TABLE 2.4 3.3.1 J

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

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

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

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

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (2.4) [2.5]	0	1 (2.2) [2.1]	0	2 (3.7) [3.4]
結腸腺癌	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
大腸腺腫	1 (2.4) [2.5]	0	0	0	0
線維腫	0	0	0	0	1 (1.9) [1.7]
皮膚乳頭腫	0	0	0	0	1 (1.9) [1.7]
神経系障害	2 (4.9) [4.9]	2 (4.4) [4.6]	5 (11.1) [11.5]	3 (6.5) [6.3]	6 (11.1) [11.5]
浮動性めまい	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
神経系障害 (Cont.)					
てんかん	1 (2.4) [2.3]	0	0	0	0
頭痛	0	2 (4.4) [4.6]	2 (4.4) [4.8]	2 (4.3) [4.5]	3 (5.6) [5.9]
感覚鈍麻	0	1 (2.2) [2.5]	1 (2.2) [2.3]	1 (2.2) [2.5]	1 (1.9) [2.0]
片頭痛	1 (2.4) [2.5]	0	0	0	0
末梢性ニューロパチー	1 (2.4) [2.5]	0	0	0	0
後頭神経痛	0	0	0	1 (2.2) [1.8]	0
ヘルペス後神経痛	0	0	0	0	1 (1.9) [1.7]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
神経系障害 (Cont.)					
くも膜下出血	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
精神障害	3 (7.3) [7.2]	1 (2.2) [2.1]	2 (4.4) [4.4]	1 (2.2) [2.0]	2 (3.7) [3.6]
不安障害	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
抑うつ気分	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
不眠症	3 (7.3) [7.2]	0	2 (4.4) [4.4]	0	2 (3.7) [3.6]
腎および尿路障害	0	0	2 (4.4) [4.2]	0	2 (3.7) [3.4]
急性腎障害	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
腎および尿路障害 (Cont.)					
尿管結石症	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
生殖系および乳房障害	1 (2.4) [2.3]	2 (4.4) [4.5]	0	2 (4.3) [4.3]	0
月経困難症	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0
不規則月経	1 (2.4) [2.3]	0	0	0	0
前立腺炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
呼吸器、胸郭および縦隔障害	3 (7.3) [7.2]	3 (6.7) [7.0]	3 (6.7) [6.7]	4 (8.7) [9.5]	5 (9.3) [9.3]
咳嗽	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)					
しゃっくり	1 (2.4) [2.5]	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]
口腔咽頭痛	0	0	2 (4.4) [4.2]	1 (2.2) [2.5]	3 (5.6) [5.0]
アレルギー性鼻炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
上気道の炎症	2 (4.9) [4.7]	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.0]
皮膚および皮下組織障害	12 (29.3) [29.2]	8 (17.8) [17.4]	11 (24.4) [24.4]	9 (19.6) [19.4]	15 (27.8) [27.7]
ざ瘡	3 (7.3) [7.2]	2 (4.4) [4.2]	2 (4.4) [4.6]	2 (4.3) [4.1]	2 (3.7) [3.9]
皮脂欠乏症	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
皮膚炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
ざ瘡様皮膚炎	0	0	0	1 (2.2) [2.5]	0
アトピー性皮膚炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0
接触皮膚炎	1 (2.4) [2.5]	0	0	0	0
湿疹	1 (2.4) [2.5]	2 (4.4) [4.6]	2 (4.4) [4.2]	3 (6.5) [6.3]	4 (7.4) [6.7]
皮脂欠乏性湿疹	1 (2.4) [2.5]	0	1 (2.2) [2.1]	0	2 (3.7) [3.6]
瘢痕そう痒感	0	0	0	0	1 (1.9) [2.0]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
脂肪織炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
光線過敏性反応	1 (2.4) [2.3]	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]
そう痒症	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0
壊疽性膿皮症	1 (2.4) [2.5]	0	0	0	0
発疹	2 (4.9) [4.7]	1 (2.2) [2.1]	1 (2.2) [2.3]	1 (2.2) [2.0]	1 (1.9) [2.0]
斑状丘疹状皮疹	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]
脂漏性皮膚炎	4 (9.8) [9.7]	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.1 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)					
蕁麻疹	0	0	4 (8.9) [9.0]	0	4 (7.4) [7.6]
血管障害	1 (2.4) [2.5]	1 (2.2) [2.5]	2 (4.4) [4.8]	1 (2.2) [2.5]	4 (7.4) [7.9]
大動脈瘤	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0
高血圧	0	0	2 (4.4) [4.8]	0	3 (5.6) [6.2]
静脈炎	0	0	0	0	1 (1.9) [1.7]
静脈血栓症	1 (2.4) [2.5]	0	0	0	0

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

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表 2.7.4.7-25.

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TABLE 2.4 3.3.5 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]			
MedDRA 23.0 Preferred Term	Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
Any adverse event	33 (80.5) [80.0]	32 (71.1) [71.5]	40 (88.9) [88.9]	34 (73.9) [74.5]	46 (85.2) [85.4]		
上咽頭炎	5 (12.2) [11.8]	8 (17.8) [18.9]	11 (24.4) [24.0]	9 (19.6) [20.5]	12 (22.2) [22.1]	7.1 (-7.9, 22.0)	12.2 (-3.5, 28.0)
血中クレアチンホスホキナーゼ増加	1 (2.4) [2.3]	5 (11.1) [11.0]	6 (13.3) [13.2]	5 (10.9) [10.6]	8 (14.8) [14.6]	8.7 (-2.6, 19.9)	10.8 (-1.2, 22.9)
帯状疱疹	0	4 (8.9) [8.6]	3 (6.7) [6.7]	5 (10.9) [10.2]	6 (11.1) [10.6]	8.6 (-1.3, 18.6)	6.7 (-2.7, 16.0)
好中球減少症	1 (2.4) [2.3]	0	4 (8.9) [8.6]	0	6 (11.1) [10.4]	-2.3 (-9.9, 5.3)	6.3 (-4.5, 17.0)
好中球数減少	1 (2.4) [2.5]	1 (2.2) [2.5]	4 (8.9) [9.0]	2 (4.3) [4.9]	5 (9.3) [9.2]	-0.1 (-9.0, 8.9)	6.4 (-4.6, 17.5)
口腔ヘルペス	0	2 (4.4) [4.2]	4 (8.9) [9.0]	2 (4.3) [4.1]	5 (9.3) [9.8]	4.2 (-4.1, 12.4)	9.0 (-1.1, 19.0)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
湿疹	1 (2.4) [2.5]	2 (4.4) [4.6]	2 (4.4) [4.2]	3 (6.5) [6.3]	4 (7.4) [6.7]	2.0 (-7.7, 11.8)	1.7 (-7.7, 11.1)
便秘	0	1 (2.2) [2.1]	3 (6.7) [6.7]	1 (2.2) [2.0]	4 (7.4) [7.3]	2.1 (-5.3, 9.5)	6.7 (-2.7, 16.0)
蕁麻疹	0	0	4 (8.9) [9.0]	0	4 (7.4) [7.6]	0.0	9.0 (-1.1, 19.0)
頭痛	0	2 (4.4) [4.6]	2 (4.4) [4.8]	2 (4.3) [4.5]	3 (5.6) [5.9]	4.6 (-4.1, 13.2)	4.8 (-3.8, 13.3)
毛包炎	1 (2.4) [2.3]	1 (2.2) [2.1]	3 (6.7) [6.9]	1 (2.2) [2.0]	3 (5.6) [5.9]	-0.2 (-8.7, 8.3)	4.5 (-5.7, 14.8)
アラニンアミノトランスフェラーゼ増加	0	1 (2.2) [2.5]	3 (6.7) [6.7]	1 (2.2) [2.5]	3 (5.6) [5.6]	2.5 (-5.2, 10.2)	6.7 (-2.7, 16.0)
口腔咽頭痛	0	0	2 (4.4) [4.2]	1 (2.2) [2.5]	3 (5.6) [5.0]	0.0	4.2 (-4.0, 12.4)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] - UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
発熱	0	1 (2.2) [2.5]	3 (6.7) [6.7]	1 (2.2) [2.5]	3 (5.6) [5.6]	2.5 (-5.2, 10.2)	6.7 (-2.7, 16.0)
高血圧	0	0	2 (4.4) [4.8]	0	3 (5.6) [6.2]	0.0	4.8 (-3.8, 13.3)
リンパ球数減少	0	0	2 (4.4) [4.4]	0	3 (5.6) [5.9]	0.0	4.4 (-4.1, 12.9)
ざ瘡	3 (7.3) [7.2]	2 (4.4) [4.2]	2 (4.4) [4.6]	2 (4.3) [4.1]	2 (3.7) [3.9]	-3.0 (-14.1, 8.1)	-2.6 (-13.8, 8.6)
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (4.4) [4.9]	2 (4.4) [4.4]	2 (4.3) [4.9]	2 (3.7) [3.6]	4.9 (-3.8, 13.7)	4.4 (-4.1, 12.9)
貧血	2 (4.9) [4.9]	1 (2.2) [2.5]	2 (4.4) [4.4]	1 (2.2) [2.5]	2 (3.7) [3.6]	-2.4 (-12.3, 7.5)	-0.5 (-11.0, 10.1)
膀胱炎	0	1 (2.2) [2.1]	2 (4.4) [4.4]	1 (2.2) [2.0]	2 (3.7) [3.6]	2.1 (-5.3, 9.5)	4.4 (-4.1, 12.9)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
高コレステロール血症	0	1 (2.2) [2.5]	1 (2.2) [2.1]	1 (2.2) [2.5]	2 (3.7) [3.9]	2.5 (-5.2, 10.2)	2.1 (-5.3, 9.5)
インフルエンザ	0	1 (2.2) [2.0]	2 (4.4) [4.8]	1 (2.2) [1.8]	2 (3.7) [4.2]	2.0 (-5.1, 9.1)	4.8 (-3.8, 13.3)
季節性アレルギー	0	1 (2.2) [2.1]	2 (4.4) [4.4]	1 (2.2) [2.0]	2 (3.7) [3.6]	2.1 (-5.3, 9.5)	4.4 (-4.1, 12.9)
不眠症	3 (7.3) [7.2]	0	2 (4.4) [4.4]	0	2 (3.7) [3.6]	-7.2 (-16.9, 2.5)	-2.8 (-14.1, 8.4)
口内炎	2 (4.9) [4.9]	0	2 (4.4) [4.4]	0	2 (3.7) [3.6]	-4.9 (-13.7, 4.0)	-0.5 (-11.0, 10.1)
皮脂欠乏性湿疹	1 (2.4) [2.5]	0	1 (2.2) [2.1]	0	2 (3.7) [3.6]	-2.5 (-10.3, 5.3)	-0.4 (-9.1, 8.2)
潜伏結核	0	0	1 (2.2) [2.1]	0	2 (3.7) [3.6]	0.0	2.1 (-5.3, 9.5)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] - UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
心室性期外収縮	0	0	0	0	2 (3.7) [3.4]	0.0	0.0
関節痛	4 (9.8) [9.9]	2 (4.4) [4.2]	1 (2.2) [2.3]	4 (8.7) [7.9]	1 (1.9) [2.0]	-5.7 (-17.7, 6.2)	-7.6 (-19.1, 3.8)
白血球数減少	1 (2.4) [2.5]	2 (4.4) [4.6]	1 (2.2) [2.5]	3 (6.5) [7.0]	1 (1.9) [2.3]	2.0 (-7.7, 11.8)	-0.1 (-8.8, 8.7)
上気道感染	0	3 (6.7) [6.7]	1 (2.2) [2.1]	3 (6.5) [6.6]	1 (1.9) [1.7]	6.7 (-2.7, 16.0)	2.1 (-5.3, 9.5)
肝機能異常	0	1 (2.2) [2.1]	0	2 (4.3) [3.8]	1 (1.9) [1.7]	2.1 (-5.3, 9.5)	0.0
回転性めまい	0	1 (2.2) [2.5]	0	2 (4.3) [4.9]	1 (1.9) [2.0]	2.5 (-5.2, 10.2)	0.0
潰瘍性大腸炎	13 (31.7) [31.5]	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [1.7]	-29.4 (-44.5, -14.3)	-31.5 (-46.1, -16.9)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]			
MedDRA 23.0 Preferred Term	Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
発疹	2 (4.9) [4.7]	1 (2.2) [2.1]	1 (2.2) [2.3]	1 (2.2) [2.0]	1 (1.9) [2.0]	-2.6 (-12.0, 6.8)	-2.4 (-11.9, 7.2)
上気道の炎症	2 (4.9) [4.7]	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.0]	-2.2 (-11.9, 7.5)	-4.7 (-13.2, 3.9)
白血球減少症	1 (2.4) [2.3]	0	0	1 (2.2) [1.8]	1 (1.9) [1.7]	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
カンピロバクター胃腸炎	0	0	0	1 (2.2) [2.5]	1 (1.9) [1.7]	0.0	0.0
齲歯	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [2.0]	2.1 (-5.3, 9.5)	0.0
歯肉炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [2.0]	2.5 (-5.2, 10.2)	0.0
感覚鈍麻	0	1 (2.2) [2.5]	1 (2.2) [2.3]	1 (2.2) [2.5]	1 (1.9) [2.0]	2.5 (-5.2, 10.2)	2.3 (-5.2, 9.8)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] - UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
大腸感染	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	1 (1.9) [1.7]	2.5 (-5.2, 10.2)	0.0
筋肉痛	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [1.7]	2.1 (-5.3, 9.5)	0.0
咽頭炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	1 (1.9) [2.3]	2.1 (-5.3, 9.5)	0.0
血中クレアチニン増加	1 (2.4) [2.3]	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	-2.3 (-9.9, 5.3)	-0.0 (-8.7, 8.6)
アレルギー性結膜炎	1 (2.4) [2.5]	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	-2.5 (-10.3, 5.3)	-0.4 (-9.1, 8.2)
しゃっくり	1 (2.4) [2.5]	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	-2.5 (-10.3, 5.3)	-0.1 (-8.8, 8.7)
末梢性浮腫	1 (2.4) [2.3]	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	-2.3 (-9.9, 5.3)	0.1 (-8.4, 8.7)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
光線過敏性反応	1 (2.4) [2.3]	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	-2.3 (-9.9, 5.3)	-0.0 (-8.7, 8.6)
肺炎	1 (2.4) [2.3]	0	0	0	1 (1.9) [2.0]	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
急性腎障害	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
結腸腺癌	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
アナフィラキシー反応	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
皮脂欠乏症	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
血中コレステロール増加	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
霰粒腫	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
胸痛	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
挫傷	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
片耳難聴	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
抑うつ気分	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
糖尿病	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
浮動性めまい	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
ドライアイ	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	0.0	2.5 (-5.0, 9.9)
感染性腸炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
腸炎	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
線維腫	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
足骨折	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
帯状疱疹性髄膜炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
炎症	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
椎間板突出	0	0	0	0	1 (1.9) [2.3]	0.0	0.0
瘢痕そう痒感	0	0	0	0	1 (1.9) [2.0]	0.0	0.0
角膜炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
腰部脊柱管狭窄症	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
メニエール病	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
小球性貧血	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	0.0	2.5 (-5.0, 9.9)
僧帽弁閉鎖不全症	0	0	0	0	1 (1.9) [2.0]	0.0	0.0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]			
MedDRA 23.0 Preferred Term	Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
好中球数増加	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
関節周囲炎	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
歯周病	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
歯周炎	0	0	1 (2.2) [2.3]	0	1 (1.9) [2.0]	0.0	2.3 (-5.2, 9.8)
静脈炎	0	0	0	0	1 (1.9) [1.7]	0.0	0.0
胸膜感染	0	0	1 (2.2) [2.5]	0	1 (1.9) [2.3]	0.0	2.5 (-5.0, 9.9)
ヘルペス後神経痛	0	0	0	0	1 (1.9) [1.7]	0.0	0.0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

