中カルシウム増加	0	0	0	1 (1.5)	0
血中コレステロール減少	0	1 (1.9)	0	1 (1.5)	0
血中コレステロール増加	0	0	2 (3.6)	0	2 (3.1)
血中クレアチンホスホキナーゼ増加	1 (2.9)	1 (1.9)	7 (12.6)	1 (1.5)	7 (11.0)
血中カリウム減少	0	1 (1.9)	0	1 (1.5)	0
血中トリグリセリド異常	0	1 (1.9)	0	1 (1.5)	0
体温上昇	0	1 (1.9)	0	1 (1.5)	0
骨密度減少	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
臨床検査 (Cont.)					
握力低下	0	1 (1.9)	0	1 (1.5)	0
ヘモグロビン減少	0	0	0	0	1 (1.6)
低比重リポ蛋白減少	0	1 (1.9)	0	1 (1.5)	0
低比重リポ蛋白増加	0	0	2 (3.6)	0	2 (3.1)
リンパ球数減少	0	0	1 (1.8)	0	1 (1.6)
リンパ球百分率増加	0	1 (1.9)	0	1 (1.5)	0
好中球数減少	1 (2.9)	2 (3.8)	1 (1.8)	3 (4.5)	1 (1.6)
好中球数増加	0	0	1 (1.8)	0	1 (1.6)
ビタミンD減少	0	0	0	0	1 (1.6)
体重増加	0	1 (1.9)	0	1 (1.5)	0
白血球数減少	1 (2.9)	1 (1.9)	0	2 (3.0)	0
尿中白血球陽性	0	1 (1.9)	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
代謝および栄養障害	1 (2.9)	6 (11.5)	4 (7.2)	7 (10.6)	4 (6.3)
食欲減退	0	0	0	1 (1.5)	0
脂質異常症	0	3 (5.7)	0	3 (4.5)	0
痛風	0	1 (1.9)	0	1 (1.5)	0
高コレステロール血症	0	2 (3.8)	1 (1.8)	2 (3.0)	1 (1.6)
低カリウム血症	1 (2.9)	0	0	0	0
低ナトリウム血症	0	0	1 (1.8)	0	1 (1.6)
ビタミンD欠乏	0	0	2 (3.6)	0	2 (3.1)
筋骨格系および結合組織障害	18 (51.4)	5 (9.6)	5 (9.0)	10 (15.1)	7 (11.0)
強直性脊椎炎	1 (2.9)	0	0	0	0
関節痛	4 (11.4)	2 (3.8)	1 (1.8)	3 (4.5)	2 (3.1)
腸炎性関節炎	1 (2.9)	0	0	0	0
関節障害	1 (2.9)	0	1 (1.8)	0	1 (1.6)
背部痛	1 (2.9)	1 (1.9)	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
軟骨軟化症	0	0	1 (1.8)	0	1 (1.6)
肋軟骨炎	1 (2.9)	0	1 (1.8)	0	1 (1.6)
側腹部痛	1 (2.9)	0	0	0	0
筋拘縮	0	0	0	1 (1.5)	0
筋骨格系胸痛	0	1 (1.9)	0	1 (1.5)	0
筋骨格硬直	1 (2.9)	0	0	0	0
筋肉痛	1 (2.9)	0	0	1 (1.5)	1 (1.6)
頚部痛	1 (2.9)	0	1 (1.8)	0	1 (1.6)
骨壊死	0	1 (1.9)	0	1 (1.5)	0
骨粗鬆症	0	0	0	1 (1.5)	0
四肢痛	1 (2.9)	0	0	0	0
肩回旋筋腱板症候群	2 (5.7)	0	0	0	0
脊椎関節障害	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
腱痛	1 (2.9)	0	0	0	0
腱鞘炎	1 (2.9)	0	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 (3.8)	2 (3.6)	3 (4.5)	4 (6.3)
基底細胞癌	0	0	2 (3.6)	0	3 (4.7)
浸潤性乳癌	0	1 (1.9)	0	1 (1.5)	0
卵巣胚細胞良性奇形腫	0	1 (1.9)	0	1 (1.5)	0
脂漏性角化症	0	0	0	0	1 (1.6)
甲状腺腺腫	0	0	0	1 (1.5)	0
神経系障害	2 (5.7)	7 (13.4)	6 (10.8)	8 (12.1)	7 (11.0)
手根管症候群	0	1 (1.9)	1 (1.8)	1 (1.5)	1 (1.6)
浮動性めまい	0	1 (1.9)	2 (3.6)	1 (1.5)	3 (4.7)
頭痛	1 (2.9)	3 (5.7)	1 (1.8)	4 (6.0)	1 (1.6)
感覚鈍麻	0	1 (1.9)	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
神経系障害 (Cont.)					
腰仙部神経根障害	0	1 (1.9)	0	1 (1.5)	0
片頭痛	1 (2.9)	0	1 (1.8)	0	1 (1.6)
錯感覚	0	0	1 (1.8)	0	1 (1.6)
精神障害	6 (17.1)	1 (1.9)	2 (3.6)	4 (6.0)	4 (6.3)
不安	2 (5.7)	0	0	1 (1.5)	1 (1.6)
抑うつ気分	0	0	1 (1.8)	0	1 (1.6)
うつ病	1 (2.9)	1 (1.9)	0	2 (3.0)	0
不眠症	1 (2.9)	0	1 (1.8)	1 (1.5)	2 (3.1)
精神障害	1 (2.9)	0	0	0	0
自殺念慮	1 (2.9)	0	0	0	0
腎および尿路障害	0	1 (1.9)	3 (5.4)	2 (3.0)	3 (4.7)
急性腎障害	0	0	1 (1.8)	0	1 (1.6)
排尿困難	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
腎および尿路障害 (Cont.)					
血尿	0	0	1 (1.8)	0	1 (1.6)
尿管結石症	0	0	1 (1.8)	0	1 (1.6)
尿閉	0	1 (1.9)	0	1 (1.5)	0
生殖系および乳房障害	0	4 (7.7)	2 (3.6)	4 (6.0)	2 (3.1)
無月経	0	1 (1.9)	0	1 (1.5)	0
乳房痛	0	1 (1.9)	0	1 (1.5)	0
子宮頚部上皮異形成	0	0	1 (1.8)	0	1 (1.6)
月経困難症	0	1 (1.9)	0	1 (1.5)	0
月経過多	0	1 (1.9)	0	1 (1.5)	0
前立腺炎	0	0	1 (1.8)	0	1 (1.6)
呼吸器、胸郭および縦隔障害	4 (11.4)	3 (5.7)	5 (9.0)	6 (9.1)	7 (11.0)
失声症	0	0	0	0	1 (1.6)
喘息	0	1 (1.9)	1 (1.8)	1 (1.5)	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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
咳嗽	1 (2.9)	0	1 (1.8)	1 (1.5)	1 (1.6)
鼻出血	0	0	1 (1.8)	0	1 (1.6)
口腔咽頭痛	2 (5.7)	1 (1.9)	2 (3.6)	3 (4.5)	2 (3.1)
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	11 (31.4)	11 (21.1)	17 (30.6)	14 (21.2)	18 (28.2)
ざ瘡	1 (2.9)	3 (5.7)	1 (1.8)	3 (4.5)	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 (3.1)
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 (3.0)	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)

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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
紅斑	0	2 (3.8)	0	2 (3.0)	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
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	5 (14.3)	1 (1.9)	4 (7.2)	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 (4.7)
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

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

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=35.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=52.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=66.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.8) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
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)
血管障害	0	1 (1.9)	2 (3.6)	2 (3.0)	2 (3.1)
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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month					
Any adverse event	109 (417.5)	150 (322.5)	132 (249.8)	191 (316.7)	156 (256.2)
血液およびリンパ系障害	8 (30.6)	5 (10.8)	1 (1.9)	7 (11.6)	2 (3.3)
貧血	5 (19.2)	2 (4.3)	1 (1.9)	2 (3.3)	1 (1.6)
鉄欠乏性貧血	2 (7.7)	0	0	0	1 (1.6)
白血球減少症	0	1 (2.2)	0	1 (1.7)	0
小球性貧血	0	0	0	1 (1.7)	0
好中球減少症	1 (3.8)	1 (2.2)	0	1 (1.7)	0
汎血球減少症	0	0	0	1 (1.7)	0
脾腫	0	1 (2.2)	0	1 (1.7)	0
心臓障害	1 (3.8)	1 (2.2)	1 (1.9)	1 (1.7)	2 (3.3)
不整脈	0	1 (2.2)	0	1 (1.7)	0
僧帽弁閉鎖不全症	0	0	0	0	1 (1.6)
心膜炎	0	0	1 (1.9)	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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
心臓障害 (Cont.)					
頻脈	1 (3.8)	0	0	0	0
先天性、家族性および遺伝性障害	0	0	1 (1.9)	0	1 (1.6)
皮様嚢腫	0	0	1 (1.9)	0	1 (1.6)
耳および迷路障害	0	2 (4.3)	1 (1.9)	2 (3.3)	1 (1.6)
感音性難聴	0	1 (2.2)	0	1 (1.7)	0
片耳難聴	0	0	1 (1.9)	0	1 (1.6)
耳痛	0	1 (2.2)	0	1 (1.7)	0
内分泌障害	0	0	0	0	1 (1.6)
甲状腺腫瘤	0	0	0	0	1 (1.6)
眼障害	1 (3.8)	1 (2.2)	0	2 (3.3)	0
白内障	0	0	0	1 (1.7)	0
角膜混濁	1 (3.8)	0	0	0	0
眼そう痒症	0	1 (2.2)	0	1 (1.7)	0

TABLE 2.4 6.1.3

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)

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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
胃腸障害	29 (111.1)	18 (38.7)	18 (34.1)	24 (39.8)	21 (34.5)
腹部膨満	0	1 (2.2)	0	1 (1.7)	0
腹部腫瘤	1 (3.8)	0	0	0	0
腹痛	3 (11.5)	1 (2.2)	1 (1.9)	2 (3.3)	1 (1.6)
下腹部痛	1 (3.8)	0	0	0	0
上腹部痛	0	0	2 (3.8)	0	3 (4.9)
痔瘻	0	0	2 (3.8)	1 (1.7)	2 (3.3)
肛門の炎症	0	0	1 (1.9)	0	1 (1.6)
肛門そう痒症	1 (3.8)	0	0	0	0
アフタ性潰瘍	0	0	1 (1.9)	0	1 (1.6)
大腸炎	1 (3.8)	0	0	0	0
潰瘍性大腸炎	11 (42.1)	8 (17.2)	3 (5.7)	11 (18.2)	3 (4.9)
便秘	1 (3.8)	2 (4.3)	1 (1.9)	2 (3.3)	2 (3.3)

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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
胃腸障害 (Cont.)					
齲歯	0	1 (2.2)	0	1 (1.7)	1 (1.6)
下痢	1 (3.8)	0	0	0	0
消化不良	1 (3.8)	0	0	0	0
鼓腸	1 (3.8)	0	0	0	0
胃炎	0	0	1 (1.9)	0	1 (1.6)
胃食道逆流性疾患	2 (7.7)	0	0	0	0
痔核	1 (3.8)	2 (4.3)	1 (1.9)	3 (5.0)	1 (1.6)
鼠径ヘルニア	0	1 (2.2)	0	1 (1.7)	0
腸閉塞	0	1 (2.2)	0	1 (1.7)	0
過敏性腸症候群	0	0	1 (1.9)	0	1 (1.6)
大腸穿孔	1 (3.8)	0	0	0	0
口腔内潰瘍形成	0	0	1 (1.9)	0	1 (1.6)
悪心	1 (3.8)	0	1 (1.9)	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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
胃腸障害 (Cont.)					
嚥下痛	1 (3.8)	0	0	0	0
肛門周囲痛	0	1 (2.2)	0	1 (1.7)	0
歯の脱落	0	0	1 (1.9)	0	1 (1.6)
臍ヘルニア	1 (3.8)	0	0	0	0
嘔吐	0	0	1 (1.9)	0	1 (1.6)
一般・全身障害および投与部位の状態	5 (19.2)	3 (6.5)	6 (11.4)	6 (9.9)	9 (14.8)
胸部不快感	0	1 (2.2)	0	1 (1.7)	0
胸痛	1 (3.8)	1 (2.2)	0	1 (1.7)	1 (1.6)
疲労	0	0	0	2 (3.3)	1 (1.6)
インフルエンザ様疾患	0	0	0	1 (1.7)	0
注射部位疼痛	0	0	2 (3.8)	0	2 (3.3)
倦怠感	0	0	1 (1.9)	0	1 (1.6)
粘膜乾燥	1 (3.8)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
一般・全身障害および投与部位の状態 (Cont.)					
末梢性浮腫	1 (3.8)	1 (2.2)	0	1 (1.7)	0
発熱	1 (3.8)	0	3 (5.7)	0	4 (6.6)
異物感	1 (3.8)	0	0	0	0
肝胆道系障害	1 (3.8)	1 (2.2)	2 (3.8)	3 (5.0)	2 (3.3)
硬化性胆管炎	0	0	0	1 (1.7)	0
薬物性肝障害	0	0	1 (1.9)	0	1 (1.6)
肝機能異常	1 (3.8)	1 (2.2)	0	1 (1.7)	0
脂肪肝	0	0	0	1 (1.7)	0
肝障害	0	0	1 (1.9)	0	1 (1.6)
免疫系障害	0	1 (2.2)	0	1 (1.7)	0
季節性アレルギー	0	1 (2.2)	0	1 (1.7)	0
感染症および寄生虫症	22 (84.3)	44 (94.6)	39 (73.8)	53 (87.9)	42 (69.0)
腹部膿瘍	1 (3.8)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
ダニ皮膚炎	0	1 (2.2)	0	1 (1.7)	0
肛門膿瘍	0	1 (2.2)	0	1 (1.7)	0
気管支炎	1 (3.8)	1 (2.2)	1 (1.9)	1 (1.7)	1 (1.6)
COVID-19	2 (7.7)	0	4 (7.6)	1 (1.7)	5 (8.2)
COVID-19肺炎	0	0	0	1 (1.7)	0
蜂巣炎	0	1 (2.2)	0	1 (1.7)	0
クロストリジウム・ディフィシレ感染	0	1 (2.2)	0	1 (1.7)	0
結膜炎	0	1 (2.2)	0	2 (3.3)	0
膀胱炎	0	2 (4.3)	1 (1.9)	2 (3.3)	1 (1.6)
毛嚢虫症	0	2 (4.3)	0	2 (3.3)	0
耳感染	0	1 (2.2)	1 (1.9)	1 (1.7)	1 (1.6)
眼感染	0	0	0	1 (1.7)	0
毛包炎	0	1 (2.2)	2 (3.8)	1 (1.7)	2 (3.3)