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

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]			
MedDRA 23.0 Preferred Term	Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
尿管結石症	0	0	1 (2.2) [2.1]	0	1 (1.9) [1.7]	0.0	2.1 (-5.3, 9.5)
背部痛	3 (7.3) [7.3]	3 (6.7) [6.9]	0	4 (8.7) [9.2]	0	-0.4 (-12.4, 11.6)	-7.3 (-17.1, 2.4)
脂質異常症	0	3 (6.7) [6.2]	0	3 (6.5) [5.9]	0	6.2 (-2.7, 15.1)	0.0
γ-グルタミルトランスフェラーゼ増加	0	3 (6.7) [7.0]	0	3 (6.5) [7.0]	0	7.0 (-2.6, 16.6)	0.0
高比重リポ蛋白増加	0	2 (4.4) [4.6]	0	3 (6.5) [6.3]	0	4.6 (-4.1, 13.2)	0.0
胃腸炎	1 (2.4) [2.5]	2 (4.4) [4.6]	0	2 (4.3) [4.5]	0	2.0 (-7.7, 11.8)	-2.5 (-10.3, 5.2)
痔核	1 (2.4) [2.3]	1 (2.2) [2.1]	0	2 (4.3) [4.5]	0	-0.2 (-8.7, 8.3)	-2.3 (-9.9, 5.2)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] - UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
ダニ皮膚炎	0	2 (4.4) [4.2]	0	2 (4.3) [4.1]	0	4.2 (-4.1, 12.4)	0.0
骨壊死	0	1 (2.2) [2.1]	0	2 (4.3) [4.1]	0	2.1 (-5.3, 9.5)	0.0
脂漏性皮膚炎	4 (9.8) [9.7]	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	-7.7 (-18.9, 3.4)	-9.7 (-20.4, 0.9)
鉄欠乏性貧血	3 (7.3) [7.4]	0	0	1 (2.2) [2.5]	0	-7.4 (-17.3, 2.5)	-7.4 (-17.3, 2.5)
上腹部痛	1 (2.4) [2.5]	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	-0.1 (-9.0, 8.9)	-2.5 (-10.3, 5.2)
アミラーゼ増加	1 (2.4) [2.5]	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	-0.4 (-9.1, 8.2)	-2.5 (-10.3, 5.2)
胃食道逆流性疾患	1 (2.4) [2.3]	0	0	1 (2.2) [2.0]	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
変形性関節症	1 (2.4) [2.3]	0	0	1 (2.2) [1.8]	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
足部白癬	1 (2.4) [2.3]	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	0.1 (-8.7, 8.9)	-2.3 (-9.9, 5.2)
腹痛	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0
下腹部痛	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
不安障害	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
大動脈瘤	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
不整脈	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]			
MedDRA 23.0 Preferred Term	Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
細菌性関節炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
白内障	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
蜂巣炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
虚血性大腸炎	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0
結膜炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
咳嗽	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
感音性難聴	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] - UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
皮膚炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
ざ瘡様皮膚炎	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
アトピー性皮膚炎	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
月経困難症	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0
消化不良	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
ヘリコバクター感染	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
鼠径ヘルニア	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	-- M14-234 Substudy 3 (Cohort 1) [A] -- Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 - (Cohorts 1 and 3) [B] - UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
腸管ポリープ	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
関節損傷	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
リパーゼ増加	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
リンパ球百分率増加	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
筋痙縮	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
筋骨格痛	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
後頭神経痛	0	0	0	1 (2.2) [1.8]	0	0.0	0.0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]			
MedDRA 23.0 Preferred Term	Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
過量投与	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
脂肪織炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
前立腺炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
そう痒症	0	1 (2.2) [2.0]	0	1 (2.2) [1.8]	0	2.0 (-5.1, 9.1)	0.0
肺挫傷	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0
アレルギー性鼻炎	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
胸椎骨折	0	1 (2.2) [2.1]	0	1 (2.2) [2.0]	0	2.1 (-5.3, 9.5)	0.0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
弾発指	0	0	0	1 (2.2) [2.5]	0	0.0	0.0
尿中白血球エステラーゼ陽性	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
硝子体浮遊物	0	0	0	1 (2.2) [1.8]	0	0.0	0.0
体重増加	0	1 (2.2) [2.5]	0	1 (2.2) [2.5]	0	2.5 (-5.2, 10.2)	0.0
麦粒腫	2 (4.9) [5.0]	0	0	0	0	-5.0 (-12.8, 2.8)	-5.0 (-12.8, 2.8)
腹部膨満	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
肛門そう痒症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]			
MedDRA 23.0 Preferred Term	Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
アフタ性潰瘍	1 (2.4) [2.5]	0	0	0	0	-2.5 (-9.9, 5.0)	-2.5 (-9.9, 5.0)
関節障害	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
眼瞼炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
骨挫傷	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
大腸腺腫	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
接触皮膚炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
てんかん	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

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

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
肝損傷	1 (2.4) [2.5]	0	0	0	0	-2.5 (-9.9, 5.0)	-2.5 (-9.9, 5.0)
リンパ球数増加	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
リンパ球減少症	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
倦怠感	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
不規則月経	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
片頭痛	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
伝染性軟属腫	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

MedDRA 23.0 Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) n (%) [SSA%]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	Differences [C] Cohort 1 30 mg - PBO RD (95% CI)
口腔嚢胞	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
筋骨格系胸痛	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
悪心	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
末梢性ニューロパチー	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
口腔カンジダ症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
外耳炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
四肢痛	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]			
MedDRA 23.0 Preferred Term	Placebo QD (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	UPA 15 mg QD (N=46) n (%) [SSA%]	UPA 30 mg QD (N=54) n (%) [SSA%]	Differences [C] Cohort 1 15 mg - PBO RD (95% CI)	30 mg - PBO RD (95% CI)
膵炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
ニューモシスチス・イロベチイ肺炎	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
直腸炎	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
壊疽性膿皮症	1 (2.4) [2.5]	0	0	0	0	-2.5 (-10.3, 5.3)	-2.5 (-10.3, 5.2)
肋骨骨折	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
肩回旋筋腱板症候群	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)
皮下血腫	1 (2.4) [2.3]	0	0	0	0	-2.3 (-9.9, 5.3)	-2.3 (-9.9, 5.2)

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

Program Source Code: [redacted]

TABLE 2.4 3.3.5 J

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

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

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

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表 2.7.4.7-26.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 3.3.2 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=21.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=37.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=37.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=60.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=59.0) Events(E/100 PYs) [SSA E/100 PYs]
Any adverse event	114 (521.1) [515.7]	111 (293.6) [295.8]	128 (345.2) [346.0]	148 (243.4) [249.5]	182 (308.2) [308.1]
血液およびリンパ系障害	10 (45.7) [44.1]	1 (2.6) [3.0]	7 (18.9) [18.6]	4 (6.6) [6.4]	10 (16.9) [16.1]
貧血	3 (13.7) [13.1]	1 (2.6) [3.0]	2 (5.4) [5.4]	1 (1.6) [2.0]	2 (3.4) [3.2]
鉄欠乏性貧血	3 (13.7) [13.7]	0	0	1 (1.6) [2.0]	0
白血球減少症	1 (4.6) [4.2]	0	0	2 (3.3) [2.4]	1 (1.7) [1.4]
リンパ球減少症	1 (4.6) [4.2]	0	0	0	0
小球性貧血	0	0	1 (2.7) [2.7]	0	1 (1.7) [2.7]
好中球減少症	1 (4.6) [4.2]	0	4 (10.8) [10.5]	0	6 (10.2) [8.9]
血小板減少症	1 (4.6) [4.8]	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	--- M14-234 Substudy 3 (Cohort 1) [A] ---			--- M14-234 Substudy 3 (Cohorts 1 and 3) [B] ---	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
心臓障害	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	3 (5.1) [4.6]
不整脈	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
僧帽弁閉鎖不全症	0	0	0	0	1 (1.7) [1.7]
心室性期外収縮	0	0	0	0	2 (3.4) [2.9]
耳および迷路障害	0	2 (5.3) [5.4]	1 (2.7) [2.8]	3 (4.9) [5.6]	3 (5.1) [4.9]
感音性難聴	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
片耳難聴	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
メニエール病	0	0	0	0	1 (1.7) [1.4]
回転性めまい	0	1 (2.6) [3.0]	0	2 (3.3) [4.0]	1 (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.
E/100PYs = Number of events per 100 patient-years.

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

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

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
内分泌障害	0	0	0	0	1 (1.7) [1.7]
甲状腺腫瘤	0	0	0	0	1 (1.7) [1.7]
眼障害	3 (13.7) [13.7]	1 (2.6) [2.5]	4 (10.8) [10.7]	2 (3.3) [2.8]	4 (6.8) [7.2]
眼瞼炎	1 (4.6) [4.8]	0	0	0	0
白内障	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
霰粒腫	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
アレルギー性結膜炎	1 (4.6) [4.8]	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
ドライアイ	0	0	1 (2.7) [2.7]	0	1 (1.7) [2.7]
角膜炎	0	0	1 (2.7) [2.8]	0	1 (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.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=21.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=37.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=37.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=60.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=59.0) Events(E/100 PYs) [SSA E/100 PYs]
眼障害 (Cont.)					
潰瘍性角膜炎	1 (4.6) [4.2]	0	0	0	0
硝子体浮遊物	0	0	0	1 (1.6) [1.2]	0
胃腸障害	29 (132.6) [131.7]	9 (23.8) [22.2]	9 (24.3) [24.7]	14 (23.0) [21.0]	14 (23.7) [22.4]
腹部膨満	1 (4.6) [4.2]	0	0	0	0
腹痛	0	1 (2.6) [2.3]	0	1 (1.6) [1.2]	0
下腹部痛	0	0	0	1 (1.6) [1.2]	0
上腹部痛	1 (4.6) [4.8]	1 (2.6) [3.0]	0	1 (1.6) [2.0]	0
肛門そう痒症	1 (4.6) [4.8]	0	0	0	0
アフタ性潰瘍	1 (4.6) [5.9]	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
虚血性大腸炎	0	1 (2.6) [2.3]	0	1 (1.6) [1.2]	0
潰瘍性大腸炎	13 (59.4) [57.8]	1 (2.6) [2.5]	0	1 (1.6) [1.6]	1 (1.7) [1.4]
便秘	0	1 (2.6) [2.5]	3 (8.1) [8.2]	1 (1.6) [1.6]	4 (6.8) [6.3]
齲歯	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	1 (1.7) [1.7]
消化不良	0	0	0	1 (1.6) [1.2]	0
腸炎	0	0	0	0	1 (1.7) [1.4]
胃食道逆流性疾患	1 (4.6) [4.2]	0	0	1 (1.6) [1.6]	0
歯肉腫脹	1 (4.6) [4.8]	0	0	0	0
舌痛	1 (4.6) [4.8]	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
痔出血	1 (4.6) [4.2]	0	0	0	0
痔核	1 (4.6) [4.2]	2 (5.3) [4.9]	0	3 (4.9) [5.2]	0
血栓性痔核	1 (4.6) [4.8]	0	0	0	0
鼠径ヘルニア	0	1 (2.6) [2.3]	0	1 (1.6) [1.2]	0
腸管ポリープ	0	0	0	1 (1.6) [1.2]	0
口腔嚢胞	1 (4.6) [4.8]	0	0	0	0
悪心	1 (4.6) [4.8]	0	0	0	0
膵炎	1 (4.6) [4.8]	0	0	0	0
歯周病	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=21.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=37.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=37.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=60.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=59.0) Events(E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)					
直腸炎	1 (4.6) [4.2]	0	0	0	0
口内炎	2 (9.1) [8.9]	0	4 (10.8) [11.1]	0	4 (6.8) [6.6]
歯の脱落	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
歯痛	0	0	0	0	1 (1.7) [1.7]
一般・全身障害および投与部位の状態	2 (9.1) [8.3]	1 (2.6) [3.0]	6 (16.2) [16.7]	1 (1.6) [2.0]	6 (10.2) [11.0]
胸痛	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
炎症	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
倦怠感	1 (4.6) [4.2]	0	0	0	0
末梢性浮腫	1 (4.6) [4.2]	0	1 (2.7) [2.7]	0	1 (1.7) [2.7]

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.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)					
発熱	0	1 (2.6) [3.0]	3 (8.1) [8.2]	1 (1.6) [2.0]	3 (5.1) [4.9]
肝胆道系障害	1 (4.6) [5.9]	1 (2.6) [2.5]	0	2 (3.3) [2.8]	1 (1.7) [1.4]
肝機能異常	0	1 (2.6) [2.5]	0	2 (3.3) [2.8]	1 (1.7) [1.4]
肝損傷	1 (4.6) [5.9]	0	0	0	0
免疫系障害	0	1 (2.6) [2.5]	2 (5.4) [5.4]	1 (1.6) [1.6]	3 (5.1) [4.9]
アナフィラキシー反応	0	0	0	0	1 (1.7) [1.7]
季節性アレルギー	0	1 (2.6) [2.5]	2 (5.4) [5.4]	1 (1.6) [1.6]	2 (3.4) [3.2]
感染症および寄生虫症	16 (73.1) [74.2]	39 (103.2) [105.5]	35 (94.4) [95.3]	44 (72.4) [76.8]	50 (84.7) [88.7]
ダニ皮膚炎	0	2 (5.3) [4.9]	0	2 (3.3) [3.2]	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
細菌性関節炎	0	1 (2.6) [3.0]	0	1 (1.6) [2.0]	0
カンピロバクター胃腸炎	0	0	0	1 (1.6) [2.0]	1 (1.7) [1.4]
蜂巣炎	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
結膜炎	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
膀胱炎	0	1 (2.6) [2.5]	2 (5.4) [5.4]	1 (1.6) [1.6]	2 (3.4) [3.2]
感染性腸炎	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
毛包炎	1 (4.6) [4.2]	1 (2.6) [2.5]	3 (8.1) [8.5]	1 (1.6) [1.6]	3 (5.1) [5.2]
胃腸炎	1 (4.6) [4.8]	2 (5.3) [5.4]	0	2 (3.3) [3.6]	0
歯肉炎	0	1 (2.6) [3.0]	0	1 (1.6) [2.0]	1 (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.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
ヘリコバクター感染	0	0	0	1 (1.6) [1.2]	0
帯状疱疹	0	4 (10.6) [10.2]	3 (8.1) [8.2]	5 (8.2) [7.7]	6 (10.2) [9.2]
帯状疱疹性髄膜炎	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
麦粒腫	2 (9.1) [11.7]	0	0	0	0
インフルエンザ	0	1 (2.6) [2.3]	2 (5.4) [5.6]	1 (1.6) [1.2]	2 (3.4) [4.4]
大腸感染	0	1 (2.6) [3.0]	0	1 (1.6) [2.0]	1 (1.7) [1.4]
潜伏結核	0	0	1 (2.7) [2.5]	0	2 (3.4) [3.2]
伝染性軟属腫	1 (4.6) [4.2]	0	0	0	0
上咽頭炎	5 (22.9) [22.5]	14 (37.0) [40.6]	14 (37.8) [37.2]	16 (26.3) [30.1]	16 (27.1) [27.7]

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.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
口腔カンジダ症	1 (4.6) [4.8]	0	0	0	0
口腔ヘルペス	0	4 (10.6) [9.8]	4 (10.8) [11.1]	4 (6.6) [6.5]	8 (13.5) [16.0]
外耳炎	1 (4.6) [4.8]	0	0	0	0
歯周炎	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
咽頭炎	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	1 (1.7) [2.7]
胸膜感染	0	0	1 (2.7) [2.7]	0	1 (1.7) [2.7]
ニューモシスチス・イロベチイ肺炎	1 (4.6) [4.8]	0	0	0	0
肺炎	1 (4.6) [4.2]	0	0	0	1 (1.7) [1.7]
白癬感染	1 (4.6) [4.2]	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)					
足部白癬	1 (4.6) [4.2]	1 (2.6) [3.0]	0	1 (1.6) [2.0]	0
扁桃炎	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
上気道感染	0	3 (7.9) [7.9]	1 (2.7) [2.5]	3 (4.9) [5.2]	1 (1.7) [1.4]
傷害、中毒および処置合併症	4 (18.3) [16.7]	3 (7.9) [7.9]	1 (2.7) [2.8]	4 (6.6) [7.2]	2 (3.4) [3.2]
骨挫傷	1 (4.6) [4.2]	0	0	0	0
挫傷	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
足骨折	0	0	0	0	1 (1.7) [1.4]
熱中症	1 (4.6) [4.2]	0	0	0	0
関節損傷	0	1 (2.6) [3.0]	0	1 (1.6) [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.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)					
過量投与	0	0	0	1 (1.6) [2.0]	0
肺挫傷	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
肋骨骨折	1 (4.6) [4.2]	0	0	0	0
皮下血腫	1 (4.6) [4.2]	0	0	0	0
胸椎骨折	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
臨床検査	7 (32.0) [32.2]	20 (52.9) [55.2]	26 (70.1) [70.0]	29 (47.7) [50.2]	31 (52.5) [50.9]
アラニンアミノトランスフェラーゼ増加	0	1 (2.6) [3.0]	3 (8.1) [8.2]	1 (1.6) [2.0]	3 (5.1) [4.9]
アミラーゼ増加	1 (4.6) [4.8]	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (5.3) [6.0]	2 (5.4) [5.4]	2 (3.3) [4.0]	2 (3.4) [3.2]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
血中コレステロール増加	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
血中クレアチンホスホキナーゼ増加	1 (4.6) [4.2]	5 (13.2) [13.0]	8 (21.6) [21.3]	7 (11.5) [10.5]	11 (18.6) [17.2]
血中クレアチニン増加	1 (4.6) [4.2]	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
γ-グルタミルトランスフェラーゼ増加	0	3 (7.9) [8.4]	0	5 (8.2) [9.6]	0
高比重リポ蛋白増加	0	2 (5.3) [5.4]	0	3 (4.9) [4.8]	0
リパーゼ増加	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
リンパ球数減少	0	0	2 (5.4) [5.4]	0	3 (5.1) [5.8]
リンパ球数増加	1 (4.6) [4.8]	0	0	0	0
リンパ球百分率増加	0	1 (2.6) [3.0]	0	1 (1.6) [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.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)					
好中球数減少	2 (9.1) [9.5]	1 (2.6) [3.0]	7 (18.9) [18.7]	2 (3.3) [4.0]	8 (13.5) [12.3]
好中球数増加	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
尿中白血球エステラーゼ陽性	0	0	0	2 (3.3) [2.4]	0
体重増加	0	1 (2.6) [3.0]	0	1 (1.6) [2.0]	0
白血球数減少	1 (4.6) [4.8]	2 (5.3) [5.4]	1 (2.7) [2.7]	3 (4.9) [5.6]	1 (1.7) [2.7]
代謝および栄養障害	2 (9.1) [9.5]	4 (10.6) [10.2]	1 (2.7) [2.5]	4 (6.6) [6.5]	3 (5.1) [5.5]
糖尿病	0	0	0	0	1 (1.7) [1.4]
脂質異常症	0	3 (7.9) [7.2]	0	3 (4.9) [4.5]	0
高コレステロール血症	0	1 (2.6) [3.0]	1 (2.7) [2.5]	1 (1.6) [2.0]	2 (3.4) [4.1]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=21.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=37.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=37.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=60.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=59.0) Events(E/100 PYs) [SSA E/100 PYs]
代謝および栄養障害 (Cont.)					
高リパーゼ血症	1 (4.6) [4.8]	0	0	0	0
低ナトリウム血症	1 (4.6) [4.8]	0	0	0	0
筋骨格系および結合組織障害	14 (64.0) [63.1]	8 (21.2) [20.6]	3 (8.1) [7.9]	15 (24.7) [24.2]	6 (10.2) [10.4]
関節痛	4 (18.3) [18.5]	2 (5.3) [4.9]	1 (2.7) [2.8]	4 (6.6) [6.1]	2 (3.4) [3.4]
関節障害	1 (4.6) [4.2]	0	0	0	0
背部痛	3 (13.7) [14.8]	3 (7.9) [8.3]	0	4 (6.6) [7.2]	0
椎間板突出	0	0	0	0	1 (1.7) [2.7]
腰部脊柱管狭窄症	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
筋痙縮	0	0	0	1 (1.6) [1.2]	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
筋骨格系胸痛	2 (9.1) [8.3]	0	0	0	0
筋骨格痛	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
筋肉痛	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	1 (1.7) [1.4]
変形性関節症	1 (4.6) [4.2]	0	0	1 (1.6) [1.2]	0
骨壊死	0	1 (2.6) [2.5]	0	2 (3.3) [3.2]	0
四肢痛	1 (4.6) [4.2]	0	0	0	0
関節周囲炎	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
肩回旋筋腱板症候群	1 (4.6) [4.2]	0	0	0	0
腱鞘炎	1 (4.6) [4.8]	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	--- M14-234 Substudy 3 (Cohort 1) [A] ---			---M14-234 Substudy 3 (Cohorts 1 and 3) [B]---	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)					
弾発指	0	0	0	1 (1.6) [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）	1 (4.6) [4.8]	0	1 (2.7) [2.5]	0	3 (5.1) [4.3]
結腸腺癌	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
大腸腺腫	1 (4.6) [4.8]	0	0	0	0
線維腫	0	0	0	0	1 (1.7) [1.4]
皮膚乳頭腫	0	0	0	0	1 (1.7) [1.4]
神経系障害	3 (13.7) [13.7]	3 (7.9) [8.4]	5 (13.5) [13.8]	4 (6.6) [6.8]	7 (11.9) [12.1]
浮動性めまい	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
てんかん	1 (4.6) [4.2]	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	--- M14-234 Substudy 3 (Cohort 1) [A] ---			--- M14-234 Substudy 3 (Cohorts 1 and 3) [B] ---	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)					
頭痛	0	2 (5.3) [5.4]	2 (5.4) [5.6]	2 (3.3) [3.6]	3 (5.1) [5.8]
感覚鈍麻	0	1 (2.6) [3.0]	1 (2.7) [2.8]	1 (1.6) [2.0]	1 (1.7) [1.7]
片頭痛	1 (4.6) [4.8]	0	0	0	0
末梢性ニューロパチー	1 (4.6) [4.8]	0	0	0	0
後頭神経痛	0	0	0	1 (1.6) [1.2]	0
ヘルペス後神経痛	0	0	0	0	1 (1.7) [1.4]
くも膜下出血	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
精神障害	3 (13.7) [13.1]	1 (2.6) [2.5]	3 (8.1) [8.2]	1 (1.6) [1.6]	3 (5.1) [4.9]
不安障害	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	--- M14-234 Substudy 3 (Cohort 1) [A] ---			--- M14-234 Substudy 3 (Cohorts 1 and 3) [B] ---	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
精神障害 (Cont.)					
抑うつ気分	0	0	1 (2.7) [2.8]	0	1 (1.7) [1.7]
不眠症	3 (13.7) [13.1]	0	2 (5.4) [5.4]	0	2 (3.4) [3.2]
腎および尿路障害	0	0	2 (5.4) [5.1]	0	2 (3.4) [2.9]
急性腎障害	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
尿管結石症	0	0	1 (2.7) [2.5]	0	1 (1.7) [1.4]
生殖系および乳房障害	1 (4.6) [4.2]	2 (5.3) [5.3]	0	2 (3.3) [3.2]	0
月経困難症	0	1 (2.6) [2.3]	0	1 (1.6) [1.2]	0
不規則月経	1 (4.6) [4.2]	0	0	0	0
前立腺炎	0	1 (2.6) [3.0]	0	1 (1.6) [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.

SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	--------- M14-234 Substudy 3 (Cohort 1) [A] ---------			---M14-234 Substudy 3 (Cohorts 1 and 3) [B]---	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]	Events(E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害	3 (13.7) [13.1]	3 (7.9) [8.4]	3 (8.1) [7.8]	4 (6.6) [7.6]	5 (8.5) [8.7]
咳嗽	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
しゃっくり	1 (4.6) [4.8]	0	1 (2.7) [2.7]	0	1 (1.7) [2.7]
口腔咽頭痛	0	0	2 (5.4) [5.1]	1 (1.6) [2.0]	3 (5.1) [4.3]
アレルギー性鼻炎	0	1 (2.6) [3.0]	0	1 (1.6) [2.0]	0
上気道の炎症	2 (9.1) [8.3]	1 (2.6) [3.0]	0	1 (1.6) [2.0]	1 (1.7) [1.7]
皮膚および皮下組織障害	14 (64.0) [62.6]	10 (26.5) [25.4]	17 (45.8) [45.5]	12 (19.7) [19.4]	21 (35.6) [34.8]
ざ瘡	3 (13.7) [13.1]	2 (5.3) [4.9]	3 (8.1) [8.0]	2 (3.3) [3.2]	3 (5.1) [6.7]
皮脂欠乏症	0	0	1 (2.7) [2.8]	0	1 (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.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=41) (PYs=21.9) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=45) (PYs=37.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=45) (PYs=37.1) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=46) (PYs=60.8) Events(E/100 PYs) [SSA E/100 PYs]	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=54) (PYs=59.0) Events(E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
皮膚炎	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
ざ瘡様皮膚炎	0	0	0	1 (1.6) [2.0]	0
アトピー性皮膚炎	0	1 (2.6) [2.5]	0	1 (1.6) [1.6]	0
接触皮膚炎	1 (4.6) [4.8]	0	0	0	0
湿疹	1 (4.6) [4.8]	2 (5.3) [5.4]	2 (5.4) [5.1]	3 (4.9) [4.8]	4 (6.8) [5.7]
皮脂欠乏性湿疹	1 (4.6) [4.8]	0	1 (2.7) [2.5]	0	2 (3.4) [3.2]
瘢痕そう痒感	0	0	0	0	1 (1.7) [1.7]
脂肪織炎	0	1 (2.6) [3.0]	0	1 (1.6) [2.0]	0
光線過敏性反応	1 (4.6) [4.2]	0	1 (2.7) [2.8]	0	1 (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.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.
SSA = Study-size adjusted.

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	--- M14-234 Substudy 3 (Cohort 1) [A] ---			--- M14-234 Substudy 3 (Cohorts 1 and 3) [B] ---	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)					
そう痒症	0	1 (2.6) [2.3]	0	1 (1.6) [1.2]	0
壊疽性膿皮症	1 (4.6) [4.8]	0	0	0	0
発疹	2 (9.1) [8.3]	1 (2.6) [2.5]	1 (2.7) [2.8]	1 (1.6) [1.6]	1 (1.7) [1.7]
斑状丘疹状皮疹	0	0	4 (10.8) [10.2]	0	4 (6.8) [5.7]
脂漏性皮膚炎	4 (18.3) [17.9]	1 (2.6) [2.3]	0	1 (1.6) [1.2]	0
蕁麻疹	0	0	4 (10.8) [11.1]	0	4 (6.8) [6.6]
血管障害	1 (4.6) [4.8]	1 (2.6) [3.0]	2 (5.4) [5.6]	1 (1.6) [2.0]	4 (6.8) [7.5]
大動脈瘤	0	1 (2.6) [3.0]	0	1 (1.6) [2.0]	0
高血圧	0	0	2 (5.4) [5.6]	0	3 (5.1) [6.1]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.2 J

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

	M14-234 Substudy 3 (Cohort 1) [A]			M14-234 Substudy 3 (Cohorts 1 and 3) [B]	
	Placebo QD (N=41) (PYs=21.9)	UPA 15 mg QD (N=45) (PYs=37.8)	UPA 30 mg QD (N=45) (PYs=37.1)	UPA 15 mg QD (N=46) (PYs=60.8)	UPA 30 mg QD (N=54) (PYs=59.0)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]
血管障害 (Cont.)					
静脈炎	0	0	0	0	1 (1.7) [1.4]
静脈血栓症	1 (4.6) [4.8]	0	0	0	0

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

Program Source Code: [redacted]