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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
皮膚真菌感染	0	0	1 (1.9)	0	1 (1.6)
ウイルス性胃腸炎	0	0	1 (1.9)	0	1 (1.6)
陰部単純ヘルペス	0	0	0	0	1 (1.6)
ヘモフィルス感染	1 (3.8)	0	0	0	0
ヘルペス性皮膚炎	0	1 (2.2)	0	1 (1.7)	0
単純ヘルペス	0	1 (2.2)	0	1 (1.7)	0
帯状疱疹	0	3 (6.5)	4 (7.6)	3 (5.0)	5 (8.2)
麦粒腫	0	0	1 (1.9)	0	1 (1.6)
インフルエンザ	1 (3.8)	2 (4.3)	3 (5.7)	4 (6.6)	3 (4.9)
喉頭炎	0	0	1 (1.9)	0	1 (1.6)
下気道感染	1 (3.8)	1 (2.2)	0	1 (1.7)	0
伝染性軟属腫	1 (3.8)	0	0	0	0
上咽頭炎	4 (15.3)	9 (19.4)	7 (13.2)	10 (16.6)	7 (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 6.1.3

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	0	2 (4.3)	3 (5.7)	2 (3.3)	3 (4.9)
咽頭炎	1 (3.8)	1 (2.2)	0	1 (1.7)	0
肺炎	1 (3.8)	0	0	0	0
クリプトコッカス性肺炎	0	0	1 (1.9)	0	1 (1.6)
ウイルス性肺炎	0	0	1 (1.9)	0	1 (1.6)
腎盂腎炎	1 (3.8)	0	0	0	0
ウイルス性気道感染	0	1 (2.2)	0	1 (1.7)	0
鼻炎	1 (3.8)	1 (2.2)	1 (1.9)	1 (1.7)	1 (1.6)
セラチア感染	1 (3.8)	0	0	0	0
副鼻腔炎	0	2 (4.3)	1 (1.9)	2 (3.3)	1 (1.6)
ブドウ球菌感染	1 (3.8)	0	0	0	0
足部白癬	0	1 (2.2)	0	1 (1.7)	0
扁桃炎	0	0	1 (1.9)	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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
歯感染	0	0	0	1 (1.7)	0
上気道感染	1 (3.8)	4 (8.6)	4 (7.6)	4 (6.6)	4 (6.6)
尿路感染	1 (3.8)	2 (4.3)	0	2 (3.3)	0
ウイルス血症	1 (3.8)	0	0	0	0
ウイルス性咽頭炎	0	0	0	1 (1.7)	0
ウイルス性上気道感染	1 (3.8)	0	0	0	0
外陰腟真菌感染	0	1 (2.2)	0	1 (1.7)	0
傷害、中毒および処置合併症	2 (7.7)	1 (2.2)	4 (7.6)	2 (3.3)	6 (9.9)
足関節部骨折	0	0	0	1 (1.7)	0
挫傷	0	0	2 (3.8)	0	3 (4.9)
転倒	0	0	0	0	1 (1.6)
熱中症	1 (3.8)	0	0	0	0
靭帯捻挫	1 (3.8)	0	1 (1.9)	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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
傷害、中毒および処置合併症 (Cont.)					
皮膚裂傷	0	1 (2.2)	0	1 (1.7)	0
手首関節骨折	0	0	1 (1.9)	0	1 (1.6)
臨床検査	7 (26.8)	35 (75.3)	17 (32.2)	38 (63.0)	19 (31.2)
アラニンアミノトランスフェラーゼ増加	1 (3.8)	3 (6.5)	1 (1.9)	3 (5.0)	1 (1.6)
アスパラギン酸アミノトランスフェラーゼ増加	1 (3.8)	1 (2.2)	0	1 (1.7)	0
血中アルブミン減少	0	2 (4.3)	0	2 (3.3)	0
血中ビリルビン増加	0	2 (4.3)	0	2 (3.3)	0
血中コレステロール増加	0	0	1 (1.9)	0	1 (1.6)
血中クレアチンホスホキナーゼ増加	2 (7.7)	4 (8.6)	3 (5.7)	6 (9.9)	5 (8.2)
血中葉酸減少	0	1 (2.2)	0	1 (1.7)	0
血中ブドウ糖増加	0	1 (2.2)	0	1 (1.7)	0
血中鉄減少	0	0	0	1 (1.7)	0
血中カリウム増加	0	1 (2.2)	0	1 (1.7)	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.
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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
臨床検査 (Cont.)					
血中ナトリウム増加	0	1 (2.2)	0	1 (1.7)	0
尿中血陽性	0	0	1 (1.9)	0	1 (1.6)
γ-グルタミルトランスフェラーゼ増加	0	3 (6.5)	0	3 (5.0)	0
糸球体濾過率減少	0	1 (2.2)	0	1 (1.7)	0
ヘモグロビン減少	0	1 (2.2)	0	1 (1.7)	0
肝酵素上昇	0	1 (2.2)	1 (1.9)	1 (1.7)	1 (1.6)
リンパ球数減少	0	2 (4.3)	1 (1.9)	2 (3.3)	1 (1.6)
リンパ球数増加	0	0	1 (1.9)	0	1 (1.6)
リンパ球百分率減少	0	1 (2.2)	0	1 (1.7)	0
好中球数減少	1 (3.8)	1 (2.2)	3 (5.7)	1 (1.7)	3 (4.9)
好中球数増加	0	1 (2.2)	1 (1.9)	1 (1.7)	1 (1.6)
血小板数減少	1 (3.8)	0	0	0	0
プレアルブミン減少	0	1 (2.2)	0	1 (1.7)	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.
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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
臨床検査 (Cont.)					
総蛋白減少	0	1 (2.2)	0	1 (1.7)	0
尿中蛋白陽性	0	1 (2.2)	0	1 (1.7)	0
血沈亢進	0	1 (2.2)	0	1 (1.7)	0
尿検査異常	0	1 (2.2)	0	1 (1.7)	0
ビタミンD減少	0	1 (2.2)	0	1 (1.7)	0
体重増加	0	0	1 (1.9)	0	1 (1.6)
白血球数減少	1 (3.8)	1 (2.2)	2 (3.8)	1 (1.7)	2 (3.3)
白血球数増加	0	1 (2.2)	1 (1.9)	1 (1.7)	1 (1.6)
代謝および栄養障害	5 (19.2)	1 (2.2)	1 (1.9)	1 (1.7)	2 (3.3)
食欲減退	1 (3.8)	0	0	0	0
脂質異常症	0	0	1 (1.9)	0	2 (3.3)
高血糖	0	1 (2.2)	0	1 (1.7)	0
低カリウム血症	1 (3.8)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
代謝および栄養障害 (Cont.)					
鉄欠乏	1 (3.8)	0	0	0	0
2型糖尿病	1 (3.8)	0	0	0	0
ビタミンD欠乏	1 (3.8)	0	0	0	0
筋骨格系および結合組織障害	9 (34.5)	15 (32.3)	7 (13.2)	18 (29.8)	7 (11.5)
関節痛	4 (15.3)	4 (8.6)	2 (3.8)	6 (9.9)	2 (3.3)
腸炎性関節炎	1 (3.8)	0	0	0	0
関節障害	0	0	0	1 (1.7)	0
背部痛	2 (7.7)	5 (10.8)	0	5 (8.3)	0
腰部脊柱管狭窄症	0	0	1 (1.9)	0	1 (1.6)
筋骨格系胸痛	1 (3.8)	0	0	0	0
筋骨格痛	1 (3.8)	1 (2.2)	0	1 (1.7)	0
筋肉痛	0	1 (2.2)	1 (1.9)	1 (1.7)	1 (1.6)
筋炎	0	1 (2.2)	0	1 (1.7)	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.
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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
頚部痛	0	1 (2.2)	0	1 (1.7)	0
骨減少症	0	1 (2.2)	0	1 (1.7)	0
四肢痛	0	1 (2.2)	1 (1.9)	1 (1.7)	1 (1.6)
関節周囲炎	0	0	2 (3.8)	0	2 (3.3)
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）	2 (7.7)	1 (2.2)	1 (1.9)	2 (3.3)	1 (1.6)
大腸腺腫	1 (3.8)	0	0	0	0
線維性組織球腫	0	0	1 (1.9)	0	1 (1.6)
皮膚血管腫	0	1 (2.2)	0	1 (1.7)	0
浸潤性乳癌	1 (3.8)	0	0	0	0
甲状腺腺腫	0	0	0	1 (1.7)	0
神経系障害	3 (11.5)	3 (6.5)	3 (5.7)	5 (8.3)	7 (11.5)
手根管症候群	1 (3.8)	0	0	0	0
浮動性めまい	0	0	0	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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
神経系障害 (Cont.)					
本態性振戦	1 (3.8)	0	0	0	0
頭痛	1 (3.8)	1 (2.2)	3 (5.7)	3 (5.0)	6 (9.9)
感覚鈍麻	0	2 (4.3)	0	2 (3.3)	0
精神障害	2 (7.7)	2 (4.3)	6 (11.4)	2 (3.3)	6 (9.9)
不安	2 (7.7)	0	1 (1.9)	0	1 (1.6)
うつ病	0	0	2 (3.8)	0	2 (3.3)
不眠症	0	1 (2.2)	3 (5.7)	1 (1.7)	3 (4.9)
睡眠障害	0	1 (2.2)	0	1 (1.7)	0
腎および尿路障害	4 (15.3)	1 (2.2)	2 (3.8)	2 (3.3)	2 (3.3)
排尿困難	0	0	0	1 (1.7)	0
血尿	2 (7.7)	0	0	0	0
水腎症	1 (3.8)	0	0	0	0
腎結石症	1 (3.8)	1 (2.2)	0	1 (1.7)	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.
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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
腎および尿路障害 (Cont.)					
腎仙痛	0	0	2 (3.8)	0	2 (3.3)
生殖系および乳房障害	1 (3.8)	4 (8.6)	0	5 (8.3)	0
良性前立腺肥大症	0	1 (2.2)	0	1 (1.7)	0
乳房嚢胞	0	1 (2.2)	0	1 (1.7)	0
勃起不全	0	0	0	1 (1.7)	0
閉経期症状	1 (3.8)	0	0	0	0
前立腺炎	0	1 (2.2)	0	1 (1.7)	0
腟出血	0	1 (2.2)	0	1 (1.7)	0
呼吸器、胸郭および縦隔障害	2 (7.7)	3 (6.5)	10 (18.9)	4 (6.6)	10 (16.4)
気管支拡張症	1 (3.8)	0	0	0	0
咳嗽	0	1 (2.2)	2 (3.8)	2 (3.3)	2 (3.3)
労作性呼吸困難	0	0	1 (1.9)	0	1 (1.6)
肺気腫	0	0	1 (1.9)	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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
肺過膨脹	0	0	1 (1.9)	0	1 (1.6)
鼻閉	1 (3.8)	0	1 (1.9)	0	1 (1.6)
非感染性気管支炎	0	0	1 (1.9)	0	1 (1.6)
口腔咽頭痛	0	1 (2.2)	2 (3.8)	1 (1.7)	2 (3.3)
湿性咳嗽	0	1 (2.2)	0	1 (1.7)	0
上気道咳症候群	0	0	1 (1.9)	0	1 (1.6)
皮膚および皮下組織障害	4 (15.3)	4 (8.6)	10 (18.9)	9 (14.9)	12 (19.7)
ざ瘡	1 (3.8)	1 (2.2)	2 (3.8)	2 (3.3)	2 (3.3)
脱毛症	0	0	0	1 (1.7)	0
皮膚炎	0	0	1 (1.9)	0	1 (1.6)
ざ瘡様皮膚炎	0	0	0	1 (1.7)	0
湿疹	0	0	1 (1.9)	0	2 (3.3)
結節性紅斑	0	0	1 (1.9)	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