表 2.7.4.7-27.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	694 (576.1)	360 (332.8)	1965 (335.3)
血液およびリンパ系障害	39 (32.4)	11 (10.2)	53 (9.0)
貧血	26 (21.6)	8 (7.4)	23 (3.9)
大球性貧血	0	0	0
失血性貧血	0	0	0
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	1 (0.9)	1 (0.2)
鉄欠乏性貧血	1 (0.8)	0	3 (0.5)
白血球増加症	0	0	4 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	239 (992.5)	1530 (426.3)	1507 (323.3)	1614 (364.0)	6441 (353.7)
血液およびリンパ系障害	23 (95.5)	69 (19.2)	83 (17.8)	57 (12.9)	260 (14.3)
貧血	17 (70.6)	23 (6.4)	25 (5.4)	18 (4.1)	99 (5.4)
大球性貧血	0	0	2 (0.4)	0	2 (0.1)
失血性貧血	0	0	0	2 (0.5)	2 (0.1)
周期性好中球減少症	0	1 (0.3)	0	0	1 (<0.1)
好酸球増加症	0	1 (0.3)	0	0	0
内出血発生の増加傾向	0	1 (0.3)	0	2 (0.5)	4 (0.2)
鉄欠乏性貧血	1 (4.2)	8 (2.2)	3 (0.6)	4 (0.9)	14 (0.8)
白血球増加症	0	1 (0.3)	0	1 (0.2)	5 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)			
白血球減少症	1 (0.8)	0	3 (0.5)
リンパ節症	0	1 (0.9)	0
リンパ球増加症	0	0	0
リンパ球減少症	4 (3.3)	1 (0.9)	8 (1.4)
小球性貧血	0	0	0
好中球減少症	3 (2.5)	0	7 (1.2)
正球性貧血	1 (0.8)	0	0
汎血球減少症	0	0	0
網状赤血球増加症	0	0	1 (0.2)
脾腫	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)					
白血球減少症	0	7 (2.0)	24 (5.1)	5 (1.1)	35 (1.9)
リンパ節症	0	1 (0.3)	0	1 (0.2)	2 (0.1)
リンパ球増加症	0	1 (0.3)	0	0	0
リンパ球減少症	3 (12.5)	10 (2.8)	8 (1.7)	7 (1.6)	34 (1.9)
小球性貧血	0	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
好中球減少症	1 (4.2)	11 (3.1)	16 (3.4)	16 (3.6)	48 (2.6)
正球性貧血	0	0	0	0	0
汎血球減少症	0	0	2 (0.4)	0	2 (0.1)
網状赤血球増加症	0	0	0	0	1 (<0.1)
脾腫	0	0	1 (0.2)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)			
血小板減少症	1 (0.8)	0	0
血小板増加症	1 (0.8)	0	2 (0.3)
心臓障害	12 (10.0)	3 (2.8)	12 (2.0)
急性心筋梗塞	0	0	0
不安定狭心症	0	1 (0.9)	0
不整脈	0	0	0
心房細動	0	0	0
第一度房室ブロック	0	0	0
二束ブロック	0	0	0
徐脈	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)					
血小板減少症	1 (4.2)	2 (0.6)	0	0	2 (0.1)
血小板増加症	0	1 (0.3)	1 (0.2)	0	4 (0.2)
心臓障害	3 (12.5)	9 (2.5)	5 (1.1)	16 (3.6)	42 (2.3)
急性心筋梗塞	0	1 (0.3)	0	0	0
不安定狭心症	0	0	0	0	1 (<0.1)
不整脈	0	0	1 (0.2)	1 (0.2)	2 (0.1)
心房細動	0	2 (0.6)	0	1 (0.2)	2 (0.1)
第一度房室ブロック	0	0	0	1 (0.2)	1 (<0.1)
二束ブロック	0	0	0	1 (0.2)	1 (<0.1)
徐脈	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
心臓障害 (Cont.)			
左脚ブロック	1 (0.8)	0	0
心不全	0	0	0
うっ血性心不全	0	0	0
心拡大	0	0	0
慢性左室不全	0	0	0
冠動脈疾患	0	1 (0.9)	1 (0.2)
虚血性心筋症	0	0	1 (0.2)
僧帽弁閉鎖不全症	0	0	0
心筋梗塞	0	0	1 (0.2)
動悸	6 (5.0)	1 (0.9)	2 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
心臓障害 (Cont.)					
左脚ブロック	0	0	0	0	0
心不全	0	0	0	1 (0.2)	1 (<0.1)
うっ血性心不全	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
心拡大	0	0	0	1 (0.2)	1 (<0.1)
慢性左室不全	0	0	0	1 (0.2)	1 (<0.1)
冠動脈疾患	0	0	0	0	2 (0.1)
虚血性心筋症	0	0	0	0	1 (<0.1)
僧帽弁閉鎖不全症	0	0	0	1 (0.2)	1 (<0.1)
心筋梗塞	0	0	0	0	1 (<0.1)
動悸	2 (8.3)	4 (1.1)	0	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
心臓障害 (Cont.)			
心膜炎	0	0	0
洞性不整脈	1 (0.8)	0	0
洞性徐脈	0	0	0
洞性頻脈	0	0	0
上室性期外収縮	1 (0.8)	0	0
上室性頻脈	0	0	2 (0.3)
頻脈	2 (1.7)	0	1 (0.2)
心室性期外収縮	1 (0.8)	0	1 (0.2)
心室性頻脈	0	0	2 (0.3)
ウォルフ・パーキンソン・ホワイト症候群	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
心臓障害 (Cont.)					
心膜炎	1 (4.2)	0	0	1 (0.2)	2 (0.1)
洞性不整脈	0	0	0	0	0
洞性徐脈	0	0	1 (0.2)	1 (0.2)	2 (0.1)
洞性頻脈	0	0	0	1 (0.2)	1 (<0.1)
上室性期外収縮	0	0	1 (0.2)	0	1 (<0.1)
上室性頻脈	0	0	0	1 (0.2)	3 (0.2)
頻脈	0	1 (0.3)	1 (0.2)	0	3 (0.2)
心室性期外収縮	0	0	0	3 (0.7)	4 (0.2)
心室性頻脈	0	0	0	0	2 (0.1)
ウォルフ・パーキンソン・ホワイト症候群	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
先天性、家族性および遺伝性障害	0	0	2 (0.3)
ジルベール症候群	0	0	1 (0.2)
魚鱗癬	0	0	1 (0.2)
歯原性嚢胞	0	0	0
耳および迷路障害	4 (3.3)	0	15 (2.6)
耳垢栓塞	0	0	1 (0.2)
感音性難聴	0	0	0
片耳難聴	0	0	0
耳不快感	0	0	0
耳痛	1 (0.8)	0	2 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
先天性、家族性および遺伝性障害	0	1 (0.3)	1 (0.2)	0	4 (0.2)
ジルベール症候群	0	0	1 (0.2)	0	2 (0.1)
魚鱗癬	0	0	0	0	1 (<0.1)
歯原性嚢胞	0	1 (0.3)	0	0	1 (<0.1)
耳および迷路障害	2 (8.3)	6 (1.7)	13 (2.8)	7 (1.6)	40 (2.2)
耳垢栓塞	0	0	0	0	1 (<0.1)
感音性難聴	0	0	1 (0.2)	1 (0.2)	2 (0.1)
片耳難聴	0	0	0	1 (0.2)	1 (<0.1)
耳不快感	0	0	1 (0.2)	0	1 (<0.1)
耳痛	0	2 (0.6)	2 (0.4)	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
耳および迷路障害 (Cont.)			
耳部腫脹	0	0	0
外耳道の外骨腫	0	0	0
外耳の炎症	0	0	0
聴力低下	0	0	0
内耳障害	0	0	1 (0.2)
メニエール病	0	0	0
中耳滲出液	0	0	0
突発性難聴	1 (0.8)	0	1 (0.2)
耳鳴	0	0	5 (0.9)
回転性めまい	2 (1.7)	0	5 (0.9)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
耳および迷路障害 (Cont.)					
耳部腫脹	0	1 (0.3)	0	0	0
外耳道の外骨腫	0	1 (0.3)	0	0	0
外耳の炎症	0	1 (0.3)	0	0	1 (<0.1)
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	2 (0.5)	2 (0.1)
中耳滲出液	0	1 (0.3)	0	0	0
突発性難聴	0	0	1 (0.2)	0	2 (0.1)
耳鳴	2 (8.3)	0	3 (0.6)	1 (0.2)	11 (0.6)
回転性めまい	0	0	4 (0.9)	2 (0.5)	11 (0.6)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
内分泌障害	1 (0.8)	1 (0.9)	6 (1.0)
アジソン病	0	0	1 (0.2)
副腎機能不全	0	0	1 (0.2)
急性副腎皮質機能不全	0	0	0
クッシング症候群	0	0	0
クッシング様症状	0	0	3 (0.5)
甲状腺腫	0	0	1 (0.2)
甲状腺機能亢進症	0	1 (0.9)	0
甲状腺機能低下症	1 (0.8)	0	0
甲状腺腫瘤	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
内分泌障害	0	1 (0.3)	2 (0.4)	4 (0.9)	13 (0.7)
アジソン病	0	0	0	0	1 (<0.1)
副腎機能不全	0	0	0	1 (0.2)	2 (0.1)
急性副腎皮質機能不全	0	0	0	1 (0.2)	1 (<0.1)
クッシング症候群	0	1 (0.3)	0	0	0
クッシング様症状	0	0	0	1 (0.2)	4 (0.2)
甲状腺腫	0	0	2 (0.4)	0	3 (0.2)
甲状腺機能亢進症	0	0	0	0	1 (<0.1)
甲状腺機能低下症	0	0	0	0	0
甲状腺腫瘤	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
眼障害	7 (5.8)	4 (3.7)	20 (3.4)
眼精疲労	0	0	0
眼瞼炎	0	0	1 (0.2)
眼瞼痙攣	0	0	1 (0.2)
白内障	1 (0.8)	1 (0.9)	3 (0.5)
霰粒腫	0	0	1 (0.2)
結膜嚢胞	0	0	0
結膜出血	0	0	1 (0.2)
結膜充血	0	0	1 (0.2)
アレルギー性結膜炎	1 (0.8)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害	4 (16.6)	30 (8.4)	17 (3.6)	25 (5.6)	85 (4.7)
眼精疲労	0	1 (0.3)	0	1 (0.2)	1 (<0.1)
眼瞼炎	0	4 (1.1)	0	3 (0.7)	7 (0.4)
眼瞼痙攣	0	0	0	0	1 (<0.1)
白内障	0	3 (0.8)	4 (0.9)	3 (0.7)	13 (0.7)
霰粒腫	1 (4.2)	0	0	4 (0.9)	6 (0.3)
結膜嚢胞	0	1 (0.3)	0	0	1 (<0.1)
結膜出血	0	1 (0.3)	0	2 (0.5)	4 (0.2)
結膜充血	0	1 (0.3)	0	1 (0.2)	2 (0.1)
アレルギー性結膜炎	0	2 (0.6)	0	1 (0.2)	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
眼障害 (Cont.)			
結膜弛緩症	0	0	1 (0.2)
角膜びらん	0	0	1 (0.2)
角膜混濁	0	0	0
後天性涙道狭窄	0	0	0
ドライアイ	0	0	2 (0.3)
上強膜炎	0	1 (0.9)	0
眼のアレルギー	1 (0.8)	0	0
眼の障害	0	0	0
眼出血	0	0	0
眼刺激	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)					
結膜弛緩症	0	0	0	0	1 (<0.1)
角膜びらん	0	0	0	0	1 (<0.1)
角膜混濁	0	1 (0.3)	0	0	0
後天性涙道狭窄	0	1 (0.3)	0	0	1 (<0.1)
ドライアイ	1 (4.2)	1 (0.3)	1 (0.2)	6 (1.4)	11 (0.6)
上強膜炎	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
眼のアレルギー	0	0	0	0	0
眼の障害	0	2 (0.6)	0	0	2 (0.1)
眼出血	0	0	1 (0.2)	0	1 (<0.1)
眼刺激	0	0	1 (0.2)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
眼障害 (Cont.)			
眼痛	0	0	1 (0.2)
眼そう痒症	0	0	0
眼部腫脹	0	0	0
眼瞼嚢胞	0	0	0
眼瞼障害	0	0	0
眼瞼刺激	0	0	0
眼瞼発疹	0	0	0
眼瞼肥厚	0	0	0
緑内障	0	0	0
虹彩毛様体炎	1 (0.8)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)					
眼痛	0	0	0	0	1 (<0.1)
眼そう痒症	0	0	1 (0.2)	0	1 (<0.1)
眼部腫脹	0	0	1 (0.2)	0	1 (<0.1)
眼瞼嚢胞	0	1 (0.3)	0	0	1 (<0.1)
眼瞼障害	0	1 (0.3)	0	0	0
眼瞼刺激	0	1 (0.3)	0	0	1 (<0.1)
眼瞼発疹	0	1 (0.3)	0	0	0
眼瞼肥厚	1 (4.2)	0	0	0	1 (<0.1)
緑内障	0	0	0	1 (0.2)	1 (<0.1)
虹彩毛様体炎	0	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
眼障害 (Cont.)			
角膜炎	0	0	0
流涙増加	0	0	0
眼部不快感	1 (0.8)	0	0
眼充血	0	0	1 (0.2)
高眼圧症	0	0	0
開放隅角緑内障	0	0	1 (0.2)
眼窩周囲腫脹	0	0	0
光視症	0	0	1 (0.2)
翼状片	1 (0.8)	0	0
潰瘍性角膜炎	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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)					
角膜炎	0	1 (0.3)	1 (0.2)	1 (0.2)	2 (0.1)
流涙増加	0	0	1 (0.2)	0	1 (<0.1)
眼部不快感	0	0	0	0	0
眼充血	0	2 (0.6)	1 (0.2)	1 (0.2)	5 (0.3)
高眼圧症	0	0	1 (0.2)	1 (0.2)	2 (0.1)
開放隅角緑内障	0	0	0	0	1 (<0.1)
眼窩周囲腫脹	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
光視症	0	0	0	0	1 (<0.1)
翼状片	0	0	0	0	0
潰瘍性角膜炎	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
眼障害 (Cont.)			
ぶどう膜炎	1 (0.8)	0	0
霧視	0	0	1 (0.2)
視力低下	0	1 (0.9)	0
視力障害	0	0	2 (0.3)
硝子体浮遊物	0	1 (0.9)	0
胃腸障害	157 (130.3)	63 (58.2)	320 (54.6)
腹部不快感	3 (2.5)	2 (1.8)	0
腹部膨満	2 (1.7)	1 (0.9)	11 (1.9)
腹部腫瘤	0	0	0
腹痛	3 (2.5)	1 (0.9)	21 (3.6)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)					
ぶどう膜炎	0	2 (0.6)	1 (0.2)	0	2 (0.1)
霧視	1 (4.2)	0	0	0	2 (0.1)
視力低下	0	0	0	0	0
視力障害	0	0	0	0	2 (0.1)
硝子体浮遊物	0	0	1 (0.2)	0	2 (0.1)
胃腸障害	48 (199.3)	272 (75.8)	213 (45.7)	230 (51.9)	973 (53.4)
腹部不快感	0	1 (0.3)	1 (0.2)	1 (0.2)	4 (0.2)
腹部膨満	2 (8.3)	6 (1.7)	2 (0.4)	11 (2.5)	31 (1.7)
腹部腫瘤	0	1 (0.3)	0	0	0
腹痛	4 (16.6)	14 (3.9)	16 (3.4)	11 (2.5)	60 (3.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
下腹部痛	1 (0.8)	0	2 (0.3)
上腹部痛	5 (4.2)	2 (1.8)	8 (1.4)
腹部圧痛	1 (0.8)	0	7 (1.2)
異常便	0	0	0
無酸症	0	0	0
裂肛	1 (0.8)	0	3 (0.5)
痔瘻	0	0	1 (0.2)
肛門失禁	0	0	1 (0.2)
肛門の炎症	1 (0.8)	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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
下腹部痛	0	7 (2.0)	3 (0.6)	2 (0.5)	10 (0.5)
上腹部痛	0	5 (1.4)	8 (1.7)	6 (1.4)	26 (1.4)
腹部圧痛	1 (4.2)	0	3 (0.6)	4 (0.9)	15 (0.8)
異常便	0	1 (0.3)	0	0	0
無酸症	0	0	0	1 (0.2)	1 (<0.1)
裂肛	1 (4.2)	3 (0.8)	3 (0.6)	2 (0.5)	11 (0.6)
痔瘻	0	0	1 (0.2)	3 (0.7)	5 (0.3)
肛門失禁	0	0	0	0	1 (<0.1)
肛門の炎症	0	0	0	1 (0.2)	1 (<0.1)
肛門そう痒症	0	3 (0.8)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
肛門潰瘍	0	0	0
口角口唇炎	0	0	1 (0.2)
肛門直腸不快感	0	0	0
アフタ性潰瘍	4 (3.3)	1 (0.9)	6 (1.0)
口唇のひび割れ	0	0	1 (0.2)
大腸炎	6 (5.0)	0	2 (0.3)
虚血性大腸炎	0	0	0
潰瘍性大腸炎	77 (63.9)	15 (13.9)	95 (16.2)
結腸異形成	0	0	3 (0.5)
便秘	3 (2.5)	0	7 (1.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (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	4 (1.1)	2 (0.4)	6 (1.4)	17 (0.9)
口唇のひび割れ	0	0	0	0	1 (<0.1)
大腸炎	0	3 (0.8)	2 (0.4)	0	4 (0.2)
虚血性大腸炎	0	0	1 (0.2)	0	1 (<0.1)
潰瘍性大腸炎	21 (87.2)	105 (29.3)	76 (16.3)	48 (10.8)	270 (14.8)
結腸異形成	0	0	2 (0.4)	1 (0.2)	6 (0.3)
便秘	3 (12.5)	8 (2.2)	10 (2.1)	14 (3.2)	40 (2.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
クローン病	0	0	1 (0.2)
便意切迫	2 (1.7)	0	3 (0.5)
齲歯	1 (0.8)	1 (0.9)	1 (0.2)
歯不快感	0	0	1 (0.2)
歯組織の壊死	0	0	1 (0.2)
横隔膜ヘルニア	1 (0.8)	0	0
下痢	0	6 (5.5)	8 (1.4)
血性下痢	0	0	0
腸憩室	0	0	0
口内乾燥	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
クローン病	0	0	0	0	1 (<0.1)
便意切迫	0	0	0	1 (0.2)	4 (0.2)
齲歯	0	4 (1.1)	1 (0.2)	2 (0.5)	8 (0.4)
歯不快感	0	0	0	0	1 (<0.1)
歯組織の壊死	0	0	0	0	1 (<0.1)
横隔膜ヘルニア	0	0	0	0	0
下痢	3 (12.5)	8 (2.2)	7 (1.5)	4 (0.9)	32 (1.8)
血性下痢	1 (4.2)	1 (0.3)	0	0	2 (0.1)
腸憩室	0	0	1 (0.2)	0	1 (<0.1)
口内乾燥	0	1 (0.3)	0	2 (0.5)	4 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
十二指腸炎	0	0	0
排便困難	1 (0.8)	0	0
消化不良	3 (2.5)	0	10 (1.7)
嚥下障害	1 (0.8)	0	1 (0.2)
小腸炎	0	0	0
腸炎	0	0	0
心窩部不快感	0	0	1 (0.2)
おくび	0	0	1 (0.2)
糞塊	1 (0.8)	0	0
変色便	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
十二指腸炎	0	0	0	1 (0.2)	1 (<0.1)
排便困難	0	0	0	0	0
消化不良	0	10 (2.8)	5 (1.1)	6 (1.4)	28 (1.5)
嚥下障害	0	1 (0.3)	2 (0.4)	1 (0.2)	4 (0.2)
小腸炎	0	0	1 (0.2)	2 (0.5)	3 (0.2)
腸炎	0	1 (0.3)	0	1 (0.2)	2 (0.1)
心窩部不快感	0	0	0	0	1 (<0.1)
おくび	0	0	0	1 (0.2)	2 (0.1)
糞塊	0	1 (0.3)	0	0	0
変色便	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
白色便	0	0	1 (0.2)
軟便	0	0	1 (0.2)
大腿ヘルニア	0	0	0
鼓腸	5 (4.2)	2 (1.8)	11 (1.9)
食中毒	3 (2.5)	0	0
排便回数増加	0	0	3 (0.5)
胃障害	0	0	1 (0.2)
胃ポリープ	0	0	0
胃潰瘍	0	0	0
胃炎	0	2 (1.8)	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
白色便	0	0	0	0	1 (<0.1)
軟便	0	0	0	0	1 (<0.1)
大腿ヘルニア	0	1 (0.3)	0	0	0
鼓腸	0	6 (1.7)	1 (0.2)	6 (1.4)	23 (1.3)
食中毒	0	2 (0.6)	0	0	2 (0.1)
排便回数増加	0	0	0	2 (0.5)	5 (0.3)
胃障害	0	0	0	0	1 (<0.1)
胃ポリープ	0	1 (0.3)	0	0	1 (<0.1)
胃潰瘍	0	0	1 (0.2)	0	1 (<0.1)
胃炎	0	3 (0.8)	4 (0.9)	1 (0.2)	9 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
びらん性胃炎	0	0	0
胃腸障害	0	0	1 (0.2)
消化管運動障害	0	0	1 (0.2)
消化器痛	0	1 (0.9)	0
胃食道逆流性疾患	3 (2.5)	3 (2.8)	9 (1.5)
歯肉痛	0	0	1 (0.2)
歯肉腫脹	0	0	0
舌痛	0	0	0
血便排泄	0	1 (0.9)	0
痔出血	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
びらん性胃炎	0	0	1 (0.2)	0	1 (<0.1)
胃腸障害	0	1 (0.3)	0	0	2 (0.1)
消化管運動障害	0	0	0	0	1 (<0.1)
消化器痛	0	1 (0.3)	0	0	1 (<0.1)
胃食道逆流性疾患	0	4 (1.1)	7 (1.5)	8 (1.8)	29 (1.6)
歯肉痛	0	0	1 (0.2)	1 (0.2)	3 (0.2)
歯肉腫脹	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
舌痛	0	1 (0.3)	0	0	0
血便排泄	0	3 (0.8)	0	0	2 (0.1)
痔出血	1 (4.2)	2 (0.6)	1 (0.2)	0	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
痔核	4 (3.3)	5 (4.6)	6 (1.0)
血栓性痔核	0	0	0
裂孔ヘルニア	0	0	1 (0.2)
胃酸過多	0	0	0
肛門肥大乳頭	0	0	1 (0.2)
回腸潰瘍	1 (0.8)	0	0
イレウス	0	1 (0.9)	1 (0.2)
単径ヘルニア	0	0	0
腸閉塞	1 (0.8)	0	1 (0.2)
腸管ポリープ	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
痔核	1 (4.2)	6 (1.7)	15 (3.2)	6 (1.4)	37 (2.0)
血栓性痔核	0	1 (0.3)	0	1 (0.2)	1 (<0.1)
裂孔ヘルニア	0	0	0	0	1 (<0.1)
胃酸過多	0	0	0	1 (0.2)	1 (<0.1)
肛門肥大乳頭	0	0	0	0	1 (<0.1)
回腸潰瘍	0	0	0	0	0
イレウス	0	0	0	0	2 (0.1)
単径ヘルニア	0	1 (0.3)	1 (0.2)	0	2 (0.1)
腸閉塞	0	0	1 (0.2)	0	2 (0.1)
腸管ポリープ	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
過敏性腸症候群	0	0	1 (0.2)
大腸穿孔	1 (0.8)	0	1 (0.2)
大腸ポリープ	0	6 (5.5)	4 (0.7)
口唇水疱	0	0	0
口唇乾燥	0	0	0
口唇腫脹	0	0	0
口唇潰瘍	0	0	1 (0.2)
口腔嚢胞	0	0	0
口腔内潰瘍形成	1 (0.8)	2 (1.8)	3 (0.5)
粘液便	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
過敏性腸症候群	0	0	2 (0.4)	1 (0.2)	4 (0.2)
大腸穿孔	0	1 (0.3)	0	0	1 (<0.1)
大腸ポリープ	0	2 (0.6)	1 (0.2)	5 (1.1)	16 (0.9)
口唇水疱	0	0	0	1 (0.2)	1 (<0.1)
口唇乾燥	1 (4.2)	0	0	0	1 (<0.1)
口唇腫脹	0	0	0	1 (0.2)	1 (<0.1)
口唇潰瘍	0	0	0	0	1 (<0.1)
口腔嚢胞	0	1 (0.3)	0	0	0
口腔内潰瘍形成	0	4 (1.1)	1 (0.2)	1 (0.2)	8 (0.4)
粘液便	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
悪心	12 (10.0)	4 (3.7)	27 (4.6)
非感染性歯肉炎	0	0	0
嚥下痛	0	1 (0.9)	0
食道運動低下	0	0	1 (0.2)
食道痛	0	0	1 (0.2)
食道潰瘍	0	0	0
食道炎	0	0	0
口腔障害	0	0	0
口腔知覚不全	0	0	0
口腔扁平苔癬	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
悪心	2 (8.3)	13 (3.6)	10 (2.1)	21 (4.7)	71 (3.9)
非感染性歯肉炎	0	0	0	1 (0.2)	1 (<0.1)
嚥下痛	0	2 (0.6)	0	2 (0.5)	3 (0.2)
食道運動低下	0	0	0	0	1 (<0.1)
食道痛	0	0	0	0	1 (<0.1)
食道潰瘍	0	0	1 (0.2)	0	1 (<0.1)
食道炎	0	0	1 (0.2)	0	1 (<0.1)
口腔障害	0	0	0	1 (0.2)	1 (<0.1)
口腔知覚不全	0	1 (0.3)	0	0	1 (<0.1)
口腔扁平苔癬	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
口腔内痛	0	0	0
膵臓障害	0	0	1 (0.2)
膵脂肪変性	0	0	1 (0.2)
膵炎	0	0	0
肛門周囲紅斑	0	0	1 (0.2)
歯周病	0	0	0
肛門周囲痛	0	0	4 (0.7)
直腸炎	0	0	2 (0.3)
偽性ポリポーシス	0	1 (0.9)	1 (0.2)
直腸分泌物	1 (0.8)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
口腔内痛	0	0	2 (0.4)	1 (0.2)	3 (0.2)
膵臓障害	0	0	0	0	1 (<0.1)
膵脂肪変性	0	0	0	0	1 (<0.1)
膵炎	1 (4.2)	1 (0.3)	0	1 (0.2)	2 (0.1)
肛門周囲紅斑	0	0	0	0	1 (<0.1)
歯周病	0	0	0	2 (0.5)	2 (0.1)
肛門周囲痛	1 (4.2)	3 (0.8)	1 (0.2)	1 (0.2)	10 (0.5)
直腸炎	0	1 (0.3)	0	0	2 (0.1)
偽性ポリポーシス	0	1 (0.3)	0	0	3 (0.2)
直腸分泌物	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
直腸異形成	0	0	0
直腸出血	0	1 (0.9)	5 (0.9)
直腸ポリープ	0	0	0
直腸しぶり	0	0	1 (0.2)
口内炎	4 (3.3)	0	3 (0.5)
舌障害	0	0	1 (0.2)
舌潰瘍	0	0	0
歯の障害	0	0	1 (0.2)
埋伏歯	0	0	1 (0.2)
歯の脱落	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
直腸異形成	1 (4.2)	0	2 (0.4)	0	3 (0.2)
直腸出血	0	2 (0.6)	1 (0.2)	2 (0.5)	9 (0.5)
直腸ポリープ	0	1 (0.3)	0	0	1 (<0.1)
直腸しぶり	1 (4.2)	1 (0.3)	0	0	2 (0.1)
口内炎	0	9 (2.5)	1 (0.2)	9 (2.0)	19 (1.0)
舌障害	0	0	0	0	1 (<0.1)
舌潰瘍	0	0	0	2 (0.5)	2 (0.1)
歯の障害	0	0	0	1 (0.2)	2 (0.1)
埋伏歯	0	0	1 (0.2)	0	2 (0.1)
歯の脱落	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
歯痛	0	1 (0.9)	7 (1.2)
臍ヘルニア	0	0	0
嘔吐	4 (3.3)	2 (1.8)	13 (2.2)
一般・全身障害および投与部位の状態	36 (29.9)	14 (12.9)	108 (18.4)
医薬品副作用	0	1 (0.9)	0
無力症	2 (1.7)	0	5 (0.9)
胸部不快感	1 (0.8)	0	0
胸痛	1 (0.8)	1 (0.9)	8 (1.4)
悪寒	2 (1.7)	1 (0.9)	6 (1.0)
状態悪化	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
歯痛	0	0	6 (1.3)	5 (1.1)	19 (1.0)
臍ヘルニア	0	2 (0.6)	0	0	1 (<0.1)
嘔吐	1 (4.2)	4 (1.1)	1 (0.2)	11 (2.5)	31 (1.7)
一般・全身障害および投与部位の状態	18 (74.8)	59 (16.4)	57 (12.2)	69 (15.6)	291 (16.0)
医薬品副作用	0	0	1 (0.2)	0	2 (0.1)
無力症	2 (8.3)	0	1 (0.2)	3 (0.7)	11 (0.6)
胸部不快感	2 (8.3)	0	2 (0.4)	1 (0.2)	5 (0.3)
胸痛	0	1 (0.3)	6 (1.3)	7 (1.6)	22 (1.2)
悪寒	0	4 (1.1)	4 (0.9)	3 (0.7)	15 (0.8)
状態悪化	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
医療機器に対する不耐性	0	0	0
不快感	0	0	0
薬効欠如	0	0	1 (0.2)
異形成	0	0	1 (0.2)
顔面浮腫	0	0	0
疲労	6 (5.0)	4 (3.7)	16 (2.7)
異常感	0	0	0
びくびく感	0	0	0
全身性浮腫	0	0	2 (0.3)
宿酔	1 (0.8)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
医療機器に対する不耐性	0	1 (0.3)	0	0	0
不快感	0	0	0	1 (0.2)	1 (<0.1)
薬効欠如	0	1 (0.3)	0	0	1 (<0.1)
異形成	0	1 (0.3)	1 (0.2)	0	3 (0.2)
顔面浮腫	0	1 (0.3)	0	0	1 (<0.1)
疲労	1 (4.2)	9 (2.5)	10 (2.1)	13 (2.9)	46 (2.5)
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	1 (0.2)	0	3 (0.2)
宿酔	0	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
過形成	0	0	0
高体温症	0	0	3 (0.5)
治癒不良	0	0	1 (0.2)
硬結	0	1 (0.9)	0
炎症	0	0	0
インフルエンザ様疾患	1 (0.8)	2 (1.8)	13 (2.2)
注入部位反応	0	0	0
医療機器関連損傷	0	0	0
倦怠感	1 (0.8)	0	2 (0.3)
腫瘤	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
過形成	0	1 (0.3)	0	0	1 (<0.1)
高体温症	0	1 (0.3)	0	0	3 (0.2)
治癒不良	0	0	0	0	1 (<0.1)
硬結	0	0	0	0	0
炎症	0	0	0	1 (0.2)	1 (<0.1)
インフルエンザ様疾患	0	2 (0.6)	2 (0.4)	2 (0.5)	19 (1.0)
注入部位反応	0	1 (0.3)	0	0	1 (<0.1)
医療機器関連損傷	0	1 (0.3)	0	0	1 (<0.1)
倦怠感	1 (4.2)	1 (0.3)	2 (0.4)	1 (0.2)	6 (0.3)
腫瘤	0	0	0	3 (0.7)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
小結節	0	0	1 (0.2)
非心臓性胸痛	0	0	0
浮腫	0	0	0
末梢性浮腫	2 (1.7)	1 (0.9)	2 (0.3)
疼痛	3 (2.5)	0	8 (1.4)
末梢腫脹	1 (0.8)	0	2 (0.3)
ポリープ	0	0	1 (0.2)
偽ポリープ	0	0	2 (0.3)
発熱	12 (10.0)	3 (2.8)	32 (5.5)
異物感	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
小結節	0	0	0	2 (0.5)	3 (0.2)
非心臓性胸痛	1 (4.2)	0	0	0	1 (<0.1)
浮腫	0	0	1 (0.2)	0	1 (<0.1)
末梢性浮腫	0	4 (1.1)	3 (0.6)	3 (0.7)	10 (0.5)
疼痛	0	3 (0.8)	2 (0.4)	1 (0.2)	13 (0.7)
末梢腫脹	0	2 (0.6)	1 (0.2)	2 (0.5)	6 (0.3)
ポリープ	0	0	0	0	1 (<0.1)
偽ポリープ	0	0	0	2 (0.5)	4 (0.2)
発熱	11 (45.7)	21 (5.9)	19 (4.1)	20 (4.5)	96 (5.3)
異物感	0	2 (0.6)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
腫脹	0	0	0
顔面腫脹	0	0	2 (0.3)
ワクチン接種部位紅斑	1 (0.8)	0	0
ワクチン接種部位疼痛	1 (0.8)	0	0
ワクチン接種部位反応	0	0	0
乾燥症	1 (0.8)	0	0
肝胆道系障害	6 (5.0)	3 (2.8)	13 (2.2)
胆道ジスキネジア	0	0	0
胆汁性嚢胞	0	0	0
硬化性胆管炎	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
腫脹	0	0	0	1 (0.2)	1 (<0.1)
顔面腫脹	0	0	0	2 (0.5)	4 (0.2)
ワクチン接種部位紅斑	0	0	0	0	0
ワクチン接種部位疼痛	0	0	0	0	0
ワクチン接種部位反応	0	1 (0.3)	0	0	1 (<0.1)
乾燥症	0	0	0	0	0
肝胆道系障害	1 (4.2)	8 (2.2)	17 (3.6)	8 (1.8)	47 (2.6)
胆道ジスキネジア	0	0	1 (0.2)	0	1 (<0.1)
胆汁性嚢胞	0	0	1 (0.2)	0	1 (<0.1)
硬化性胆管炎	0	0	3 (0.6)	1 (0.2)	5 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