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
寝汗	0	0	1 (1.9)	0	1 (1.6)
爪甲剥離症	0	0	1 (1.9)	0	1 (1.6)
発疹	0	2 (4.3)	1 (1.9)	3 (5.0)	1 (1.6)
紅斑性皮疹	1 (3.8)	0	0	0	0
毛孔性皮疹	0	0	0	1 (1.7)	0
斑状皮疹	0	1 (2.2)	0	1 (1.7)	0
そう痒性皮疹	0	0	0	0	1 (1.6)
脂漏性皮膚炎	1 (3.8)	0	0	0	0
皮膚病変	0	0	2 (3.8)	0	2 (3.3)
蕁麻疹	1 (3.8)	0	0	0	0
外科および内科処置	0	2 (4.3)	0	2 (3.3)	0
人工流産	0	2 (4.3)	0	2 (3.3)	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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=119) (PYs=26.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=196) (PYs=46.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=216) (PYs=52.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=253) (PYs=60.3) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=249) (PYs=60.9) Events (E/100PYs)
Subgroup:>= 6 - < 9 Month (Cont.)					
血管障害	1 (3.8)	2 (4.3)	2 (3.8)	2 (3.3)	3 (4.9)
深部静脈血栓症	0	0	1 (1.9)	0	1 (1.6)
高血圧	1 (3.8)	2 (4.3)	1 (1.9)	2 (3.3)	2 (3.3)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month					
Any adverse event	64 (322.3)	73 (179.1)	91 (190.6)	107 (192.3)	130 (231.7)
血液およびリンパ系障害	3 (15.1)	1 (2.5)	4 (8.4)	2 (3.6)	4 (7.1)
貧血	0	0	2 (4.2)	0	2 (3.6)
鉄欠乏性貧血	1 (5.0)	0	0	0	0
白血球増加症	1 (5.0)	0	0	0	0
白血球減少症	1 (5.0)	1 (2.5)	0	1 (1.8)	0
リンパ球減少症	0	0	0	1 (1.8)	0
小球性貧血	0	0	1 (2.1)	0	1 (1.8)
好中球減少症	0	0	1 (2.1)	0	1 (1.8)
心臓障害	1 (5.0)	0	2 (4.2)	0	3 (5.3)
急性心筋梗塞	1 (5.0)	0	0	0	0
二束ブロック	0	0	1 (2.1)	0	1 (1.8)
上室性頻脈	0	0	1 (2.1)	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
心臓障害 (Cont.)					
心室性期外収縮	0	0	0	0	1 (1.8)
先天性、家族性および遺伝性障害	0	1 (2.5)	0	1 (1.8)	0
ジルベール症候群	0	1 (2.5)	0	1 (1.8)	0
耳および迷路障害	1 (5.0)	2 (4.9)	0	3 (5.4)	0
耳痛	0	0	0	1 (1.8)	0
中耳滲出液	1 (5.0)	0	0	0	0
回転性めまい	0	2 (4.9)	0	2 (3.6)	0
眼障害	2 (10.1)	1 (2.5)	3 (6.3)	2 (3.6)	3 (5.3)
眼瞼炎	0	0	1 (2.1)	0	1 (1.8)
白内障	0	0	1 (2.1)	1 (1.8)	1 (1.8)
結膜充血	1 (5.0)	0	0	0	0
アレルギー性結膜炎	0	1 (2.5)	0	1 (1.8)	0
ドライアイ	0	0	1 (2.1)	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
眼障害 (Cont.)					
眼瞼発疹	1 (5.0)	0	0	0	0
胃腸障害	17 (85.6)	12 (29.4)	12 (25.1)	19 (34.1)	17 (30.3)
腹部膨満	0	1 (2.5)	0	1 (1.8)	1 (1.8)
腹痛	0	1 (2.5)	1 (2.1)	1 (1.8)	1 (1.8)
下腹部痛	1 (5.0)	0	0	0	0
上腹部痛	0	1 (2.5)	0	2 (3.6)	0
腹部圧痛	0	0	1 (2.1)	0	1 (1.8)
異常便	1 (5.0)	0	0	0	0
潰瘍性大腸炎	7 (35.3)	3 (7.4)	3 (6.3)	8 (14.4)	3 (5.3)
結腸異形成	0	1 (2.5)	0	1 (1.8)	0
便秘	0	0	1 (2.1)	0	1 (1.8)
歯嚢胞	0	0	1 (2.1)	0	1 (1.8)
下痢	0	0	0	1 (1.8)	0

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
胃腸障害 (Cont.)					
消化不良	2 (10.1)	1 (2.5)	0	1 (1.8)	0
嚥下障害	1 (5.0)	0	0	0	0
小腸炎	0	0	1 (2.1)	0	1 (1.8)
大腿ヘルニア	1 (5.0)	0	0	0	0
胃潰瘍	0	1 (2.5)	0	1 (1.8)	0
胃炎	0	1 (2.5)	0	1 (1.8)	0
胃食道逆流性疾患	1 (5.0)	0	1 (2.1)	0	1 (1.8)
舌痛	1 (5.0)	0	0	0	0
痔出血	1 (5.0)	0	0	0	0
痔核	0	1 (2.5)	0	1 (1.8)	0
悪心	0	0	1 (2.1)	0	2 (3.6)
口腔障害	0	0	1 (2.1)	0	1 (1.8)
歯周病	1 (5.0)	0	0	0	0

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
胃腸障害 (Cont.)					
歯痛	0	1 (2.5)	1 (2.1)	1 (1.8)	3 (5.3)
臍ヘルニア	0	0	0	0	1 (1.8)
一般・全身障害および投与部位の状態	6 (30.2)	3 (7.4)	14 (29.3)	5 (9.0)	15 (26.7)
胸痛	0	0	1 (2.1)	0	1 (1.8)
医療機器に対する不耐性	1 (5.0)	0	0	0	0
疲労	1 (5.0)	0	1 (2.1)	0	2 (3.6)
炎症	0	0	1 (2.1)	0	1 (1.8)
注射部位疼痛	0	1 (2.5)	2 (4.2)	2 (3.6)	2 (3.6)
倦怠感	0	0	0	1 (1.8)	0
非心臓性胸痛	1 (5.0)	0	0	0	0
疼痛	1 (5.0)	0	0	0	0
末梢腫脹	1 (5.0)	0	0	0	0
発熱	1 (5.0)	2 (4.9)	9 (18.8)	2 (3.6)	9 (16.0)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
肝胆道系障害	1 (5.0)	2 (4.9)	0	2 (3.6)	1 (1.8)
肝機能異常	1 (5.0)	0	0	0	1 (1.8)
脂肪肝	0	1 (2.5)	0	1 (1.8)	0
肝損傷	0	1 (2.5)	0	1 (1.8)	0
免疫系障害	0	1 (2.5)	0	1 (1.8)	0
季節性アレルギー	0	1 (2.5)	0	1 (1.8)	0
感染症および寄生虫症	6 (30.2)	18 (44.2)	25 (52.3)	30 (53.9)	28 (49.9)
腹壁膿瘍	0	0	0	1 (1.8)	0
COVID-19	1 (5.0)	1 (2.5)	4 (8.4)	2 (3.6)	4 (7.1)
COVID-19肺炎	0	1 (2.5)	0	1 (1.8)	0
カンピロバクター感染	0	0	0	1 (1.8)	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	1 (1.8)	0
膀胱炎	0	0	1 (2.1)	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
憩室炎	0	0	1 (2.1)	0	1 (1.8)
感染性腸炎	0	0	1 (2.1)	0	1 (1.8)
毛包炎	0	0	1 (2.1)	0	1 (1.8)
せつ	0	1 (2.5)	0	1 (1.8)	0
胃腸炎	0	1 (2.5)	0	1 (1.8)	0
ウイルス性胃腸炎	0	0	0	1 (1.8)	0
歯肉炎	0	0	0	0	1 (1.8)
帯状疱疹	0	2 (4.9)	3 (6.3)	3 (5.4)	3 (5.3)
麦粒腫	0	0	1 (2.1)	0	1 (1.8)
膿痂疹	0	1 (2.5)	0	1 (1.8)	0
インフルエンザ	0	1 (2.5)	1 (2.1)	1 (1.8)	1 (1.8)
潜伏結核	0	0	0	0	1 (1.8)
下気道感染	0	0	0	1 (1.8)	0

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
上咽頭炎	0	3 (7.4)	3 (6.3)	4 (7.2)	3 (5.3)
口腔ヘルペス	0	1 (2.5)	1 (2.1)	1 (1.8)	1 (1.8)
歯周炎	1 (5.0)	0	0	0	0
咽頭炎	2 (10.1)	0	0	0	0
肺炎	0	0	1 (2.1)	0	1 (1.8)
膿皮症	0	0	1 (2.1)	0	1 (1.8)
ウイルス性気道感染	1 (5.0)	0	0	1 (1.8)	0
鼻炎	0	0	1 (2.1)	0	1 (1.8)
副鼻腔炎	0	0	1 (2.1)	0	1 (1.8)
歯感染	0	0	1 (2.1)	0	1 (1.8)
上気道感染	1 (5.0)	3 (7.4)	0	4 (7.2)	0
尿路感染	0	3 (7.4)	2 (4.2)	5 (9.0)	2 (3.6)
ウイルス性上気道感染	0	0	1 (2.1)	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
外陰部腟カンジダ症	0	0	0	0	1 (1.8)
傷害、中毒および処置合併症	0	5 (12.3)	0	6 (10.8)	0
足骨折	0	0	0	1 (1.8)	0
靭帯捻挫	0	1 (2.5)	0	1 (1.8)	0
四肢損傷	0	1 (2.5)	0	1 (1.8)	0
肉離れ	0	1 (2.5)	0	1 (1.8)	0
外傷後疼痛	0	1 (2.5)	0	1 (1.8)	0
皮膚裂傷	0	1 (2.5)	0	1 (1.8)	0
臨床検査	0	7 (17.2)	11 (23.0)	10 (18.0)	21 (37.4)
アラニンアミノトランスフェラーゼ増加	0	1 (2.5)	2 (4.2)	1 (1.8)	2 (3.6)
アミラーゼ増加	0	1 (2.5)	0	1 (1.8)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (4.9)	2 (4.2)	2 (3.6)	2 (3.6)
血中クレアチンホスホキナーゼ増加	0	1 (2.5)	2 (4.2)	2 (3.6)	4 (7.1)

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
臨床検査 (Cont.)					
血中ブドウ糖増加	0	0	1 (2.1)	0	1 (1.8)
血中鉄減少	0	0	0	0	1 (1.8)
血中トリグリセリド増加	0	0	0	0	1 (1.8)
リパーゼ増加	0	1 (2.5)	0	1 (1.8)	0
肝機能検査値上昇	0	0	1 (2.1)	0	1 (1.8)
リンパ球数減少	0	0	1 (2.1)	0	2 (3.6)
好中球数減少	0	0	1 (2.1)	0	1 (1.8)
好中球数増加	0	0	0	0	1 (1.8)
血小板数増加	0	0	0	0	1 (1.8)
前立腺特異性抗原増加	0	0	0	1 (1.8)	0
網状赤血球数減少	0	0	0	1 (1.8)	0
ブドウ球菌検査陽性	0	1 (2.5)	0	1 (1.8)	0
尿中ケトン体陽性	0	0	0	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
臨床検査 (Cont.)					
白血球数減少	0	0	1 (2.1)	0	2 (3.6)
尿中白血球陽性	0	0	0	0	1 (1.8)
代謝および栄養障害	1 (5.0)	1 (2.5)	1 (2.1)	2 (3.6)	4 (7.1)
糖尿病	0	0	0	0	1 (1.8)
耐糖能障害	1 (5.0)	0	0	0	0
痛風	0	1 (2.5)	0	1 (1.8)	0
高コレステロール血症	0	0	0	1 (1.8)	1 (1.8)
高脂血症	0	0	1 (2.1)	0	2 (3.6)
筋骨格系および結合組織障害	12 (60.4)	6 (14.7)	2 (4.2)	6 (10.8)	4 (7.1)
関節痛	0	3 (7.4)	1 (2.1)	3 (5.4)	1 (1.8)
腸炎性関節炎	1 (5.0)	0	0	0	0
関節障害	1 (5.0)	0	0	0	0
背部痛	4 (20.1)	0	0	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
尾骨痛	1 (5.0)	0	0	0	0
外骨腫	0	1 (2.5)	0	1 (1.8)	0
側腹部痛	0	0	1 (2.1)	0	1 (1.8)
関節腫脹	0	1 (2.5)	0	1 (1.8)	0
筋力低下	1 (5.0)	0	0	0	0
筋骨格系胸痛	1 (5.0)	0	0	0	0
筋肉痛	0	0	0	0	1 (1.8)
四肢痛	2 (10.1)	0	0	0	0
肩回旋筋腱板症候群	0	1 (2.5)	0	1 (1.8)	0
変形性脊椎症	1 (5.0)	0	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	0	2 (4.2)	0	3 (5.3)
基底細胞癌	0	0	1 (2.1)	0	2 (3.6)
小細胞癌	0	0	1 (2.1)	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
神経系障害	3 (15.1)	2 (4.9)	2 (4.2)	3 (5.4)	7 (12.5)
灼熱感	0	0	0	1 (1.8)	0
頭痛	1 (5.0)	1 (2.5)	1 (2.1)	1 (1.8)	4 (7.1)
感覚鈍麻	0	1 (2.5)	0	1 (1.8)	0
片頭痛	2 (10.1)	0	1 (2.1)	0	1 (1.8)
ヘルペス後神経痛	0	0	0	0	1 (1.8)
傾眠	0	0	0	0	1 (1.8)
精神障害	1 (5.0)	1 (2.5)	1 (2.1)	1 (1.8)	1 (1.8)
不眠症	1 (5.0)	0	1 (2.1)	0	1 (1.8)
パニック発作	0	1 (2.5)	0	1 (1.8)	0
腎および尿路障害	2 (10.1)	2 (4.9)	2 (4.2)	2 (3.6)	2 (3.6)
排尿困難	0	0	1 (2.1)	0	1 (1.8)
緊張性膀胱	0	0	1 (2.1)	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
腎および尿路障害 (Cont.)					
腎石灰沈着症	1 (5.0)	0	0	0	0
腎結石症	1 (5.0)	1 (2.5)	0	1 (1.8)	0
腎機能障害	0	1 (2.5)	0	1 (1.8)	0
生殖系および乳房障害	3 (15.1)	0	0	1 (1.8)	1 (1.8)
機能不全性子宮出血	1 (5.0)	0	0	0	0
月経過多	0	0	0	1 (1.8)	0
不規則月経	1 (5.0)	0	0	0	0
前立腺炎	1 (5.0)	0	0	0	0
腟分泌物	0	0	0	0	1 (1.8)
呼吸器、胸郭および縦隔障害	2 (10.1)	1 (2.5)	3 (6.3)	1 (1.8)	4 (7.1)
急性呼吸不全	0	0	1 (2.1)	0	1 (1.8)
咳嗽	1 (5.0)	0	0	0	0
鼻出血	0	0	0	0	1 (1.8)