胆石症	0	0	3 (0.5)
胆汁うっ滞	1 (0.8)	0	0
薬物性肝障害	0	0	0
肝嚢胞	0	0	1 (0.2)
肝機能異常	0	0	3 (0.5)
脂肪肝	0	2 (1.8)	2 (0.3)
肝炎	0	0	1 (0.2)
肝細胞損傷	0	0	1 (0.2)
肝腫大	0	0	0
高ビリルビン血症	2 (1.7)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
肝胆道系障害 (Cont.)					
胆石症	0	0	0	2 (0.5)	5 (0.3)
胆汁うっ滞	0	0	0	0	0
薬物性肝障害	0	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
肝嚢胞	0	0	0	0	1 (<0.1)
肝機能異常	0	2 (0.6)	6 (1.3)	3 (0.7)	12 (0.7)
脂肪肝	0	1 (0.3)	3 (0.6)	0	8 (0.4)
肝炎	0	0	0	0	1 (<0.1)
肝細胞損傷	0	0	0	0	1 (<0.1)
肝腫大	0	1 (0.3)	0	0	1 (<0.1)
高ビリルビン血症	0	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
高トランスアミナーゼ血症	0	0	0
肝障害	1 (0.8)	0	0
肝損傷	1 (0.8)	0	0
非アルコール性脂肪性肝炎	0	0	1 (0.2)
非アルコール性脂肪性肝疾患	0	0	1 (0.2)
門脈血栓症	1 (0.8)	0	0
免疫系障害	5 (4.2)	1 (0.9)	13 (2.2)
動物アレルギー	1 (0.8)	0	1 (0.2)
アミロイドーシス	1 (0.8)	0	0
アナフィラキシー反応	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
肝胆道系障害 (Cont.)					
高トランスアミナーゼ血症	1 (4.2)	0	1 (0.2)	0	2 (0.1)
肝障害	0	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
肝損傷	0	1 (0.3)	0	0	0
非アルコール性脂肪性肝炎	0	0	0	0	1 (<0.1)
非アルコール性脂肪性肝疾患	0	1 (0.3)	0	0	2 (0.1)
門脈血栓症	0	0	0	0	0
免疫系障害	0	3 (0.8)	7 (1.5)	4 (0.9)	27 (1.5)
動物アレルギー	0	0	0	0	1 (<0.1)
アミロイドーシス	0	0	0	0	0
アナフィラキシー反応	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
免疫系障害 (Cont.)			
薬物過敏症	1 (0.8)	0	0
粉塵アレルギー	1 (0.8)	0	1 (0.2)
過敏症	0	0	1 (0.2)
ダニアレルギー	0	0	1 (0.2)
季節性アレルギー	1 (0.8)	1 (0.9)	9 (1.5)
感染症および寄生虫症	107 (88.8)	74 (68.4)	468 (79.9)
腹部膿瘍	0	0	1 (0.2)
腹壁膿瘍	0	0	0
膿瘍	1 (0.8)	0	0
頚部膿瘍	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
免疫系障害 (Cont.)					
薬物過敏症	0	1 (0.3)	3 (0.6)	0	3 (0.2)
粉塵アレルギー	0	0	0	0	1 (<0.1)
過敏症	0	1 (0.3)	1 (0.2)	1 (0.2)	4 (0.2)
ダニアレルギー	0	0	0	0	1 (<0.1)
季節性アレルギー	0	1 (0.3)	3 (0.6)	2 (0.5)	16 (0.9)
感染症および寄生虫症	39 (162.0)	335 (93.3)	357 (76.6)	376 (84.8)	1503 (82.5)
腹部膿瘍	0	1 (0.3)	0	0	1 (<0.1)
腹壁膿瘍	0	0	1 (0.2)	0	1 (<0.1)
膿瘍	0	1 (0.3)	0	0	1 (<0.1)
頚部膿瘍	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ダニ皮膚炎	0	0	2 (0.3)
急性心内膜炎	0	0	0
急性副鼻腔炎	0	0	0
歯槽骨炎	0	0	1 (0.2)
肛門膿瘍	1 (0.8)	0	2 (0.3)
肛門直腸感染	0	0	0
虫垂炎	0	0	0
細菌性関節炎	0	0	0
無症候性COVID-19	0	0	2 (0.3)
無症候性細菌尿	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ダニ皮膚炎	0	1 (0.3)	2 (0.4)	0	5 (0.3)
急性心内膜炎	0	1 (0.3)	0	0	0
急性副鼻腔炎	0	1 (0.3)	0	0	1 (<0.1)
歯槽骨炎	0	0	0	0	1 (<0.1)
肛門膿瘍	0	1 (0.3)	3 (0.6)	2 (0.5)	8 (0.4)
肛門直腸感染	0	2 (0.6)	0	0	0
虫垂炎	0	0	3 (0.6)	0	3 (0.2)
細菌性関節炎	0	0	1 (0.2)	0	1 (<0.1)
無症候性COVID-19	0	1 (0.3)	1 (0.2)	3 (0.7)	6 (0.3)
無症候性細菌尿	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
異型肺炎	0	0	1 (0.2)
細菌感染	0	0	0
細菌性膣症	1 (0.8)	0	2 (0.3)
細菌尿	0	1 (0.9)	0
バルトリン腺炎	0	0	0
ブラストシスティス感染	0	0	0
体部白癬	0	0	0
ボレリア感染	0	0	0
乳房膿瘍	0	0	0
気管支炎	3 (2.5)	1 (0.9)	22 (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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
異型肺炎	0	0	0	1 (0.2)	2 (0.1)
細菌感染	0	1 (0.3)	0	1 (0.2)	2 (0.1)
細菌性膣症	0	0	1 (0.2)	0	3 (0.2)
細菌尿	0	0	0	0	1 (<0.1)
バルトリン腺炎	0	1 (0.3)	0	0	1 (<0.1)
ブラストシスティス感染	0	0	1 (0.2)	0	1 (<0.1)
体部白癬	1 (4.2)	0	0	0	1 (<0.1)
ボレリア感染	0	0	1 (0.2)	0	1 (<0.1)
乳房膿瘍	0	0	1 (0.2)	0	1 (<0.1)
気管支炎	2 (8.3)	10 (2.8)	9 (1.9)	4 (0.9)	45 (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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
感染性滑液包炎	0	0	0
COVID-19	3 (2.5)	0	14 (2.4)
COVID-19肺炎	0	0	2 (0.3)
カンピロバクター胃腸炎	0	0	1 (0.2)
カンピロバクター感染	0	0	0
カンジダ感染	0	0	0
蜂巣炎	8 (6.6)	1 (0.9)	4 (0.7)
条虫感染	0	0	0
感染性胆嚢炎	0	0	0
慢性副鼻腔炎	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
感染性滑液包炎	0	0	0	1 (0.2)	1 (<0.1)
COVID-19	1 (4.2)	23 (6.4)	13 (2.8)	22 (5.0)	63 (3.5)
COVID-19肺炎	0	4 (1.1)	5 (1.1)	6 (1.4)	16 (0.9)
カンピロバクター胃腸炎	0	0	1 (0.2)	1 (0.2)	3 (0.2)
カンピロバクター感染	0	0	3 (0.6)	0	3 (0.2)
カンジダ感染	0	1 (0.3)	0	2 (0.5)	2 (0.1)
蜂巣炎	0	0	5 (1.1)	3 (0.7)	12 (0.7)
条虫感染	1 (4.2)	0	0	0	1 (<0.1)
感染性胆嚢炎	0	0	1 (0.2)	0	1 (<0.1)
慢性副鼻腔炎	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.2)
クロストリジウム・ディフィシレ感染	3 (2.5)	2 (1.8)	9 (1.5)
結腸膿瘍	0	0	0
結膜炎	2 (1.7)	0	0
ウイルス性結膜炎	1 (0.8)	0	0
コロナウイルス感染	0	0	0
サイクロスポリジウム感染	0	0	0
膀胱炎	0	3 (2.8)	14 (2.4)
サイトメガロウイルス性大腸炎	0	0	0
サイトメガロウイルス感染	1 (0.8)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.2)	0	2 (0.1)
クロストリジウム・ディフィシレ感染	0	2 (0.6)	3 (0.6)	7 (1.6)	21 (1.2)
結腸膿瘍	0	0	1 (0.2)	0	1 (<0.1)
結膜炎	0	0	3 (0.6)	3 (0.7)	6 (0.3)
ウイルス性結膜炎	0	1 (0.3)	0	0	1 (<0.1)
コロナウイルス感染	0	1 (0.3)	0	0	1 (<0.1)
サイクロスポリジウム感染	0	1 (0.3)	0	0	1 (<0.1)
膀胱炎	1 (4.2)	4 (1.1)	7 (1.5)	2 (0.5)	30 (1.6)
サイトメガロウイルス性大腸炎	0	0	0	1 (0.2)	1 (<0.1)
サイトメガロウイルス感染	1 (4.2)	1 (0.3)	1 (0.2)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
毛嚢虫症	0	1 (0.9)	2 (0.3)
デング熱	0	0	0
感染性皮膚炎	0	0	0
皮膚糸状菌症	0	0	1 (0.2)
爪の皮膚糸状菌症	0	0	1 (0.2)
医療機器関連敗血症	0	0	0
感染性下痢	0	0	0
憩室炎	0	0	1 (0.2)
耳感染	2 (1.7)	0	8 (1.4)
感染性腸炎	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
毛嚢虫症	0	0	4 (0.9)	4 (0.9)	11 (0.6)
デング熱	0	0	0	1 (0.2)	1 (<0.1)
感染性皮膚炎	0	1 (0.3)	0	0	1 (<0.1)
皮膚糸状菌症	0	1 (0.3)	0	0	1 (<0.1)
爪の皮膚糸状菌症	0	0	0	3 (0.7)	4 (0.2)
医療機器関連敗血症	0	0	0	1 (0.2)	1 (<0.1)
感染性下痢	0	1 (0.3)	0	2 (0.5)	3 (0.2)
憩室炎	0	0	0	0	1 (<0.1)
耳感染	0	0	5 (1.1)	3 (0.7)	16 (0.9)
感染性腸炎	0	0	0	1 (0.2)	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
蟯虫症	0	0	1 (0.2)
腸球菌感染	1 (0.8)	0	0
エンテロウイルス感染	0	0	0
丹毒	0	0	2 (0.3)
遊走性紅斑	0	0	1 (0.2)
大腸菌感染	2 (1.7)	0	1 (0.2)
大腸菌性敗血症	0	0	1 (0.2)
大腸菌性尿路感染	0	0	0
眼感染	0	0	0
眼瞼感染	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
蟯虫症	0	0	0	0	1 (<0.1)
腸球菌感染	0	0	0	0	0
エンテロウイルス感染	0	0	0	1 (0.2)	1 (<0.1)
丹毒	0	0	0	0	2 (0.1)
遊走性紅斑	0	0	0	0	1 (<0.1)
大腸菌感染	0	1 (0.3)	1 (0.2)	0	3 (0.2)
大腸菌性敗血症	0	0	0	0	1 (<0.1)
大腸菌性尿路感染	0	0	1 (0.2)	0	1 (<0.1)
眼感染	0	0	1 (0.2)	0	1 (<0.1)
眼瞼感染	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
毛包炎	2 (1.7)	0	5 (0.9)
真菌感染	1 (0.8)	0	0
皮膚真菌感染	2 (1.7)	0	1 (0.2)
せつ	0	0	1 (0.2)
胃腸炎	4 (3.3)	2 (1.8)	15 (2.6)
ノロウイルス性胃腸炎	1 (0.8)	0	0
ウイルス性胃腸炎	0	1 (0.9)	6 (1.0)
消化管内細菌過剰増殖	0	0	1 (0.2)
消化管感染	0	0	1 (0.2)
性器カンジダ症	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
毛包炎	2 (8.3)	7 (2.0)	11 (2.4)	22 (5.0)	43 (2.4)
真菌感染	0	0	0	1 (0.2)	1 (<0.1)
皮膚真菌感染	0	1 (0.3)	0	2 (0.5)	4 (0.2)
せつ	0	0	1 (0.2)	1 (0.2)	3 (0.2)
胃腸炎	1 (4.2)	9 (2.5)	9 (1.9)	7 (1.6)	39 (2.1)
ノロウイルス性胃腸炎	1 (4.2)	0	0	0	1 (<0.1)
ウイルス性胃腸炎	0	1 (0.3)	4 (0.9)	4 (0.9)	16 (0.9)
消化管内細菌過剰増殖	0	0	0	0	1 (<0.1)
消化管感染	0	0	0	1 (0.2)	2 (0.1)
性器カンジダ症	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
陰部ヘルペス	0	0	1 (0.2)
陰部単純ヘルペス	0	0	0
歯肉膿瘍	0	0	0
歯肉炎	1 (0.8)	0	0
単径部膿瘍	0	0	0
ヘモフィルス感染	0	0	0
ヘリコバクター性胃炎	0	0	0
ヘリコバクター感染	0	0	1 (0.2)
伝染性単核症肝炎	0	0	1 (0.2)
単純ヘルペス	0	6 (5.5)	4 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
陰部ヘルペス	0	0	1 (0.2)	2 (0.5)	4 (0.2)
陰部単純ヘルペス	0	2 (0.6)	1 (0.2)	1 (0.2)	4 (0.2)
歯肉膿瘍	0	0	1 (0.2)	1 (0.2)	2 (0.1)
歯肉炎	0	5 (1.4)	1 (0.2)	1 (0.2)	7 (0.4)
単径部膿瘍	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
ヘモフィルス感染	0	1 (0.3)	0	0	0
ヘリコバクター性胃炎	0	1 (0.3)	0	0	1 (<0.1)
ヘリコバクター感染	0	0	1 (0.2)	0	2 (0.1)
伝染性単核症肝炎	0	0	0	0	1 (<0.1)
単純ヘルペス	0	5 (1.4)	4 (0.9)	2 (0.5)	21 (1.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
単純ヘルペス性咽頭炎	0	1 (0.9)	0
帯状疱疹	0	4 (3.7)	17 (2.9)
播種性帯状疱疹	0	0	0
神経合併症を伴う帯状疱疹感染	0	0	1 (0.2)
帯状疱疹性髄膜炎	0	0	0
耳帯状疱疹	0	0	0
麦粒腫	1 (0.8)	3 (2.8)	4 (0.7)
膿痂疹	0	0	2 (0.3)
咬傷感染	0	0	0
感染性嚢腫	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
単純ヘルペス性咽頭炎	0	0	0	0	1 (<0.1)
帯状疱疹	7 (29.1)	7 (2.0)	28 (6.0)	20 (4.5)	81 (4.4)
播種性帯状疱疹	0	1 (0.3)	0	0	1 (<0.1)
神経合併症を伴う帯状疱疹感染	0	0	0	0	1 (<0.1)
帯状疱疹性髄膜炎	0	0	0	1 (0.2)	1 (<0.1)
耳帯状疱疹	0	0	1 (0.2)	0	1 (<0.1)
麦粒腫	0	4 (1.1)	4 (0.9)	3 (0.7)	15 (0.8)
膿痂疹	0	1 (0.3)	1 (0.2)	1 (0.2)	4 (0.2)
咬傷感染	0	0	0	1 (0.2)	1 (<0.1)
感染性嚢腫	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
感染性皮膚嚢腫	0	0	0
感染	0	1 (0.9)	1 (0.2)
伝染性単核症	0	0	2 (0.3)
インフルエンザ	1 (0.8)	1 (0.9)	24 (4.1)
クレブシエラ感染	0	0	1 (0.2)
大腸感染	0	0	0
喉頭炎	0	0	1 (0.2)
潜伏結核	0	0	4 (0.7)
限局性感染	1 (0.8)	0	1 (0.2)
下気道感染	2 (1.7)	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
感染性皮膚嚢腫	0	0	1 (0.2)	0	1 (<0.1)
感染	0	0	0	0	1 (<0.1)
伝染性単核症	0	0	0	0	2 (0.1)
インフルエンザ	3 (12.5)	9 (2.5)	18 (3.9)	17 (3.8)	68 (3.7)
クレブシエラ感染	0	0	0	0	1 (<0.1)
大腸感染	0	0	1 (0.2)	1 (0.2)	2 (0.1)
喉頭炎	0	2 (0.6)	1 (0.2)	2 (0.5)	5 (0.3)
潜伏結核	0	1 (0.3)	2 (0.4)	4 (0.9)	11 (0.6)
限局性感染	0	0	0	0	1 (<0.1)
下気道感染	0	2 (0.6)	2 (0.4)	1 (0.2)	6 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ライム病	0	0	0
乳腺炎	0	0	0
伝染性軟属腫	0	0	0
筋膿瘍	1 (0.8)	0	0
上咽頭炎	16 (13.3)	12 (11.1)	63 (10.8)
食道カンジダ症	0	0	0
爪真菌症	0	0	2 (0.3)
口腔カンジダ症	0	0	0
口腔真菌感染	0	0	1 (0.2)
口腔ヘルペス	3 (2.5)	7 (6.5)	22 (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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ライム病	0	0	0	1 (0.2)	1 (<0.1)
乳腺炎	0	0	1 (0.2)	0	1 (<0.1)
伝染性軟属腫	0	1 (0.3)	0	0	0
筋膿瘍	0	0	0	0	0
上咽頭炎	2 (8.3)	54 (15.0)	60 (12.9)	69 (15.6)	235 (12.9)
食道カンジダ症	0	0	1 (0.2)	0	1 (<0.1)
爪真菌症	0	7 (2.0)	2 (0.4)	1 (0.2)	10 (0.5)
口腔カンジダ症	1 (4.2)	2 (0.6)	1 (0.2)	2 (0.5)	4 (0.2)
口腔真菌感染	1 (4.2)	0	0	0	2 (0.1)
口腔ヘルペス	1 (4.2)	29 (8.1)	15 (3.2)	17 (3.8)	84 (4.6)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
精巣炎	0	0	1 (0.2)
外耳炎	0	0	0
真菌性外耳炎	0	0	0
中耳炎	0	0	0
急性中耳炎	0	0	0
乳頭腫ウイルス感染	0	0	0
爪囲炎	0	0	0
歯周炎	0	0	2 (0.3)
直腸周囲膿瘍	0	0	0
咽頭炎	2 (1.7)	0	4 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
精巣炎	0	0	0	0	1 (<0.1)
外耳炎	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
真菌性外耳炎	0	1 (0.3)	0	0	1 (<0.1)
中耳炎	0	1 (0.3)	1 (0.2)	0	2 (0.1)
急性中耳炎	0	1 (0.3)	0	0	1 (<0.1)
乳頭腫ウイルス感染	0	0	0	1 (0.2)	1 (<0.1)
爪囲炎	0	1 (0.3)	1 (0.2)	0	2 (0.1)
歯周炎	0	3 (0.8)	0	2 (0.5)	7 (0.4)
直腸周囲膿瘍	0	2 (0.6)	0	0	2 (0.1)
咽頭炎	1 (4.2)	6 (1.7)	4 (0.9)	7 (1.6)	19 (1.0)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
レンサ球菌性咽頭炎	0	0	2 (0.3)
毛巣嚢胞	0	0	2 (0.3)
胸膜感染	0	0	0
ニューモシスチス・イロベチイ感染	0	0	1 (0.2)
ニューモシスチス・イロベチイ肺炎	0	0	0
肺炎	2 (1.7)	2 (1.8)	11 (1.9)
細菌性肺炎	0	0	1 (0.2)
クリプトコッカス性肺炎	0	0	0
肺炎球菌性肺炎	0	0	1 (0.2)
ウイルス性肺炎	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
レンサ球菌性咽頭炎	1 (4.2)	1 (0.3)	2 (0.4)	1 (0.2)	6 (0.3)
毛巣嚢胞	0	0	2 (0.4)	0	4 (0.2)
胸膜感染	0	0	0	1 (0.2)	1 (<0.1)
ニューモシスチス・イロベチイ感染	0	0	0	0	1 (<0.1)
ニューモシスチス・イロベチイ肺炎	0	1 (0.3)	0	0	0
肺炎	1 (4.2)	5 (1.4)	1 (0.2)	7 (1.6)	23 (1.3)
細菌性肺炎	0	0	0	0	1 (<0.1)
クリプトコッカス性肺炎	0	0	0	1 (0.2)	1 (<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)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
処置後感染	2 (1.7)	0	0
歯髄炎	1 (0.8)	0	1 (0.2)
膿疱	0	0	2 (0.3)
腎盂腎炎	0	1 (0.9)	1 (0.2)
膿皮症	0	0	0
膿尿	1 (0.8)	0	0
膿疱性皮疹	0	0	0
RSウイルス感染	0	0	0
気道感染	1 (0.8)	0	6 (1.0)
ウイルス性気道感染	1 (0.8)	0	2 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
処置後感染	0	0	0	0	0
歯髄炎	0	1 (0.3)	2 (0.4)	1 (0.2)	5 (0.3)
膿疱	1 (4.2)	1 (0.3)	2 (0.4)	2 (0.5)	7 (0.4)
腎盂腎炎	0	2 (0.6)	1 (0.2)	0	4 (0.2)
膿皮症	0	0	0	1 (0.2)	1 (<0.1)
膿尿	0	0	0	1 (0.2)	1 (<0.1)
膿疱性皮疹	0	1 (0.3)	1 (0.2)	0	2 (0.1)
RSウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
気道感染	0	0	2 (0.4)	0	8 (0.4)
ウイルス性気道感染	1 (4.2)	1 (0.3)	4 (0.9)	2 (0.5)	9 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
鼻炎	2 (1.7)	0	2 (0.3)
根管感染	0	0	1 (0.2)
敗血症	0	0	2 (0.3)
セラチア感染	0	0	0
副鼻腔炎	8 (6.6)	1 (0.9)	19 (3.2)
皮膚カンジダ	0	0	1 (0.2)
皮膚感染	0	0	0
ブドウ球菌感染	0	0	1 (0.2)
レンサ球菌性尿路感染	0	0	1 (0.2)
皮下組織膿瘍	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
鼻炎	0	2 (0.6)	1 (0.2)	2 (0.5)	5 (0.3)
根管感染	0	0	0	0	1 (<0.1)
敗血症	0	0	1 (0.2)	0	3 (0.2)
セラチア感染	0	1 (0.3)	0	0	0
副鼻腔炎	1 (4.2)	10 (2.8)	7 (1.5)	7 (1.6)	41 (2.3)
皮膚カンジダ	0	0	0	0	1 (<0.1)
皮膚感染	0	0	0	3 (0.7)	3 (0.2)
ブドウ球菌感染	0	1 (0.3)	0	0	1 (<0.1)
レンサ球菌性尿路感染	0	0	0	0	1 (<0.1)
皮下組織膿瘍	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
股部白癬	0	0	1 (0.2)
白癬感染	0	0	0
手白癬	0	1 (0.9)	0
足部白癬	0	1 (0.9)	1 (0.2)
癜風	0	1 (0.9)	0
扁桃炎	0	0	5 (0.9)
歯膿瘍	1 (0.8)	1 (0.9)	5 (0.9)
歯感染	0	0	4 (0.7)
トリコモナス症	0	0	0
結核	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
股部白癬	0	0	1 (0.2)	0	2 (0.1)
白癬感染	1 (4.2)	2 (0.6)	0	1 (0.2)	2 (0.1)
手白癬	0	0	0	0	0
足部白癬	0	3 (0.8)	3 (0.6)	4 (0.9)	9 (0.5)
癜風	0	0	2 (0.4)	1 (0.2)	4 (0.2)
扁桃炎	0	1 (0.3)	3 (0.6)	4 (0.9)	12 (0.7)
歯膿瘍	0	1 (0.3)	2 (0.4)	2 (0.5)	10 (0.5)
歯感染	0	4 (1.1)	2 (0.4)	3 (0.7)	10 (0.5)
トリコモナス症	0	1 (0.3)	0	0	0
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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
上気道感染	8 (6.6)	12 (11.1)	53 (9.0)
尿路感染	9 (7.5)	4 (3.7)	28 (4.8)
尿路性敗血症	0	0	1 (0.2)
膣膿瘍	1 (0.8)	0	0
膣感染	0	0	4 (0.7)
水痘	0	0	1 (0.2)
水痘帯状疱疹ウイルス感染	0	0	0
ウイルス血症	0	0	0
ウイルス性下痢	0	0	0
ウイルス感染	1 (0.8)	0	2 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
上気道感染	3 (12.5)	33 (9.2)	29 (6.2)	35 (7.9)	154 (8.5)
尿路感染	1 (4.2)	18 (5.0)	18 (3.9)	9 (2.0)	69 (3.8)
尿路性敗血症	0	0	0	0	1 (<0.1)
膣膿瘍	0	0	0	0	0
膣感染	0	0	0	0	4 (0.2)
水痘	0	0	0	0	1 (<0.1)
水痘帯状疱疹ウイルス感染	0	0	1 (0.2)	0	1 (<0.1)
ウイルス血症	0	1 (0.3)	0	0	0
ウイルス性下痢	0	1 (0.3)	0	0	1 (<0.1)
ウイルス感染	1 (4.2)	1 (0.3)	1 (0.2)	3 (0.7)	8 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ウイルス性心膜炎	0	1 (0.9)	0
ウイルス性咽頭炎	0	0	0
ウイルス性上気道感染	0	1 (0.9)	4 (0.7)
女性外陰部蜂巣炎	0	0	1 (0.2)
外陰部腟カンジダ症	1 (0.8)	0	4 (0.7)
外陰腟真菌感染	0	0	2 (0.3)
外陰腟炎	0	1 (0.9)	0
創傷感染	1 (0.8)	0	0
傷害、中毒および処置合併症	12 (10.0)	17 (15.7)	79 (13.5)
偶発的過量投与	3 (2.5)	2 (1.8)	5 (0.9)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ウイルス性心膜炎	0	0	0	0	0
ウイルス性咽頭炎	1 (4.2)	0	1 (0.2)	0	2 (0.1)
ウイルス性上気道感染	0	5 (1.4)	2 (0.4)	5 (1.1)	13 (0.7)
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	2 (0.6)	2 (0.4)	7 (1.6)	14 (0.8)
外陰腟真菌感染	0	2 (0.6)	1 (0.2)	1 (0.2)	5 (0.3)
外陰腟炎	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	7 (29.1)	58 (16.2)	31 (6.7)	30 (6.8)	205 (11.3)
偶発的過量投与	0	0	1 (0.2)	2 (0.5)	10 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
吻合部漏出	1 (0.8)	0	0
動物咬傷	0	0	0
動物による引っかき傷	0	0	1 (0.2)
足関節部骨折	0	1 (0.9)	0
節足動物咬傷	0	0	2 (0.3)
節足動物刺傷	0	0	0
骨挫傷	0	0	1 (0.2)
第2度熱傷	0	0	0
挫傷	2 (1.7)	2 (1.8)	2 (0.3)
上顎炎	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
吻合部漏出	0	0	0	0	0
動物咬傷	0	0	0	1 (0.2)	1 (<0.1)
動物による引っかき傷	0	1 (0.3)	0	0	1 (<0.1)
足関節部骨折	0	0	0	0	1 (<0.1)
節足動物咬傷	0	1 (0.3)	0	0	3 (0.2)
節足動物刺傷	0	0	1 (0.2)	0	1 (<0.1)
骨挫傷	0	1 (0.3)	0	1 (0.2)	2 (0.1)
第2度熱傷	0	1 (0.3)	0	1 (0.2)	2 (0.1)
挫傷	2 (8.3)	6 (1.7)	1 (0.2)	4 (0.9)	16 (0.9)
上顎炎	0	0	0	1 (0.2)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
毒性物質曝露	0	0	0
眼外傷	0	1 (0.9)	1 (0.2)
転倒	0	1 (0.9)	5 (0.9)
腓骨骨折	0	0	0
足骨折	0	0	1 (0.2)
骨折	0	0	0
仙骨骨折	0	0	0
消化管ストーマ壊死	1 (0.8)	0	0
手骨折	0	0	0
頭部損傷	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
毒性物質曝露	0	0	1 (0.2)	0	1 (<0.1)
眼外傷	0	0	0	1 (0.2)	3 (0.2)
転倒	0	9 (2.5)	0	1 (0.2)	16 (0.9)
腓骨骨折	0	1 (0.3)	0	0	1 (<0.1)
足骨折	0	0	3 (0.6)	1 (0.2)	5 (0.3)
骨折	0	1 (0.3)	0	0	1 (<0.1)
仙骨骨折	0	0	1 (0.2)	0	1 (<0.1)
消化管ストーマ壊死	0	0	0	0	0
手骨折	0	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
頭部損傷	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
熱疲労	0	0	0
熱中症	0	0	0
熱射病	1 (0.8)	0	0
股関節部骨折	1 (0.8)	0	0
損傷	0	0	1 (0.2)
企図的過量投与	0	0	0
関節脱臼	0	0	1 (0.2)
関節損傷	0	2 (1.8)	1 (0.2)
靱帯断裂	0	0	0
靱帯捻挫	2 (1.7)	1 (0.9)	3 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
熱疲労	0	0	0	1 (0.2)	1 (<0.1)
熱中症	0	1 (0.3)	0	0	0
熱射病	0	0	0	0	0
股関節部骨折	0	0	0	0	0
損傷	1 (4.2)	1 (0.3)	0	1 (0.2)	3 (0.2)
企図的過量投与	0	1 (0.3)	0	0	1 (<0.1)
関節脱臼	0	0	0	0	1 (<0.1)
関節損傷	0	0	3 (0.6)	0	5 (0.3)
靭帯断裂	0	0	1 (0.2)	0	1 (<0.1)
靭帯捻挫	1 (4.2)	2 (0.6)	0	3 (0.7)	8 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
四肢損傷	0	0	2 (0.3)
四肢外傷性切断	0	0	0
腰椎骨折	0	0	0
つち指	0	0	0
半月板損傷	0	1 (0.9)	1 (0.2)
筋断裂	0	0	3 (0.5)
肉離れ	0	0	7 (1.2)
筋骨格内異物	0	0	0
過量投与	0	0	2 (0.3)
膝蓋骨骨折	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
四肢損傷	0	1 (0.3)	1 (0.2)	1 (0.2)	4 (0.2)
四肢外傷性切断	0	0	0	1 (0.2)	1 (<0.1)
腰椎骨折	0	0	0	1 (0.2)	1 (<0.1)
つち指	0	1 (0.3)	0	0	1 (<0.1)
半月板損傷	0	0	1 (0.2)	0	2 (0.1)
筋断裂	0	1 (0.3)	1 (0.2)	1 (0.2)	6 (0.3)
肉離れ	0	1 (0.3)	2 (0.4)	2 (0.5)	11 (0.6)
筋骨格内異物	0	0	1 (0.2)	0	1 (<0.1)
過量投与	1 (4.2)	0	2 (0.4)	0	5 (0.3)
膝蓋骨骨折	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
骨盤骨折	0	0	0
処置後血尿	0	0	0
処置後出血	0	0	3 (0.5)
外傷後頚部症候群	0	0	0
外傷後疼痛	0	0	1 (0.2)
術後イレウス	0	0	1 (0.2)
処置による腸管穿孔	0	0	1 (0.2)
処置による疼痛	0	1 (0.9)	2 (0.3)
肺挫傷	0	0	1 (0.2)
橈骨骨折	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
骨盤骨折	0	1 (0.3)	0	0	1 (<0.1)
処置後血尿	0	0	0	1 (0.2)	1 (<0.1)
処置後出血	0	0	0	0	3 (0.2)
外傷後頚部症候群	0	1 (0.3)	1 (0.2)	0	2 (0.1)
外傷後疼痛	0	0	2 (0.4)	0	3 (0.2)
術後イレウス	0	0	0	0	1 (<0.1)
処置による腸管穿孔	0	0	0	0	1 (<0.1)
処置による疼痛	0	0	0	0	3 (0.2)
肺挫傷	0	0	1 (0.2)	0	2 (0.1)
橈骨骨折	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
肋骨骨折	0	0	4 (0.7)
交通事故	0	1 (0.9)	3 (0.5)
瘢痕	0	0	1 (0.2)
陰嚢血腫	0	0	1 (0.2)
皮膚擦過傷	1 (0.8)	3 (2.8)	1 (0.2)
皮膚裂傷	0	0	2 (0.3)
軟部組織損傷	0	0	0
脊柱損傷	0	0	0
脊椎圧迫骨折	0	0	1 (0.2)
スポーツ損傷	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
肋骨骨折	1 (4.2)	3 (0.8)	0	1 (0.2)	8 (0.4)
交通事故	0	2 (0.6)	0	0	5 (0.3)
瘢痕	0	0	0	0	1 (<0.1)
陰嚢血腫	0	0	0	0	1 (<0.1)
皮膚擦過傷	0	2 (0.6)	0	0	6 (0.3)
皮膚裂傷	1 (4.2)	3 (0.8)	3 (0.6)	0	8 (0.4)
軟部組織損傷	0	1 (0.3)	0	0	1 (<0.1)
脊柱損傷	0	1 (0.3)	0	0	1 (<0.1)
脊椎圧迫骨折	0	1 (0.3)	0	0	1 (<0.1)
スポーツ損傷	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
ストレス骨折	0	0	3 (0.5)
皮下血腫	0	0	1 (0.2)
腱損傷	0	0	1 (0.2)
腱断裂	0	0	1 (0.2)
熱傷	0	0	1 (0.2)
胸椎骨折	0	0	0
脛骨骨折	0	0	1 (0.2)
歯牙破折	0	0	2 (0.3)
子宮穿孔	0	0	1 (0.2)
ワクチン接種合併症	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
ストレス骨折	0	2 (0.6)	0	0	5 (0.3)
皮下血腫	0	2 (0.6)	0	0	2 (0.1)
腱損傷	0	0	0	0	1 (<0.1)
腱断裂	0	0	0	0	1 (<0.1)
熱傷	0	0	0	0	1 (<0.1)
胸椎骨折	0	0	1 (0.2)	0	1 (<0.1)
脛骨骨折	0	1 (0.3)	0	0	2 (0.1)
歯牙破折	0	2 (0.6)	0	1 (0.2)	4 (0.2)
子宮穿孔	0	0	0	0	1 (<0.1)
ワクチン接種合併症	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
創傷	0	0	1 (0.2)
創合併症	0	1 (0.9)	0
手首関節骨折	0	0	1 (0.2)
臨床検査	57 (47.3)	29 (26.8)	179 (30.5)
アラニンアミノトランスフェラーゼ増加	6 (5.0)	2 (1.8)	10 (1.7)
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
抗好中球細胞質抗体陽性	0	0	0
抗核抗体増加	0	0	0
大動脈雑音	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