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
肺浸潤	0	0	1 (2.1)	0	1 (1.8)
鼻閉	0	0	1 (2.1)	0	1 (1.8)
アレルギー性鼻炎	0	1 (2.5)	0	1 (1.8)	0
副鼻腔うっ血	1 (5.0)	0	0	0	0
皮膚および皮下組織障害	3 (15.1)	7 (17.2)	4 (8.4)	9 (16.2)	7 (12.5)
ざ瘡	0	0	1 (2.1)	0	2 (3.6)
皮膚嚢腫	0	1 (2.5)	1 (2.1)	1 (1.8)	1 (1.8)
皮膚炎	1 (5.0)	0	0	0	0
アトピー性皮膚炎	0	2 (4.9)	0	2 (3.6)	0
湿疹	0	1 (2.5)	0	1 (1.8)	0
掌蹠膿疱症	0	1 (2.5)	0	1 (1.8)	0
光線性皮膚症	1 (5.0)	0	0	0	0
そう痒症	0	0	0	1 (1.8)	0

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

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=89) (PYs=19.9) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=178) (PYs=40.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=206) (PYs=47.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=232) (PYs=55.6) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=237) (PYs=56.1) Events (E/100PYs)
Subgroup:>= 9 - < 12 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
発疹	0	1 (2.5)	0	1 (1.8)	0
紅斑性皮疹	0	0	0	1 (1.8)	0
毛孔性皮疹	0	1 (2.5)	0	1 (1.8)	0
脂漏性皮膚炎	1 (5.0)	0	1 (2.1)	0	1 (1.8)
皮膚剥脱	0	0	0	0	1 (1.8)
皮膚病変	0	0	0	0	1 (1.8)
蕁麻疹	0	0	1 (2.1)	0	1 (1.8)
血管障害	0	0	3 (6.3)	1 (1.8)	5 (8.9)
血腫	0	0	1 (2.1)	0	1 (1.8)
高血圧	0	0	1 (2.1)	1 (1.8)	2 (3.6)
起立性低血圧	0	0	0	0	1 (1.8)
末梢動脈閉塞性疾患	0	0	1 (2.1)	0	1 (1.8)

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

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=30) (PYs=0.5) Events (E/100PYs)	 UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	 UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	 UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month					
Any adverse event	2 (392.7)	0	12 (726.9)	90 (249.2)	161 (334.2)
血液およびリンパ系障害	0	0	1 (60.6)	3 (8.3)	8 (16.6)
貧血	0	0	1 (60.6)	1 (2.8)	3 (6.2)
白血球減少症	0	0	0	1 (2.8)	1 (2.1)
リンパ節症	0	0	0	1 (2.8)	0
リンパ球減少症	0	0	0	0	2 (4.2)
好中球減少症	0	0	0	0	2 (4.2)
心臓障害	0	0	1 (60.6)	0	4 (8.3)
不整脈	0	0	0	0	1 (2.1)
第一度房室ブロック	0	0	0	0	1 (2.1)
心不全	0	0	1 (60.6)	0	1 (2.1)
心室性期外収縮	0	0	0	0	1 (2.1)

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

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
先天性、家族性および遺伝性障害	0	0	1 (60.6)	0	1 (2.1)
胃腸管動静脈奇形	0	0	1 (60.6)	0	1 (2.1)
耳および迷路障害	0	0	0	1 (2.8)	1 (2.1)
回転性めまい	0	0	0	1 (2.8)	1 (2.1)
胃腸障害	1 (196.4)	0	1 (60.6)	15 (41.5)	12 (24.9)
腹痛	0	0	0	0	1 (2.1)
腹部圧痛	0	0	0	0	1 (2.1)
潰瘍性大腸炎	1 (196.4)	0	0	5 (13.8)	2 (4.2)
結腸異形成	0	0	0	0	1 (2.1)
便秘	0	0	0	2 (5.5)	1 (2.1)
下痢	0	0	0	1 (2.8)	0
腸炎	0	0	0	0	1 (2.1)
鼓腸	0	0	0	1 (2.8)	0
胃食道逆流性疾患	0	0	0	1 (2.8)	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

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
胃腸障害 (Cont.)					
痔核	0	0	0	1 (2.8)	0
過敏性腸症候群	0	0	0	1 (2.8)	0
大腸ポリープ	0	0	1 (60.6)	0	3 (6.2)
口腔内潰瘍形成	0	0	0	1 (2.8)	0
直腸異形成	0	0	0	2 (5.5)	0
歯痛	0	0	0	0	1 (2.1)
嘔吐	0	0	0	0	1 (2.1)
一般・全身障害および投与部位の状態	0	0	0	7 (19.4)	6 (12.5)
悪寒	0	0	0	0	1 (2.1)
異形成	0	0	0	1 (2.8)	1 (2.1)
注射部位疼痛	0	0	0	2 (5.5)	2 (4.2)
倦怠感	0	0	0	1 (2.8)	0
末梢腫脹	0	0	0	0	1 (2.1)

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

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) 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.)					
発熱	0	0	0	2 (5.5)	0
腫脹	0	0	0	1 (2.8)	0
ワクチン接種部位疼痛	0	0	0	0	1 (2.1)
感染症および寄生虫症	0	0	2 (121.1)	16 (44.3)	37 (76.8)
肛門膿瘍	0	0	0	1 (2.8)	0
虫垂炎	0	0	0	0	1 (2.1)
気管支炎	0	0	0	0	1 (2.1)
COVID-19	0	0	0	2 (5.5)	5 (10.4)
COVID-19肺炎	0	0	0	1 (2.8)	1 (2.1)
カンピロバクター胃腸炎	0	0	0	0	1 (2.1)
結膜炎	0	0	0	0	1 (2.1)
膀胱炎	0	0	0	2 (5.5)	0
サイトメガロウイルス性大腸炎	0	0	0	0	1 (2.1)

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

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
毛包炎	0	0	0	0	1 (2.1)
せつ	0	0	0	0	1 (2.1)
胃腸炎	0	0	0	0	2 (4.2)
ウイルス性胃腸炎	0	0	0	0	1 (2.1)
手足口病	0	0	0	0	1 (2.1)
帯状疱疹	0	0	1 (60.6)	3 (8.3)	2 (4.2)
耳帯状疱疹	0	0	0	1 (2.8)	0
麦粒腫	0	0	0	1 (2.8)	0
インフルエンザ	0	0	0	1 (2.8)	1 (2.1)
潜伏結核	0	0	0	0	1 (2.1)
上咽頭炎	0	0	0	2 (5.5)	3 (6.2)
爪真菌症	0	0	0	1 (2.8)	0
口腔ヘルペス	0	0	0	0	3 (6.2)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
歯周炎	0	0	0	0	1 (2.1)
ウイルス性気道感染	0	0	0	0	1 (2.1)
副鼻腔炎	0	0	0	0	1 (2.1)
扁桃炎	0	0	0	1 (2.8)	0
細菌性扁桃炎	0	0	0	0	1 (2.1)
上気道感染	0	0	1 (60.6)	0	1 (2.1)
尿路感染	0	0	0	0	2 (4.2)
外陰部腟カンジダ症	0	0	0	0	3 (6.2)
傷害、中毒および処置合併症	0	0	0	4 (11.1)	1 (2.1)
足関節部骨折	0	0	0	0	1 (2.1)
節足動物咬傷	0	0	0	1 (2.8)	0
挫傷	0	0	0	1 (2.8)	0
仙骨骨折	0	0	0	1 (2.8)	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

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
傷害、中毒および処置合併症 (Cont.)					
過量投与	0	0	0	1 (2.8)	0
臨床検査	0	0	1 (60.6)	14 (38.8)	42 (87.2)
アラニンアミノトランスフェラーゼ増加	0	0	0	1 (2.8)	3 (6.2)
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	4 (8.3)
血中アルカリホスファターゼ増加	0	0	0	0	1 (2.1)
血中重炭酸塩減少	0	0	0	1 (2.8)	0
血中ビリルビン増加	0	0	0	0	2 (4.2)
血中コレステロール増加	0	0	0	0	1 (2.1)
血中クレアチンホスホキナーゼ増加	0	0	0	3 (8.3)	9 (18.7)
血中ブドウ糖減少	0	0	0	0	1 (2.1)
血中リン減少	0	0	0	0	1 (2.1)
血圧上昇	0	0	0	0	1 (2.1)
尿中血陽性	0	0	1 (60.6)	0	1 (2.1)

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

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=30) (PYs=0.5) Events (E/100PYs)	 UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	 UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	 UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
臨床検査 (Cont.)					
炭水化物耐性低下	0	0	0	0	1 (2.1)
γ-グルタミルトランスフェラーゼ増加	0	0	0	3 (8.3)	2 (4.2)
ヘモグロビン減少	0	0	0	0	2 (4.2)
肝酵素上昇	0	0	0	0	1 (2.1)
肝機能検査値上昇	0	0	0	0	1 (2.1)
リンパ球数減少	0	0	0	1 (2.8)	1 (2.1)
平均赤血球容積増加	0	0	0	0	1 (2.1)
好中球数減少	0	0	0	3 (8.3)	4 (8.3)
好中球数増加	0	0	0	1 (2.8)	0
赤血球数減少	0	0	0	0	2 (4.2)
白血球数減少	0	0	0	1 (2.8)	3 (6.2)
代謝および栄養障害	0	0	0	4 (11.1)	5 (10.4)
食欲減退	0	0	0	0	1 (2.1)

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

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=30) (PYs=0.5) Events (E/100PYs)	 UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	 UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	 UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
代謝および栄養障害 (Cont.)					
糖尿病	0	0	0	0	1 (2.1)
高コレステロール血症	0	0	0	1 (2.8)	1 (2.1)
高血糖	0	0	0	1 (2.8)	0
高脂血症	0	0	0	1 (2.8)	0
肥満	0	0	0	0	1 (2.1)
2型糖尿病	0	0	0	1 (2.8)	0
ビタミンD欠乏	0	0	0	0	1 (2.1)
筋骨格系および結合組織障害	1 (196.4)	0	1 (60.6)	9 (24.9)	8 (16.6)
関節痛	1 (196.4)	0	1 (60.6)	0	2 (4.2)
関節障害	0	0	0	1 (2.8)	0
背部痛	0	0	0	0	1 (2.1)
椎間板突出	0	0	0	1 (2.8)	0
筋肉痛	0	0	0	1 (2.8)	2 (4.2)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=30) (PYs=0.5) Events (E/100PYs)	 UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	 UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	 UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
変形性関節症	0	0	0	2 (5.5)	0
骨壊死	0	0	0	1 (2.8)	0
四肢痛	0	0	0	2 (5.5)	2 (4.2)
足底筋膜炎	0	0	0	1 (2.8)	0
腱炎	0	0	0	0	1 (2.1)
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	0	0	0	4 (8.3)
ボーエン病	0	0	0	0	1 (2.1)
線維腫	0	0	0	0	1 (2.1)
脂漏性角化症	0	0	0	0	1 (2.1)
皮膚乳頭腫	0	0	0	0	1 (2.1)
神経系障害	0	0	0	1 (2.8)	6 (12.5)
浮動性めまい	0	0	0	1 (2.8)	0
頭痛	0	0	0	0	4 (8.3)

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

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
神経系障害 (Cont.)					
坐骨神経痛	0	0	0	0	1 (2.1)
失神	0	0	0	0	1 (2.1)
精神障害	0	0	0	2 (5.5)	1 (2.1)
不安	0	0	0	1 (2.8)	0
うつ病	0	0	0	0	1 (2.1)
不眠症	0	0	0	1 (2.8)	0
腎および尿路障害	0	0	0	0	1 (2.1)
蛋白尿	0	0	0	0	1 (2.1)
生殖系および乳房障害	0	0	2 (121.1)	2 (5.5)	2 (4.2)
良性前立腺肥大症	0	0	1 (60.6)	1 (2.8)	1 (2.1)
不正子宮出血	0	0	0	1 (2.8)	0
前立腺腫瘤	0	0	1 (60.6)	0	1 (2.1)

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

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=30) (PYs=0.5) Events (E/100PYs)	 UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	 UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	 UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
呼吸器、胸郭および縦隔障害	0	0	0	6 (16.6)	2 (4.2)
咳嗽	0	0	0	1 (2.8)	0
鼻潰瘍	0	0	0	2 (5.5)	0
口腔咽頭痛	0	0	0	1 (2.8)	1 (2.1)
湿性咳嗽	0	0	0	0	1 (2.1)
肺塞栓症	0	0	0	1 (2.8)	0
睡眠時無呼吸症候群	0	0	0	1 (2.8)	0
皮膚および皮下組織障害	0	0	2 (121.1)	3 (8.3)	16 (33.2)
ざ瘡	0	0	0	1 (2.8)	3 (6.2)
脱毛症	0	0	0	0	2 (4.2)
ざ瘡様皮膚炎	0	0	0	1 (2.8)	0
アレルギー性皮膚炎	0	0	0	0	1 (2.1)
湿疹	0	0	0	0	1 (2.1)
皮脂欠乏性湿疹	0	0	0	0	2 (4.2)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
紅斑	0	0	0	0	1 (2.1)
多汗症	0	0	0	1 (2.8)	0
黒子	0	0	0	0	1 (2.1)
発疹	0	0	0	0	2 (4.2)
斑状皮疹	0	0	0	0	1 (2.1)
蕁麻疹	0	0	2 (121.1)	0	2 (4.2)
社会環境	0	0	0	0	1 (2.1)
閉経後	0	0	0	0	1 (2.1)
外科および内科処置	0	0	0	1 (2.8)	0
抜歯	0	0	0	1 (2.8)	0
血管障害	0	0	0	2 (5.5)	3 (6.2)
高血圧	0	0	0	1 (2.8)	1 (2.1)
静脈炎	0	0	0	0	1 (2.1)

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

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=30) (PYs=0.5) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=65) (PYs=0.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=82) (PYs=1.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=178) (PYs=36.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=212) (PYs=48.2) Events (E/100PYs)
Subgroup:>= 12 - < 15 Month (Cont.)					
血管障害 (Cont.)					
レイノー現象	0	0	0	1 (2.8)	0
白衣性高血圧	0	0	0	0	1 (2.1)

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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month					
Any adverse event	0	0	0	68 (231.6)	73 (186.9)
血液およびリンパ系障害	0	0	0	2 (6.8)	3 (7.7)
貧血	0	0	0	1 (3.4)	0
鉄欠乏性貧血	0	0	0	1 (3.4)	0
白血球減少症	0	0	0	0	1 (2.6)
好中球減少症	0	0	0	0	2 (5.1)
心臓障害	0	0	0	1 (3.4)	0
完全房室ブロック	0	0	0	1 (3.4)	0
耳および迷路障害	0	0	0	0	2 (5.1)
メニエール病	0	0	0	0	1 (2.6)
耳鳴	0	0	0	0	1 (2.6)
眼障害	0	0	0	0	3 (7.7)
無水晶体眼	0	0	0	0	1 (2.6)

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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
眼障害 (Cont.)					
白内障	0	0	0	0	1 (2.6)
角膜浮腫	0	0	0	0	1 (2.6)
胃腸障害	0	0	0	8 (27.2)	4 (10.2)
上腹部痛	0	0	0	1 (3.4)	0
腹部圧痛	0	0	0	1 (3.4)	0
潰瘍性大腸炎	0	0	0	2 (6.8)	2 (5.1)
齲歯	0	0	0	0	1 (2.6)
口唇障害	0	0	0	1 (3.4)	0
悪心	0	0	0	2 (6.8)	0
歯痛	0	0	0	1 (3.4)	0
嘔吐	0	0	0	0	1 (2.6)
一般・全身障害および投与部位の状態	0	0	0	11 (37.5)	3 (7.7)
悪寒	0	0	0	1 (3.4)	1 (2.6)

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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
一般・全身障害および投与部位の状態 (Cont.)					
疲労	0	0	0	2 (6.8)	1 (2.6)
注射部位疼痛	0	0	0	5 (17.0)	1 (2.6)
倦怠感	0	0	0	2 (6.8)	0
発熱	0	0	0	1 (3.4)	0
肝胆道系障害	0	0	0	2 (6.8)	0
胆道ジスキネジア	0	0	0	1 (3.4)	0
脂肪肝	0	0	0	1 (3.4)	0
免疫系障害	0	0	0	0	1 (2.6)
アナフィラキシー反応	0	0	0	0	1 (2.6)
感染症および寄生虫症	0	0	0	17 (57.9)	19 (48.6)
気管支炎	0	0	0	0	1 (2.6)
COVID-19	0	0	0	2 (6.8)	4 (10.2)
COVID-19肺炎	0	0	0	0	1 (2.6)

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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
カンピロバクター胃腸炎	0	0	0	1 (3.4)	0
蜂巣炎	0	0	0	3 (10.2)	1 (2.6)
クロストリジウム・ディフィシレ感染	0	0	0	1 (3.4)	1 (2.6)
膀胱炎	0	0	0	1 (3.4)	1 (2.6)
耳感染	0	0	0	1 (3.4)	0
帯状疱疹	0	0	0	0	1 (2.6)
麦粒腫	0	0	0	1 (3.4)	0
上咽頭炎	0	0	0	2 (6.8)	1 (2.6)
口腔ヘルペス	0	0	0	0	1 (2.6)
歯周炎	0	0	0	0	1 (2.6)
扁桃周囲炎	0	0	0	1 (3.4)	0
ウイルス性気道感染	0	0	0	1 (3.4)	0
副鼻腔炎	0	0	0	1 (3.4)	2 (5.1)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=128) (PYs=29.4) Events (E/100PYs)	 UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
足部白癬	0	0	0	0	1 (2.6)
扁桃炎	0	0	0	1 (3.4)	0
上気道感染	0	0	0	1 (3.4)	0
尿路感染	0	0	0	0	1 (2.6)
ウイルス性上気道感染	0	0	0	0	1 (2.6)
外陰部腟カンジダ症	0	0	0	0	1 (2.6)
傷害、中毒および処置合併症	0	0	0	1 (3.4)	2 (5.1)
挫傷	0	0	0	1 (3.4)	0
足骨折	0	0	0	0	1 (2.6)
四肢損傷	0	0	0	0	1 (2.6)
臨床検査	0	0	0	5 (17.0)	8 (20.5)
細菌検査陽性	0	0	0	1 (3.4)	0
血中コレステロール増加	0	0	0	0	1 (2.6)

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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
臨床検査 (Cont.)					
血中クレアチンホスホキナーゼ増加	0	0	0	0	3 (7.7)
血中リン減少	0	0	0	0	1 (2.6)
尿中血陽性	0	0	0	0	1 (2.6)
γ-グルタミルトランスフェラーゼ増加	0	0	0	1 (3.4)	0
尿中ブドウ糖陽性	0	0	0	1 (3.4)	0
高比重リポ蛋白増加	0	0	0	1 (3.4)	0
好中球数減少	0	0	0	0	1 (2.6)
尿中蛋白陽性	0	0	0	1 (3.4)	0
白血球数減少	0	0	0	0	1 (2.6)
代謝および栄養障害	0	0	0	2 (6.8)	2 (5.1)
高コレステロール血症	0	0	0	0	1 (2.6)
高血糖	0	0	0	1 (3.4)	0
ビタミンD欠乏	0	0	0	1 (3.4)	1 (2.6)

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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
筋骨格系および結合組織障害	0	0	0	5 (17.0)	8 (20.5)
関節痛	0	0	0	1 (3.4)	2 (5.1)
背部痛	0	0	0	1 (3.4)	1 (2.6)
椎間板突出	0	0	0	0	1 (2.6)
筋痙縮	0	0	0	0	1 (2.6)
筋骨格痛	0	0	0	1 (3.4)	0
筋肉痛	0	0	0	2 (6.8)	1 (2.6)
四肢痛	0	0	0	0	2 (5.1)
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	0	0	1 (3.4)	3 (7.7)
基底細胞癌	0	0	0	0	1 (2.6)
髄膜腫	0	0	0	0	1 (2.6)
子宮頚部扁平上皮癌	0	0	0	0	1 (2.6)
子宮平滑筋腫	0	0	0	1 (3.4)	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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
神経系障害	0	0	0	7 (23.8)	5 (12.8)
頚髄圧迫	0	0	0	0	1 (2.6)
注意力障害	0	0	0	1 (3.4)	0
頭痛	0	0	0	4 (13.6)	0
感覚鈍麻	0	0	0	0	1 (2.6)
片頭痛	0	0	0	1 (3.4)	0
脊髄症	0	0	0	0	1 (2.6)
睡眠の質低下	0	0	0	0	1 (2.6)
会話障害	0	0	0	1 (3.4)	0
視野欠損	0	0	0	0	1 (2.6)
精神障害	0	0	0	0	1 (2.6)
故意の自傷行為	0	0	0	0	1 (2.6)

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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
腎および尿路障害	0	0	0	0	1 (2.6)
蛋白尿	0	0	0	0	1 (2.6)
生殖系および乳房障害	0	0	0	0	1 (2.6)
閉経後出血	0	0	0	0	1 (2.6)
呼吸器、胸郭および縦隔障害	0	0	0	1 (3.4)	1 (2.6)
呼吸困難	0	0	0	1 (3.4)	0
肺塞栓症	0	0	0	0	1 (2.6)
皮膚および皮下組織障害	0	0	0	4 (13.6)	5 (12.8)
ざ瘡	0	0	0	0	1 (2.6)
光線角化症	0	0	0	0	1 (2.6)
ざ瘡様皮膚炎	0	0	0	0	1 (2.6)
接触皮膚炎	0	0	0	1 (3.4)	0
異汗性湿疹	0	0	0	0	1 (2.6)
斑状出血	0	0	0	1 (3.4)	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

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=128) (PYs=29.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=172) (PYs=39.1) Events (E/100PYs)
Subgroup:>= 15 - < 18 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
発疹	0	0	0	1 (3.4)	0
紅斑性皮疹	0	0	0	1 (3.4)	0
皮膚病変	0	0	0	0	1 (2.6)
外科および内科処置	0	0	0	0	1 (2.6)
抜歯	0	0	0	0	1 (2.6)
血管障害	0	0	0	1 (3.4)	0
大動脈硬化症	0	0	0	1 (3.4)	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

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=109) (PYs=25.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=140) (PYs=30.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month					
Any adverse event	0	0	0	43 (171.7)	56 (183.1)
耳および迷路障害	0	0	0	1 (4.0)	0
耳痛	0	0	0	1 (4.0)	0
眼障害	0	0	0	2 (8.0)	1 (3.3)
アレルギー性結膜炎	0	0	0	0	1 (3.3)
黄斑浮腫	0	0	0	1 (4.0)	0
網膜静脈閉塞	0	0	0	1 (4.0)	0
胃腸障害	0	0	0	1 (4.0)	8 (26.2)
潰瘍性大腸炎	0	0	0	0	2 (6.5)
腸炎	0	0	0	0	1 (3.3)
胃食道逆流性疾患	0	0	0	1 (4.0)	0
痔核	0	0	0	0	1 (3.3)
鼠径ヘルニア	0	0	0	0	1 (3.3)

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

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=109) (PYs=25.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=140) (PYs=30.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month (Cont.)					
胃腸障害 (Cont.)					
悪心	0	0	0	0	1 (3.3)
歯痛	0	0	0	0	1 (3.3)
嘔吐	0	0	0	0	1 (3.3)
一般・全身障害および投与部位の状態	0	0	0	8 (31.9)	6 (19.6)
無力症	0	0	0	1 (4.0)	0
悪寒	0	0	0	1 (4.0)	0
疲労	0	0	0	1 (4.0)	0
注射部位疼痛	0	0	0	2 (8.0)	1 (3.3)
倦怠感	0	0	0	1 (4.0)	0
発熱	0	0	0	2 (8.0)	5 (16.4)
感染症および寄生虫症	0	0	0	10 (39.9)	21 (68.7)
肛門膿瘍	0	0	0	0	1 (3.3)
虫垂炎	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

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=109) (PYs=25.0) Events (E/100PYs)	 UPA 30 mg QD (N=140) (PYs=30.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
COVID-19	0	0	0	1 (4.0)	5 (16.4)
COVID-19肺炎	0	0	0	1 (4.0)	1 (3.3)
クロストリジウム・ディフィシレ感染	0	0	0	0	1 (3.3)
膀胱炎	0	0	0	2 (8.0)	0
毛嚢虫症	0	0	0	0	1 (3.3)
胃腸炎	0	0	0	0	2 (6.5)
ヘルペス眼感染	0	0	0	0	1 (3.3)
帯状疱疹	0	0	0	2 (8.0)	3 (9.8)
大腸感染	0	0	0	0	1 (3.3)
上咽頭炎	0	0	0	1 (4.0)	1 (3.3)
外耳炎	0	0	0	1 (4.0)	0
副鼻腔炎	0	0	0	1 (4.0)	0
皮下組織膿瘍	0	0	0	0	1 (3.3)

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

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=109) (PYs=25.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=140) (PYs=30.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
尿路感染	0	0	0	0	1 (3.3)
ガードネレラ菌性膣炎	0	0	0	0	1 (3.3)
創傷感染	0	0	0	0	1 (3.3)
傷害、中毒および処置合併症	0	0	0	2 (8.0)	0
足骨折	0	0	0	1 (4.0)	0
ストレス骨折	0	0	0	1 (4.0)	0
臨床検査	0	0	0	2 (8.0)	3 (9.8)
尿中血陽性	0	0	0	0	1 (3.3)
ヘモグロビン減少	0	0	0	1 (4.0)	0
好中球数減少	0	0	0	0	1 (3.3)
尿中蛋白陽性	0	0	0	0	1 (3.3)
尿中白血球エステラーゼ陽性	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

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=109) (PYs=25.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=140) (PYs=30.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month (Cont.)					
代謝および栄養障害	0	0	0	0	1 (3.3)
高ナトリウム血症	0	0	0	0	1 (3.3)
筋骨格系および結合組織障害	0	0	0	7 (27.9)	1 (3.3)
関節痛	0	0	0	5 (20.0)	1 (3.3)
四肢拘縮	0	0	0	1 (4.0)	0
弾発指	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	1 (4.0)	0
血管腫	0	0	0	1 (4.0)	0
神経系障害	0	0	0	4 (16.0)	4 (13.1)
頭痛	0	0	0	2 (8.0)	1 (3.3)
片頭痛	0	0	0	1 (4.0)	0
後頭神経痛	0	0	0	1 (4.0)	0
失神寸前の状態	0	0	0	0	2 (6.5)
坐骨神経痛	0	0	0	0	1 (3.3)

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

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=109) (PYs=25.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=140) (PYs=30.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month (Cont.)					
精神障害	0	0	0	0	1 (3.3)
不眠症	0	0	0	0	1 (3.3)
腎および尿路障害	0	0	0	0	1 (3.3)
急性腎障害	0	0	0	0	1 (3.3)
生殖系および乳房障害	0	0	0	1 (4.0)	2 (6.5)
良性前立腺肥大症	0	0	0	0	1 (3.3)
不規則月経	0	0	0	1 (4.0)	0
前立腺炎	0	0	0	0	1 (3.3)
呼吸器、胸郭および縦隔障害	0	0	0	0	1 (3.3)
肺塞栓症	0	0	0	0	1 (3.3)
皮膚および皮下組織障害	0	0	0	3 (12.0)	5 (16.4)
ざ瘡	0	0	0	2 (8.0)	1 (3.3)
異汗性湿疹	0	0	0	0	1 (3.3)

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

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=109) (PYs=25.0) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=140) (PYs=30.6) Events (E/100PYs)
Subgroup:>= 18 - < 21 Month (Cont.)					
皮膚および皮下組織障害 (Cont.)					
湿疹	0	0	0	1 (4.0)	0
皮脂欠乏性湿疹	0	0	0	0	1 (3.3)
発疹	0	0	0	0	1 (3.3)
乾皮症	0	0	0	0	1 (3.3)
血管障害	0	0	0	1 (4.0)	1 (3.3)
深部静脈血栓症	0	0	0	0	1 (3.3)
高血圧	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

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=90) (PYs=19.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=109) (PYs=23.4) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month					
Any adverse event	0	0	0	31 (159.7)	44 (188.0)
耳および迷路障害	0	0	0	0	3 (12.8)
聴力低下	0	0	0	0	1 (4.3)
耳漏	0	0	0	0	1 (4.3)
回転性めまい	0	0	0	0	1 (4.3)
眼障害	0	0	0	0	1 (4.3)
ドライアイ	0	0	0	0	1 (4.3)
胃腸障害	0	0	0	5 (25.8)	10 (42.7)
腹痛	0	0	0	0	2 (8.5)
肛門ポリープ	0	0	0	0	1 (4.3)
潰瘍性大腸炎	0	0	0	1 (5.2)	3 (12.8)
便秘	0	0	0	0	1 (4.3)
下痢	0	0	0	1 (5.2)	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

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=90) (PYs=19.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=109) (PYs=23.4) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month (Cont.)					
胃腸障害 (Cont.)					
消化不良	0	0	0	1 (5.2)	0
痔核	0	0	0	1 (5.2)	0
大腸ポリープ	0	0	0	1 (5.2)	1 (4.3)
直腸ポリープ	0	0	0	0	1 (4.3)
埋伏歯	0	0	0	0	1 (4.3)
一般・全身障害および投与部位の状態	0	0	0	3 (15.5)	5 (21.4)
疲労	0	0	0	1 (5.2)	1 (4.3)
注射部位疼痛	0	0	0	1 (5.2)	3 (12.8)
疼痛	0	0	0	1 (5.2)	0
発熱	0	0	0	0	1 (4.3)
肝胆道系障害	0	0	0	2 (10.3)	0
硬化性胆管炎	0	0	0	1 (5.2)	0
肝機能異常	0	0	0	1 (5.2)	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

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=90) (PYs=19.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=109) (PYs=23.4) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month (Cont.)					
感染症および寄生虫症	0	0	0	7 (36.1)	14 (59.8)
肛門膿瘍	0	0	0	0	1 (4.3)
COVID-19	0	0	0	1 (5.2)	2 (8.5)
膀胱炎	0	0	0	1 (5.2)	0
耳感染	0	0	0	0	1 (4.3)
胃腸炎	0	0	0	0	1 (4.3)
鼠径部膿瘍	0	0	0	1 (5.2)	0
帯状疱疹	0	0	0	2 (10.3)	4 (17.1)
上咽頭炎	0	0	0	0	2 (8.5)
口腔カンジダ症	0	0	0	0	1 (4.3)
上気道感染	0	0	0	2 (10.3)	1 (4.3)
尿路感染	0	0	0	0	1 (4.3)

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

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=90) (PYs=19.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=109) (PYs=23.4) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month (Cont.)					
傷害、中毒および処置合併症	0	0	0	0	2 (8.5)
節足動物咬傷	0	0	0	0	1 (4.3)
処置後出血	0	0	0	0	1 (4.3)
臨床検査	0	0	0	3 (15.5)	1 (4.3)
血中クレアチンホスホキナーゼ増加	0	0	0	1 (5.2)	1 (4.3)
γ-グルタミルトランスフェラーゼ増加	0	0	0	1 (5.2)	0
単球数増加	0	0	0	1 (5.2)	0
代謝および栄養障害	0	0	0	3 (15.5)	0
食欲減退	0	0	0	1 (5.2)	0
高脂血症	0	0	0	2 (10.3)	0
筋骨格系および結合組織障害	0	0	0	6 (30.9)	2 (8.5)
関節痛	0	0	0	1 (5.2)	1 (4.3)
滑液包炎	0	0	0	0	1 (4.3)
ばち状指	0	0	0	1 (5.2)	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

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=90) (PYs=19.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=109) (PYs=23.4) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
筋骨格系胸痛	0	0	0	1 (5.2)	0
筋肉痛	0	0	0	3 (15.5)	0
神経系障害	0	0	0	2 (10.3)	0
頭痛	0	0	0	2 (10.3)	0
腎および尿路障害	0	0	0	0	1 (4.3)
膀胱結石	0	0	0	0	1 (4.3)
生殖系および乳房障害	0	0	0	0	1 (4.3)
不正子宮出血	0	0	0	0	1 (4.3)
呼吸器、胸郭および縦隔障害	0	0	0	0	1 (4.3)
過換気	0	0	0	0	1 (4.3)
皮膚および皮下組織障害	0	0	0	0	2 (8.5)
寝汗	0	0	0	0	1 (4.3)
蕁麻疹	0	0	0	0	1 (4.3)

TABLE 2.4 6.1.3

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=90) (PYs=19.4) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=109) (PYs=23.4) Events (E/100PYs)

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

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=90) (PYs=19.4) Events (E/100PYs)	 UPA 30 mg QD (N=109) (PYs=23.4) Events (E/100PYs)
Subgroup:>= 21 - < 24 Month (Cont.)					
外科および内科処置	0	0	0	0	1 (4.3)
歯科インプラント埋込み	0	0	0	0	1 (4.3)

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

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=67) (PYs=51.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month					
Any adverse event	0	0	0	103 (201.2)	60 (181.5)
血液およびリンパ系障害	0	0	0	4 (7.8)	2 (6.0)
貧血	0	0	0	1 (2.0)	0
内出血発生の増加傾向	0	0	0	0	1 (3.0)
白血球減少症	0	0	0	3 (5.9)	1 (3.0)
先天性、家族性および遺伝性障害	0	0	0	1 (2.0)	0
陰嚢水瘤	0	0	0	1 (2.0)	0
耳および迷路障害	0	0	0	1 (2.0)	0
回転性めまい	0	0	0	1 (2.0)	0
眼障害	0	0	0	2 (3.9)	1 (3.0)
緑内障	0	0	0	0	1 (3.0)
近視	0	0	0	1 (2.0)	0
硝子体浮遊物	0	0	0	1 (2.0)	0

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

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=67) (PYs=51.2) Events (E/100PYs)	 UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
胃腸障害	0	0	0	11 (21.5)	8 (24.2)
腹痛	0	0	0	2 (3.9)	0
下腹部痛	0	0	0	1 (2.0)	0
上腹部痛	0	0	0	0	1 (3.0)
痔瘻	0	0	0	0	1 (3.0)
潰瘍性大腸炎	0	0	0	1 (2.0)	4 (12.1)
便秘	0	0	0	0	1 (3.0)
消化器痛	0	0	0	1 (2.0)	0
痔核	0	0	0	0	1 (3.0)
腸管ポリープ	0	0	0	1 (2.0)	0
過敏性腸症候群	0	0	0	1 (2.0)	0
大腸ポリープ	0	0	0	1 (2.0)	0
悪心	0	0	0	3 (5.9)	0

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

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=67) (PYs=51.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
一般・全身障害および投与部位の状態	0	0	0	8 (15.6)	7 (21.2)
疲労	0	0	0	4 (7.8)	1 (3.0)
注射部位疼痛	0	0	0	2 (3.9)	2 (6.0)
疼痛	0	0	0	1 (2.0)	1 (3.0)
発熱	0	0	0	1 (2.0)	3 (9.1)
感染症および寄生虫症	0	0	0	17 (33.2)	14 (42.3)
COVID-19	0	0	0	2 (3.9)	2 (6.0)
COVID-19肺炎	0	0	0	1 (2.0)	1 (3.0)
カンピロバクター感染	0	0	0	1 (2.0)	0
カンジダ感染	0	0	0	1 (2.0)	0
結膜炎	0	0	0	1 (2.0)	0
コロナウイルス感染	0	0	0	1 (2.0)	0
膀胱炎	0	0	0	1 (2.0)	0

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

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=67) (PYs=51.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
胃腸炎	0	0	0	0	1 (3.0)
ヘリコバクター感染	0	0	0	1 (2.0)	0
膿痂疹	0	0	0	1 (2.0)	0
インフルエンザ	0	0	0	0	1 (3.0)
潜伏結核	0	0	0	1 (2.0)	0
上咽頭炎	0	0	0	2 (3.9)	1 (3.0)
口腔ヘルペス	0	0	0	0	4 (12.1)
爪囲炎	0	0	0	0	1 (3.0)
咽頭炎	0	0	0	0	2 (6.0)
歯髄炎	0	0	0	1 (2.0)	0
白癬感染	0	0	0	0	1 (3.0)
足部白癬	0	0	0	1 (2.0)	0
尿路感染	0	0	0	2 (3.9)	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

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=67) (PYs=51.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
傷害、中毒および処置合併症	0	0	0	5 (9.8)	0
熱射病	0	0	0	1 (2.0)	0
関節損傷	0	0	0	1 (2.0)	0
靭帯断裂	0	0	0	1 (2.0)	0
過量投与	0	0	0	1 (2.0)	0
脛骨骨折	0	0	0	1 (2.0)	0
臨床検査	0	0	0	15 (29.3)	2 (6.0)
アラニンアミノトランスフェラーゼ増加	0	0	0	2 (3.9)	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	1 (2.0)	0
血中クレアチンホスホキナーゼ増加	0	0	0	0	1 (3.0)
血圧上昇	0	0	0	1 (2.0)	0
ヘマトクリット減少	0	0	0	1 (2.0)	0
ヘモグロビン減少	0	0	0	1 (2.0)	0

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

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=67) (PYs=51.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
臨床検査 (Cont.)					
肝酵素上昇	0	0	0	1 (2.0)	0
リンパ球数減少	0	0	0	2 (3.9)	1 (3.0)
平均赤血球容積増加	0	0	0	1 (2.0)	0
好中球数減少	0	0	0	1 (2.0)	0
好中球数増加	0	0	0	1 (2.0)	0
赤血球数減少	0	0	0	1 (2.0)	0
尿中白血球エステラーゼ陽性	0	0	0	1 (2.0)	0
白血球数減少	0	0	0	1 (2.0)	0
代謝および栄養障害	0	0	0	3 (5.9)	2 (6.0)
高コレステロール血症	0	0	0	0	2 (6.0)
高脂血症	0	0	0	1 (2.0)	0
鉄欠乏	0	0	0	1 (2.0)	0
過少体重	0	0	0	1 (2.0)	0

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

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=67) (PYs=51.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
筋骨格系および結合組織障害	0	0	0	14 (27.3)	9 (27.2)
関節痛	0	0	0	2 (3.9)	5 (15.1)
関節障害	0	0	0	1 (2.0)	0
背部痛	0	0	0	2 (3.9)	0
軟骨萎縮	0	0	0	1 (2.0)	0
椎間板突出	0	0	0	1 (2.0)	1 (3.0)
関節滲出液	0	0	0	1 (2.0)	0
筋痙縮	0	0	0	1 (2.0)	0
筋骨格硬直	0	0	0	1 (2.0)	0
頚部痛	0	0	0	1 (2.0)	0
変形性関節症	0	0	0	1 (2.0)	0
四肢痛	0	0	0	0	2 (6.0)
肩回旋筋腱板症候群	0	0	0	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=67) (PYs=51.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
脊椎関節障害	0	0	0	1 (2.0)	0
軟骨下機能不全骨折	0	0	0	1 (2.0)	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 (3.9)	2 (6.0)
基底細胞癌	0	0	0	0	1 (3.0)
肺の良性新生物	0	0	0	1 (2.0)	0
気管支の良性新生物	0	0	0	1 (2.0)	0
皮膚有棘細胞癌	0	0	0	0	1 (3.0)
神経系障害	0	0	0	6 (11.7)	5 (15.1)
脳損傷	0	0	0	1 (2.0)	0
頚動脈硬化症	0	0	0	0	1 (3.0)
手根管症候群	0	0	0	1 (2.0)	0
浮動性めまい	0	0	0	1 (2.0)	1 (3.0)
頭痛	0	0	0	2 (3.9)	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=67) (PYs=51.2) Events (E/100PYs)	 UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
神経系障害 (Cont.)					
前兆を伴う片頭痛	0	0	0	1 (2.0)	0
坐骨神経痛	0	0	0	0	1 (3.0)
傾眠	0	0	0	0	1 (3.0)
精神障害	0	0	0	2 (3.9)	3 (9.1)
不安	0	0	0	1 (2.0)	1 (3.0)
うつ病	0	0	0	0	1 (3.0)
不眠症	0	0	0	1 (2.0)	1 (3.0)
生殖系および乳房障害	0	0	0	2 (3.9)	0
性交出血	0	0	0	1 (2.0)	0
性交困難	0	0	0	1 (2.0)	0
呼吸器、胸郭および縦隔障害	0	0	0	2 (3.9)	2 (6.0)
呼吸困難	0	0	0	1 (2.0)	0
鼻出血	0	0	0	0	1 (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.

Program Source Code: [redacted]

TABLE 2.4 6.1.3

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=67) (PYs=51.2) Events (E/100PYs)	 UPA 30 mg QD (N=77) (PYs=33.1) Events (E/100PYs)
Subgroup:>= 24 Month (Cont.)					
呼吸器、胸郭および縦隔障害 (Cont.)					
肺塞栓症	0	0	0	0	1 (3.0)
副鼻腔うっ血	0	0	0	1 (2.0)	0
皮膚および皮下組織障害	0	0	0	8 (15.6)	3 (9.1)
光線角化症	0	0	0	0	1 (3.0)
脱毛症	0	0	0	1 (2.0)	0
湿疹	0	0	0	1 (2.0)	0
間擦疹	0	0	0	1 (2.0)	0
汗疹	0	0	0	1 (2.0)	0
神経皮膚炎	0	0	0	1 (2.0)	0
発疹	0	0	0	3 (5.9)	1 (3.0)
皮膚病変	0	0	0	0	1 (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).
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Program Source Code: [redacted]

表 2.7.4.7-109.

[redacted]20[redacted] 16:43 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/1541 - CLINICAL/STATISTICAL

TABLE 14.3 2.5.2.1

Listing of Subjects with Treatment-Emergent Adverse Events Leading to Death
(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/UPA 30 MG QD									
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg									
		C1-3 0OL	76 to 665	550	625 /550	N: [redacted] R: EPITHELIOID ANGIOSARCOMA 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: 血管肉腫 L: Angiosarcoma	E: 665 L: 41 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (Concomitant medication or therapy started, DISCONTINUED STUDY, Other: HOSPITALIZATION)	AE: No/No/No/No/No/No S: Yes, death of subject, 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.

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)

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	Interval	Day	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 635	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 2 - UPA 30 MG QD							
[redacted]# Age:5[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted].[redacted] kg							
	C2-3 0DB	1 to 291	168 168	N: [redacted] R: WORSENING OF COVID-19 INFECTION S: 感染症および寄生虫症 P: COVID-19 L: COVID-19	E: 184 L: 17 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, death of subject, hospitalization or prolonged hospitalization O: COVID-19

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	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:5[redacted] Sex:Male Race:MULTIPLE Weight:9[redacted].[redacted] kg								
(Cont.)	C2-3 0DB	1 to 291	184	184	N: [redacted] R: PULMONARY THROMBOEMBOLISM S: 呼吸器、胸郭および縦隔障害 P: 肺塞栓症 L: Pulmonary thromboembolism	E: 184 L: 1 Day	S: SEVERE C: Yes R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: NONE	AE: No/No/No/No/No/Yes S: Yes, death of subject 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.

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							
[redacted]	C1-15OL	1 to 1273	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 2.7.4.7-110.

[redacted]20[redacted] 11:17 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL

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	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 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

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.
& 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	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.
& 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:4[redacted].[redacted] kg								
		SS3-DB	1 to 369	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.
& 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] 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.
& 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:5[redacted].[redacted] kg								
		SS3-DB	1 to 378	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.
& 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:5[redacted].[redacted] kg								
(Cont.)	SS3-DB	1 to 378	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.
& 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] 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.
& 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:5[redacted] Sex:Female Race:WHITE Weight:4[redacted].[redacted] kg									
		SS3-DB	1 to 283	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.
& 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.
& 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.
& 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:								
[redacted] Age:7[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg								
(Cont.)	SS3-DB	1 to 364	106	106 &	S: [redacted] R: SKIN BASAL CELL CARINOMA OF RIGHT TEMPLE 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 face	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.
& 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	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.
& 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.
& 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: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.
& 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: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.
& 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 367	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.
& 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 367	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.
& 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:7[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg									
		SS3-DB	1 to 371	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.
& 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] kg								
	SS3-DB	1 to 263	256	256	S: [redacted] R: PULMONARY CRYPTOCOCCUS NEOFORMANS INFECTION S1: 感染症および寄生虫症 P: クリプトコッカス性肺炎 L: Pulmonary cryptococcosis	O: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN 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.
& 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] kg								
	SS3-DB	1 to 161	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	O: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN 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.
& 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:4[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg									
		SS3-DB	1 to 83	72	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.
& 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 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] kg									
		SS3-DB	1 to 355	42	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.
& 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:4[redacted] kg								
		SS3-DB	1 to 318	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.
& 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	1	9	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 WITHDRAWN 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.
& 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:ASIAN Weight:4[redacted].[redacted] kg								
		SS3-DB	1 to 366	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.
& 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	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.
& 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:10[redacted] kg								
		SS3-DB	1 to 355	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.
& 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 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.
& 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.
& 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 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 m								
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg								
	FU	151 to 784	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.
& 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] 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.
& 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:2[redacted] Sex:Female Race:WHITE Weight:5[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.
& 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:10[redacted] kg								
		SS3-DB	1 to 45	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.
& 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: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.
& 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 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]	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.
& 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:WHITE Weight:8[redacted] kg								
	SS3-DB	1 to 308	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.
& 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: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

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.
& 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] kg								
		SS3-DB	1 to 365	199	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: 18 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.
& 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 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	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.
& 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.
& 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 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.
& 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] kg								
		SS3-DB	1 to 367	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.
& 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:5[redacted].[redacted] kg								
		SS3-DB	1 to 364	276	S: [redacted] R: POLYSEGMENTAL BILATERAL COVID-19 PNEUMONIA S1: 感染症および寄生虫症 P: ＣＯＶＩＤ－１９肺炎 L: COVID-19 pneumonia	E: 288 L: 13 Days	S: MILD 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 PANDEMIC 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.
& 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] kg								
		SS3-DB	1 to 368	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.
& 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] 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.
& 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:4[redacted] Sex:Male Race:WHITE Weight:7[redacted] kg							
		SS3-DB 1 to 319	198	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.
& 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: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.
& 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] 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.
& 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:BLACK OR AFRICAN AMERICAN Weight:7[redacted] kg								
	SS3-DB	1 to 379	308	308	S: [redacted] R: WORSENING ANEMIA S1: 血液およびリンパ系障害 P: 貧血 L: Anemia aggravated	E: 309 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: PER DISCUSSION WITH PI, OTHER CAUSE IS LIKELY CHRONIC UC. SUBJECT'S LAST COLON IN [redacted]20[redacted] SHOWED ACTIVE UC. SUBJECT IS SCHEDULED TO BE EVALUATED [redacted] 20[redacted] 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.
& 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] 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.
& 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] 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.
& 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:2[redacted]	Sex:Female	Race:WHITE	Weight:5[redacted].[redacted] kg				
	SS3-DB	1 to 33	23	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.
& 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:2[redacted] Sex:Female Race:WHITE Weight:5[redacted] kg									
		SS3-DB	1 to 224	14	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.
& 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.
& 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:Female Race:WHITE Weight:5[redacted] kg								
		SS3-DB	1 to 308	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.
& 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: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.
& 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.
& Date is estimated.

Program Source Code: [redacted]

表 2.7.4.7-111.

[redacted]20[redacted] 16:43 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/1541 - 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 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 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)

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	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 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 2 - UPA 30 MG QD								
[redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:7[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	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:7[redacted].[redacted] kg							
	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 2 - UPA 15 MG QD								
[redacted]# Age:4[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg								
	C2-1 5DB	1 to 345	244	244	N: [redacted] R: CONDYLOMA ACUMINATUM 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: 肛門性器疣贅 L: Condyloma acuminatum	E: 313 L: 70 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: TIME LAG FROM THE START OF STUDY MEDICATION ADMINISTRATION TO THE ONSET OF SAE. THE SUBJECT REPORTED NO CLOSE CONTACT WITH INFECTED. THECAUSE REMAINED 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 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] kg							
	C1-3 0OL	61 to 343	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)

INV: [redacted] ([redacted])
TRT: COHORT 1 - UPA 15 MG QD

[redacted]# Age:6[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg

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
	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	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	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:4[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] kg							
	C1-1 5OL	1 to 1100	715	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	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 D								
[redacted]# Age:7[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 1100	715	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	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:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg							
	C2-3 0DB	1 to	218 218	N: [redacted] R: RIGHT INGUINAL HERNIA S: 胃腸障害 P: 鼠径ヘルニア L: Right inguinal hernia	E: 223 L: 6 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: NO EVIDENCE OF THE CAUSE OF HERNIA. 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:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg							
[redacted]	(Cont.) C2-30DB	1 to	218 218	N: [redacted] R: WORSENING OF THE PROSTATIC HYPERTROPHY S: 生殖系および乳房障害 P: 良性前立腺肥大症 L: Prostatic hypertrophy	E: 223 L: 6 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: TRANSURETHRAL RESECTION OF HE PROSTATE WITH GREENLIGHT LASER. O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: RELATED TO AE#2 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:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted] kg							
(Cont.)	C2-30DB	1 to 316	316	N: [redacted] R: BLADDER STONES S: 腎および尿路障害 P: 膀胱結石 L: Stone urinary bladder	E: 319 L: 4 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: MEDICAL HISTORY OF UROLITHIASIS. 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:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg							
(Cont.)	C2-30DB	1 to 338	338	N: [redacted] R: HERPES ZOSTER S: 感染症および寄生虫症 P: 帯状疱疹 L: Herpes zoster		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

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] kg							
	C1-15OL	1 to 368	260	260	N: [redacted] R: MICROCYTIC ANEMIA S: 血液およびリンパ系障害 P: 小球性貧血 L: Microcytic anemia		S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: NONE	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: UPPER AND LOWER ENDOSCOPY WERE PERFORMED, NO BLEEDING LESIONS WERE DETERMINED. GYNECOLOGY REPORT IDENTIFIED MYOMA. BIOPSY OF BONE MARROW CONFIRMED TOXIC MYELOSUPPRESSION, CAUSE STILL 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/UPA 30 MG QD [redacted] Age:3[redacted] Sex:Female Race:WHITE Weight:6[redacted].[redacted] kg							
	C1-1 5OL	1 to 489	434 /-56	N: [redacted] R: CLOSTRIDIUM 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		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: CLOSTRIDIUM DIFFICILE INFECTION IS MORE COMMON IN PATIENTS WITH IBD 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 15 MG QD								
[redacted] Age:5[redacted] Sex:Female Race:MULTIPLE Weight:8[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] ([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	E: 511 L: 378 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 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 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: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	E: 511 L: 378 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: 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 1 - UPA 15 MG QD [redacted] Age:6[redacted] Sex:Male Race:WHITE Weight:10[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.
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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:Male Race:WHITE Weight:7[redacted].[redacted] kg							
	C1-15OL	1 to 164	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 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								
(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	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:2[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg								
[redacted]	C2-1 5DB	1 to 150	150		N: [redacted] R: WORSENING OF MAXILLARY AMELOBLASTOMA. 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: エナメル上皮腫 L: Ameloblastoma	E: 150 L: 1 Day	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: SCHEDULED SURGERY	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization, important medical or surgical intervention O: CEBACEOUS CYST 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 15 MG QD							
[redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:6[redacted].[redacted] kg							
(Cont.)	C2-1 5DB	1 to 164	164	N: [redacted] R: INFECTION IN THE AREA OF EXTRACTION OF THE LEFT FIBULAR SURGICAL FLAP S: 感染症および寄生虫症 P: 術後創感染 L: Surgical site infection	E: 181 L: 18 Days	S: MODERATE C: No R: NO REASONABLE POSSIBILITY A: DRUG INTERRUPTED A: Other: IP WAS ALREDY INTERRUPED SINCE [redacted] O: Concomitant medication or therapy started	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: THE PATIENT UNDERWENT MAXILLARY SURGERY ON [redacted] FOR WHICH HE REQUIRED A SURGICAL FLAP THAT WAS OBTAINED FROM THE LEFT FIBULA AT THE SITE OF THE CURRENT 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.
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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/UPA 30 MG QD							
[redacted] Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
[redacted]	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/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 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	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 1258	153 /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			
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] 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	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: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	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:9[redacted].[redacted] kg							
	C2-3 0DB	1 to	324 324	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: 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: GASTROENTERITIS 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: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: 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	833	875 /833 &	N: [redacted] R: SKIN BASAL CELL CARCINOMA ON TOP OF THE 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	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: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							
[redacted]# Age:3[redacted] Sex:Female Race:BLACK OR AFRICAN AMERICAN Weight:6[redacted].[redacted] kg							
	C2-1 5DB	1 to 365	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							
	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 102	204 /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)

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			
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)

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	Interval	Rx Day of Onset /Dose Escal-ation				
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.)	C1-3 0OL	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	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.)	C1-3 0OL	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	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:9[redacted] kg								
[redacted]	(Cont.) C1-3 0OL	103 to 1260	1362 /1260	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: 1375 L: 14 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: PROSTATA HYPERPLASY 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	1274	1376 /1274	N: [redacted] R: WORSENING PROSTATITIS S: 生殖系および乳房障害 P: 前立腺炎 L: Prostatitis	O: 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 O: PROSTATA HYPERPLASY 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:Female Race:WHITE Weight:6[redacted] kg								
	C1-3 0OL	237 to 1086	812	1048 /812	N: [redacted] R: BREAST CARCINOMA 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: 乳癌 L: 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, hospitalization or prolonged hospitalization O: PATIENT GOT SURGERY ON [redacted]20[redacted] 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	E: 264 L: 216 Days	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							
[redacted]	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 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							
[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 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							
[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	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: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: 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: 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 1134	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	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:6[redacted].[redacted] kg								
	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] 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)

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:BLACK OR AFRICAN AMERICAN Weight:9[redacted].[redacted] kg							
	C1-15OL	1 to 1413	1413	N: [redacted] R: GASTRITIS S: 胃腸障害 P: 胃炎 L: Gastritis	E: 1416 L: 4 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: SUBJECT HISTORY OF GERD AND GASTROPARESIS 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: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	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 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.
# 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:Male Race:WHITE Weight:9[redacted].[redacted] kg								
	C1-15OL	1 to 269	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	E: 247 L: 22 Days	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.
$ Cerebral vascular accident or 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:3[redacted] Sex:Male Race:WHITE Weight:9[redacted].[redacted] kg								
(Cont.)	C1-15OL	1 to 269	253	253	N: [redacted] R: ILEUS S: 胃腸障害 P: イレウス L: Ileus	E: 265 L: 13 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: INTESTINAL 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	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 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.
$ Cerebral vascular accident or 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							
(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.
* 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: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.
* 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							
(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:6[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg							
[redacted]	C1-15OL	1 to 651	651	N: [redacted] R: COVID-19 INFECTION S: 感染症および寄生虫症 P: COVID-19 L: COVID-19		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: DROPLET INFECTION FROM FAMILY 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							
[redacted]	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 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: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 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:ASIAN Weight:6[redacted].[redacted] kg							
(Cont.)	C1-3 0OL	325 to 289	613 /289	N: [redacted] R: UNILATERAL INGUINAL HERNIA, WITHOUT OBSTRUCTION OR GANGRENE, NOT SPECIFIED AS RECURRENT S: 胃腸障害 P: 鼠径ヘルニア L: Inguinal hernia, without mention of obstruction or gangrene		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: RIGHT INGUINAL HERNIA 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:5[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg							
	C2-3 0DB	1 to	424 424	N: [redacted] R: LEFT ANTERIOR PERIANAL FISTULA. S: 胃腸障害 P: 痔瘻 L: Perianal fistula		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: ANAL PAIN AND SWELLING SOMETIMES 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 640	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 640	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)

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			
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD						
[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] kg							
	C2-3 0DB	1 to 406	406	N: [redacted] R: COVID-19 RELATED PNEUMONIA S: 感染症および寄生虫症 P: COVID-19肺炎 L: COVID-19 pneumonia	E: 437 L: 32 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 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:6[redacted].[redacted] kg							
	C1-3 0OL	56 to 816	871 /816	N: [redacted] R: ISCHIORECTAL ABSCESS S: 感染症および寄生虫症 P: 直腸膿瘍 L: Ischiorectal abscess		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

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	64 to	781	844 /781	N: [redacted] R: BIPOLAR DISORDER MANIC EPISODE S: 精神障害 P: 双極1型障害 L: Bipolar affective disorder, manic		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: BIPOLAR DISORDER 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:WHITE	Weight:7[redacted].[redacted] kg				
	C1-3 0OL	76 to 665	471	546 /471	N: [redacted] R: PERICARDITIS, PERICARDIAL EFFUSION S: 心臓障害 P: 心嚢液貯留 L: Pericardial effusion	O: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/Yes/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: MOST LIKELY A VIRAL 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:2[redacted]	Sex:Male	Race:WHITE	Weight:7[redacted] kg				
(Cont.)	C1-3 0OL	76 to 665	471	546 /471	N: [redacted] R: PERICARDITIS, PERICARDIAL EFFUSION S: 心臓障害 P: 心膜炎 L: Pericarditis	O: Yes	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG INTERRUPTED O: Concomitant medication or therapy started	AE: No/Yes/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: MOST LIKELY A VIRAL 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	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] kg							
(Cont.)	C1-3 0OL	76 to 665	548 623 /548	N: [redacted] R: BILATERAL PLURAL EFFUSIONS S: 呼吸器、胸郭および縦隔障害 P: 胸水 L: Effusion pleural	O: Yes	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, life threatening, 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/UPA 30 MG QD							
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted].[redacted] kg							
(Cont.)	C1-30OL	76 to 665	550 625 /550	N: [redacted] R: EPITHELIOID ANGIOSARCOMA 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: 血管肉腫 L: Angiosarcoma	E: 665 L: 41 Days	S: SEVERE C: No R: REASONABLE POSSIBILITY A: DRUG WITHDRAWN O: MULTIPLE (Concomitant medication or therapy started, DISCONTINUED STUDY, Other: HOSPITALIZATION)	AE: No/No/No/No/No/No S: Yes, death of subject, 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:4[redacted] Sex:Female Race:WHITE Weight:8[redacted].[redacted] kg							
	C1-15OL	1 to 180	180	N: [redacted] R: ACUTE APPENDICITIS S: 感染症および寄生虫症 P: 虫垂炎 L: Acute appendicitis	E: 185 L: 6 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, important medical or surgical intervention O: LIKELY A RANDOM EVENT OR POSSIBLY RELATED TO THE IBD PROCESS 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:5[redacted] Sex:Male Race:BLACK OR AFRICAN AMERICAN Weight:10[redacted].[redacted] kg								
	C2-3 0DB	1 to 183	7	7	N: [redacted] R: RIGHT PULMONARY UPPER LOBE SEGMENTAL PULMONARY EMBOLISM S: 呼吸器、胸郭および縦隔障害 P: 肺塞栓症 L: Pulmonary embolism	E: 9 L: 3 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/Yes S: Yes, hospitalization or prolonged hospitalization O: THROMBOPHELIA 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:BLACK OR AFRICAN AMERICAN Weight:10[redacted].[redacted] kg							
(Cont.)	C2-3 0DB	1 to 183	32	32	N: [redacted] R: CHEMICAL USE DISORDER - DEPENDENCE S: 精神障害 P: 薬物依存 L: Drug dependence	E: 58 L: 27 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: ALCOHOL AND COCAINE ADDICTION 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:8[redacted].[redacted] kg							
	C1-15OL	1 to 1184	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)

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	Interval	Rx Day of Onset /Dose Escal-ation	V/N/R/S/P/L	E/L/I	S/C/R/A/O	AE/S/O/A/E
INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 15 MG QD							
[redacted]# Age:6[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
[redacted]	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 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							
[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	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)

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: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	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:3[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg								
[redacted]	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)

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			
INV: [redacted] ([redacted]) TRT: COHORT 1 - UP 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 /-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)

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			
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	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								
	C1-3 0OL	71 to 284	44	114 /44	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)

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			
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 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							
	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 - PLACEBO								
[redacted]# Age:3[redacted] Sex:Female Race:WHITE Weight:5[redacted] kg								
	C2-PBO	1 to	314	314	N: [redacted] R: WORSENING ULCERATIVE COLITIES S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 401 & L: 88 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: WORSENING UC 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:3[redacted] Sex:Female Race:WHITE Weight:5[redacted] kg							
(Cont.)	C2-PBO	1 to 436	436	N: [redacted] R: WORSENING ULCERATIVE COLITIES S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	O: Yes I: 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 O: WORSENING ULCERATIVE COLITIES 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 - PLACEBO							
[redacted] Age:4[redacted] Sex:Male Race:WHITE Weight:8[redacted] kg							
[redacted]	C2-PBO	1 to 384	384	N: [redacted] R: HEADACHE S: 神経系障害 P: 頭痛 L: Headache	E: 389 L: 6 Days 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 O: HYDROCEPHALUS 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	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:Female Race:WHITE Weight:8[redacted].[redacted] kg							
	C2-3 0DB	1 to 514	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 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:ASIAN Weight:6[redacted].[redacted] kg								
[redacted]	C1-15OL	1 to 406	406		N: [redacted] R: HIGHER BRAIN DYSFUNCTION S: 神経系障害 P: 大脳障害 L: Brain disorder NOS	E: 417 L: 12 Days	S: MILD C: No R: NO REASONABLE POSSIBILITY A: DOSE NOT CHANGED O: STRETCHING, LOWER LIMB/TRUNK MUSCLE FACILITATION, STANDING PRACTICE, WALKING PRACTICE, COGNITIVE FUNCTION EVALUATION/TRAINING, NEUROPSYCHOLOGICAL TEST.	AE: No/No/No/No/No/No S: Yes, hospitalization or prolonged hospitalization O: THIS EVENT IS A HOSPITALIZATION FOR TREATMENT OF COMPLICATIONS. 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:1[redacted] Sex:Male Race:ASIAN Weight:6[redacted].[redacted] kg								
	C2-3 0DB	1 to 439	401	401	N: [redacted] R: WORSENING OF UC S: 胃腸障害 P: 潰瘍性大腸炎 L: UC aggravated	E: 412 L: 12 Days	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 O: WORSENING OF UC 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:5[redacted] Sex:Male Race:ASIAN Weight:7[redacted].[redacted] kg							
[redacted]	C2-3 0DB	1 to 463	463	N: [redacted] R: CYTOMEGALOVIRUS INFECTION S: 感染症および寄生虫症 P: サイトメガロウイルス感染 L: Cytomegalovirus infection		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: 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 640	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	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:6[redacted] kg							
[redacted]	C1-15OL	1 to 42	34 /-9	N: [redacted] R: ULCERATIVE COLITIS WORSENING S: 胃腸障害 P: 潰瘍性大腸炎 L: Colitis ulcerative aggravated	E: 127 L: 94 Days 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 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)

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INV: [redacted] ([redacted]) TRT: COHORT 2 - UPA 30 MG QD [redacted] Age:5[redacted] Sex:Male Race:WHITE Weight:8[redacted].[redacted] kg							
	C2-3 0DB	1 to	207 207	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: 225 L: 19 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 PNEUMONIA 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.
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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 2 - UPA 30 MG QD							
[redacted] Age:7[redacted] Sex:Male Race:WHITE Weight:7[redacted] kg							
	C2-3 0DB	1 to	128 128	N: [redacted] R: RIGHT EYE CORNEAL OEDEMA, APHAKIA - RIGHT EYE S: 眼障害 P: 無水晶体眼 L: Aphakia	E: 443 L: 316 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: APHAKIC FOLLOWING PREVIOUS CATARACT 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	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:Male Race:WHITE Weight:7[redacted].[redacted] kg							
[redacted]	(Cont.) C2-30DB	1 to	128 128	N: [redacted] R: RIGHT EYE CORNEAL OEDEMA, APHAKIA - RIGHT EYE S: 眼障害 P: 角膜浮腫 L: Corneal oedema	E: 443 L: 316 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: APHAKIC FOLLOWING PREVIOUS CATARACT SURGERY

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:7[redacted] Sex:Male Race:WHITE Weight:7[redacted] kg								
(Cont.)	C2-30DB	1 to	314	314	N: [redacted] R: VERTIGO S: 耳および迷路障害 P: 回転性めまい L: Vertigo	E: 316 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: SYMPTOMS LIKELY RESIDUAL FROM PREVIOUS STROKE 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 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: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.
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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:Female Race:WHITE Weight:5[redacted].[redacted] kg							
	C1-15OL	1 to 351	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.
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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/UPA 30 MG QD								
[redacted]# Age:2[redacted] Sex:Male Race:WHITE Weight:7[redacted] kg								
	C1-3 0OL	37 to 200	131	167 /131	N: [redacted] R: INTRAABDOMINAL ABSCESS S: 感染症および寄生虫症 P: 腹部膿瘍 L: Intra-abdominal abscess	E: 200 L: 34 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/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 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] 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 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:4[redacted] Sex:Male Race:ASIAN Weight:5[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	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] kg								
(Cont.)	C1-3 0OL	46 to 977	876	921 /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 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:5[redacted] Sex:Female Race:WHITE Weight:5[redacted].[redacted] kg							
[redacted]	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 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: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 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]