Treatment-Emergent Adverse 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
創傷	0	3 (0.8)	1 (0.2)	1 (0.2)	6 (0.3)
創合併症	0	1 (0.3)	0	0	2 (0.1)
手首関節骨折	0	0	0	1 (0.2)	2 (0.1)
臨床検査	27 (112.1)	124 (34.6)	235 (50.4)	256 (57.7)	814 (44.7)
アラニンアミノトランスフェラーゼ増加	0	5 (1.4)	14 (3.0)	15 (3.4)	44 (2.4)
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.3)	0	0	1 (<0.1)
アミラーゼ増加	1 (4.2)	1 (0.3)	2 (0.4)	0	3 (0.2)
抗好中球細胞質抗体陽性	0	0	0	1 (0.2)	1 (<0.1)
抗核抗体増加	0	1 (0.3)	0	0	0
大動脈雑音	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
関節鏡検査	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	7 (5.8)	1 (0.9)	10 (1.7)
細菌検査陽性	0	0	0
好塩基球数増加	0	0	1 (0.2)
血中アルブミン減少	0	0	0
血中アルブミン増加	0	0	1 (0.2)
血中アルカリホスファターゼ減少	0	0	0
血中アルカリホスファターゼ増加	1 (0.8)	0	0
血中重炭酸塩減少	0	0	1 (0.2)
血中ビリルビン増加	0	0	2 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
関節鏡検査	0	1 (0.3)	0	0	1 (<0.1)
アスパラギン酸アミノトランスフェラーゼ増加	1 (4.2)	9 (2.5)	16 (3.4)	13 (2.9)	48 (2.6)
細菌検査陽性	0	0	1 (0.2)	0	1 (<0.1)
好塩基球数増加	0	0	0	0	1 (<0.1)
血中アルブミン減少	0	0	2 (0.4)	0	2 (0.1)
血中アルブミン増加	0	0	1 (0.2)	1 (0.2)	3 (0.2)
血中アルカリホスファターゼ減少	0	0	0	1 (0.2)	1 (<0.1)
血中アルカリホスファターゼ増加	0	0	2 (0.4)	1 (0.2)	3 (0.2)
血中重炭酸塩減少	0	0	1 (0.2)	0	2 (0.1)
血中ビリルビン増加	0	0	7 (1.5)	8 (1.8)	17 (0.9)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
血中非抱合ビリルビン増加	0	0	0
血中カルシウム増加	0	0	0
血中クロール減少	0	0	0
血中コレステロール減少	0	0	1 (0.2)
血中コレステロール増加	0	1 (0.9)	5 (0.9)
血中クレアチン増加	0	0	1 (0.2)
血中クレアチンホスホキナーゼMB増加	0	0	0
血中クレアチンホスホキナーゼ増加	6 (5.0)	11 (10.2)	30 (5.1)
血中クレアチニン増加	1 (0.8)	0	2 (0.3)
血中葉酸減少	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
血中非抱合ビリルビン増加	0	0	0	1 (0.2)	1 (<0.1)
血中カルシウム増加	0	0	2 (0.4)	0	2 (0.1)
血中クロール減少	0	1 (0.3)	0	0	1 (<0.1)
血中コレステロール減少	0	1 (0.3)	1 (0.2)	0	3 (0.2)
血中コレステロール増加	0	1 (0.3)	3 (0.6)	11 (2.5)	21 (1.2)
血中クレアチン増加	0	0	0	1 (0.2)	2 (0.1)
血中クレアチンホスホキナーゼMB増加	0	1 (0.3)	0	0	1 (<0.1)
血中クレアチンホスホキナーゼ増加	8 (33.2)	27 (7.5)	46 (9.9)	63 (14.2)	178 (9.8)
血中クレアチニン増加	0	2 (0.6)	1 (0.2)	8 (1.8)	11 (0.6)
血中葉酸減少	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
血中ブドウ糖	1 (0.8)	0	0
血中ブドウ糖減少	0	0	0
血中ブドウ糖増加	3 (2.5)	0	4 (0.7)
血中鉄減少	0	0	1 (0.2)
血中乳酸脱水素酵素増加	0	0	0
血中マグネシウム減少	0	0	0
血中リン減少	0	0	1 (0.2)
血中カリウム減少	0	0	2 (0.3)
血中カリウム増加	0	0	1 (0.2)
血圧上昇	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
血中ブドウ糖	0	0	0	0	0
血中ブドウ糖減少	0	0	0	1 (0.2)	1 (<0.1)
血中ブドウ糖増加	0	0	1 (0.2)	1 (0.2)	6 (0.3)
血中鉄減少	0	1 (0.3)	0	0	2 (0.1)
血中乳酸脱水素酵素増加	0	1 (0.3)	0	0	1 (<0.1)
血中マグネシウム減少	0	1 (0.3)	0	0	1 (<0.1)
血中リン減少	0	2 (0.6)	1 (0.2)	2 (0.5)	6 (0.3)
血中カリウム減少	0	0	2 (0.4)	0	4 (0.2)
血中カリウム増加	0	0	1 (0.2)	0	2 (0.1)
血圧上昇	0	1 (0.3)	1 (0.2)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
血中ナトリウム増加	0	0	0
血中トリグリセリド異常	0	0	0
血中トリグリセリド減少	0	0	1 (0.2)
血中トリグリセリド増加	0	2 (1.8)	2 (0.3)
血中尿素増加	0	0	1 (0.2)
血中尿酸増加	0	0	0
尿中血陽性	0	0	3 (0.5)
体温上昇	0	0	0
骨密度減少	0	0	0
心雑音	1 (0.8)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
血中ナトリウム増加	0	0	1 (0.2)	0	1 (<0.1)
血中トリグリセリド異常	0	0	1 (0.2)	0	1 (<0.1)
血中トリグリセリド減少	0	0	0	0	1 (<0.1)
血中トリグリセリド増加	0	0	1 (0.2)	1 (0.2)	6 (0.3)
血中尿素増加	0	0	1 (0.2)	0	2 (0.1)
血中尿酸増加	0	1 (0.3)	0	0	1 (<0.1)
尿中血陽性	0	0	0	4 (0.9)	7 (0.4)
体温上昇	0	0	1 (0.2)	2 (0.5)	3 (0.2)
骨密度減少	0	0	1 (0.2)	0	1 (<0.1)
心雑音	0	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
クロストリジウム検査陽性	0	0	2 (0.3)
凝固時間延長	0	0	1 (0.2)
尿中結晶陽性	1 (0.8)	0	0
心電図QT延長	0	0	1 (0.2)
心電図異常	0	0	0
心電図再分極異常	0	0	1 (0.2)
便中カルプロテクチン増加	0	0	3 (0.5)
γ-グルタミルトランスフェラーゼ増加	6 (5.0)	2 (1.8)	2 (0.3)
糸球体濾過率減少	0	0	0
尿中ブドウ糖陽性	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
クロストリジウム検査陽性	1 (4.2)	0	2 (0.4)	0	5 (0.3)
凝固時間延長	0	0	0	0	1 (<0.1)
尿中結晶陽性	0	1 (0.3)	0	0	1 (<0.1)
心電図QT延長	0	0	0	0	1 (<0.1)
心電図異常	0	0	1 (0.2)	0	1 (<0.1)
心電図再分極異常	0	0	0	0	1 (<0.1)
便中カルプロテクチン増加	0	0	0	1 (0.2)	4 (0.2)
γ-グルタミルトランスフェラーゼ増加	0	4 (1.1)	11 (2.4)	4 (0.9)	21 (1.2)
糸球体濾過率減少	1 (4.2)	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
尿中ブドウ糖陽性	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
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	1 (0.2)
ヘモグロビン減少	4 (3.3)	1 (0.9)	5 (0.9)
尿中ヘモグロビン陽性	0	0	0
肝酵素上昇	0	0	9 (1.5)
B型肝炎DNA測定陽性	1 (0.8)	0	2 (0.3)
高比重リポ蛋白増加	0	0	1 (0.2)
ヒト乳頭腫ウイルス検査陽性	0	0	0
眼圧上昇	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
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	2 (0.1)
ヘモグロビン減少	1 (4.2)	3 (0.8)	6 (1.3)	5 (1.1)	20 (1.1)
尿中ヘモグロビン陽性	0	0	0	1 (0.2)	1 (<0.1)
肝酵素上昇	4 (16.6)	1 (0.3)	4 (0.9)	4 (0.9)	22 (1.2)
B型肝炎DNA測定陽性	0	0	0	1 (0.2)	3 (0.2)
高比重リポ蛋白増加	0	1 (0.3)	4 (0.9)	3 (0.7)	9 (0.5)
ヒト乳頭腫ウイルス検査陽性	0	1 (0.3)	0	0	1 (<0.1)
眼圧上昇	0	1 (0.3)	0	1 (0.2)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
臨床検査異常	0	0	1 (0.2)
リパーゼ増加	0	0	0
肝機能検査異常	0	1 (0.9)	0
肝機能検査値上昇	1 (0.8)	0	2 (0.3)
低比重リポ蛋白減少	0	0	2 (0.3)
低比重リポ蛋白増加	0	1 (0.9)	0
リンパ球数減少	1 (0.8)	0	11 (1.9)
リンパ球数増加	0	0	1 (0.2)
リンパ球百分率減少	0	0	0
リンパ球百分率増加	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
臨床検査異常	0	0	0	0	1 (<0.1)
リパーゼ増加	1 (4.2)	0	2 (0.4)	0	3 (0.2)
肝機能検査異常	0	0	0	0	1 (<0.1)
肝機能検査値上昇	0	1 (0.3)	0	2 (0.5)	5 (0.3)
低比重リポ蛋白減少	0	1 (0.3)	1 (0.2)	0	4 (0.2)
低比重リポ蛋白増加	0	0	1 (0.2)	7 (1.6)	9 (0.5)
リンパ球数減少	0	5 (1.4)	15 (3.2)	9 (2.0)	38 (2.1)
リンパ球数増加	1 (4.2)	2 (0.6)	1 (0.2)	4 (0.9)	8 (0.4)
リンパ球百分率減少	0	0	6 (1.3)	2 (0.5)	8 (0.4)
リンパ球百分率増加	0	0	2 (0.4)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
平均赤血球容積異常	0	0	0
平均赤血球容積増加	0	0	0
単球数増加	0	0	3 (0.5)
結核菌群検査陽性	0	0	0
好中球数減少	0	1 (0.9)	5 (0.9)
好中球数増加	1 (0.8)	0	7 (1.2)
好中球百分率増加	0	0	0
血小板数減少	0	0	1 (0.2)
血小板数増加	0	1 (0.9)	0
プレアルブミン減少	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
平均赤血球容積異常	0	0	0	1 (0.2)	1 (<0.1)
平均赤血球容積増加	0	0	1 (0.2)	1 (0.2)	2 (0.1)
単球数増加	0	0	1 (0.2)	0	4 (0.2)
結核菌群検査陽性	0	1 (0.3)	0	0	1 (<0.1)
好中球数減少	4 (16.6)	17 (4.7)	21 (4.5)	23 (5.2)	67 (3.7)
好中球数増加	0	2 (0.6)	4 (0.9)	6 (1.4)	17 (0.9)
好中球百分率増加	0	0	0	2 (0.5)	2 (0.1)
血小板数減少	0	1 (0.3)	0	1 (0.2)	2 (0.1)
血小板数増加	0	1 (0.3)	1 (0.2)	3 (0.7)	6 (0.3)
プレアルブミン減少	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
前立腺特異性抗原増加	0	0	0
総蛋白減少	0	0	0
総蛋白増加	0	0	0
尿中蛋白陽性	5 (4.2)	0	4 (0.7)
赤血球数減少	0	0	3 (0.5)
赤血球数増加	0	0	1 (0.2)
血沈亢進	0	0	0
網状赤血球数減少	0	0	0
網状赤血球数増加	0	0	2 (0.3)
血清フェリチン減少	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
前立腺特異性抗原増加	1 (4.2)	0	1 (0.2)	0	2 (0.1)
総蛋白減少	0	0	1 (0.2)	0	1 (<0.1)
総蛋白増加	0	0	0	1 (0.2)	1 (<0.1)
尿中蛋白陽性	0	1 (0.3)	3 (0.6)	2 (0.5)	9 (0.5)
赤血球数減少	0	0	2 (0.4)	5 (1.1)	10 (0.5)
赤血球数増加	0	0	0	0	1 (<0.1)
血沈亢進	0	0	1 (0.2)	0	1 (<0.1)
網状赤血球数減少	0	0	1 (0.2)	0	1 (<0.1)
網状赤血球数増加	0	0	1 (0.2)	0	3 (0.2)
血清フェリチン減少	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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
尿比重増加	0	0	1 (0.2)
ブドウ球菌検査陽性	0	0	0
トランスアミナーゼ上昇	0	0	0
尿検査異常	1 (0.8)	0	1 (0.2)
尿中ケトン体陽性	1 (0.8)	0	3 (0.5)
尿中白血球エステラーゼ陽性	0	0	3 (0.5)
尿量減少	0	0	1 (0.2)
ビタミンB12減少	0	0	0
ビタミンD減少	1 (0.8)	0	0
体重減少	2 (1.7)	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
尿比重増加	0	0	0	0	1 (<0.1)
ブドウ球菌検査陽性	0	0	1 (0.2)	0	1 (<0.1)
トランスアミナーゼ上昇	0	1 (0.3)	3 (0.6)	1 (0.2)	5 (0.3)
尿検査異常	0	0	1 (0.2)	0	2 (0.1)
尿中ケトン体陽性	0	0	0	1 (0.2)	4 (0.2)
尿中白血球エステラーゼ陽性	0	0	2 (0.4)	0	5 (0.3)
尿量減少	0	0	0	0	1 (<0.1)
ビタミンB12減少	0	1 (0.3)	0	0	1 (<0.1)
ビタミンD減少	0	1 (0.3)	0	1 (0.2)	2 (0.1)
体重減少	0	1 (0.3)	0	2 (0.5)	4 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
体重増加	1 (0.8)	0	4 (0.7)
白血球数減少	3 (2.5)	1 (0.9)	6 (1.0)
白血球数増加	1 (0.8)	1 (0.9)	4 (0.7)
尿中白血球陽性	0	0	4 (0.7)
代謝および栄養障害	33 (27.4)	9 (8.3)	59 (10.1)
食欲減退	4 (3.3)	1 (0.9)	4 (0.7)
脱水	2 (1.7)	0	2 (0.3)
糖尿病	1 (0.8)	0	0
糖尿病性代謝代償不全	0	0	1 (0.2)
脂質異常症	0	0	2 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
体重増加	0	2 (0.6)	2 (0.4)	5 (1.1)	12 (0.7)
白血球数減少	2 (8.3)	15 (4.2)	14 (3.0)	15 (3.4)	49 (2.7)
白血球数増加	1 (4.2)	0	1 (0.2)	3 (0.7)	10 (0.5)
尿中白血球陽性	0	0	1 (0.2)	1 (0.2)	6 (0.3)
代謝および栄養障害	1 (4.2)	33 (9.2)	42 (9.0)	42 (9.5)	170 (9.3)
食欲減退	0	2 (0.6)	1 (0.2)	0	7 (0.4)
脱水	0	0	0	0	2 (0.1)
糖尿病	0	0	0	2 (0.5)	2 (0.1)
糖尿病性代謝代償不全	0	0	0	0	1 (<0.1)
脂質異常症	0	2 (0.6)	4 (0.9)	2 (0.5)	10 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
体液貯留	0	0	1 (0.2)
葉酸欠乏	0	0	0
耐糖能障害	0	0	0
痛風	0	1 (0.9)	0
ヒスタミン不耐性	0	0	1 (0.2)
高カルシウム血症	0	0	0
高コレステロール血症	2 (1.7)	2 (1.8)	8 (1.4)
高血糖	6 (5.0)	0	8 (1.4)
高ホモシステイン血症	0	0	1 (0.2)
高カリウム血症	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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
体液貯留	0	0	0	0	1 (<0.1)
葉酸欠乏	0	0	2 (0.4)	1 (0.2)	3 (0.2)
耐糖能障害	0	2 (0.6)	0	0	1 (<0.1)
痛風	0	0	3 (0.6)	1 (0.2)	5 (0.3)
ヒスタミン不耐性	0	0	0	0	1 (<0.1)
高カルシウム血症	0	0	0	1 (0.2)	1 (<0.1)
高コレステロール血症	0	4 (1.1)	5 (1.1)	7 (1.6)	24 (1.3)
高血糖	0	1 (0.3)	6 (1.3)	4 (0.9)	18 (1.0)
高ホモシステイン血症	0	1 (0.3)	0	0	2 (0.1)
高カリウム血症	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
高リパーゼ血症	0	0	0
高脂血症	2 (1.7)	0	5 (0.9)
高ナトリウム血症	0	0	0
高トリグリセリド血症	2 (1.7)	0	2 (0.3)
高尿酸血症	1 (0.8)	1 (0.9)	0
低アルブミン血症	1 (0.8)	0	1 (0.2)
低カリウム血症	2 (1.7)	0	6 (1.0)
低マグネシウム血症	0	0	3 (0.5)
低ナトリウム血症	1 (0.8)	0	0
低リン酸血症	2 (1.7)	1 (0.9)	4 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
高リパーゼ血症	0	1 (0.3)	0	0	0
高脂血症	0	0	7 (1.5)	2 (0.5)	14 (0.8)
高ナトリウム血症	0	0	0	1 (0.2)	1 (<0.1)
高トリグリセリド血症	0	0	0	1 (0.2)	3 (0.2)
高尿酸血症	0	1 (0.3)	0	2 (0.5)	4 (0.2)
低アルブミン血症	0	0	1 (0.2)	1 (0.2)	3 (0.2)
低カリウム血症	0	4 (1.1)	2 (0.4)	1 (0.2)	10 (0.5)
低マグネシウム血症	0	0	0	0	3 (0.2)
低ナトリウム血症	0	3 (0.8)	1 (0.2)	1 (0.2)	3 (0.2)
低リン酸血症	0	2 (0.6)	1 (0.2)	4 (0.9)	11 (0.6)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
低蛋白血症	0	0	0
食欲亢進	0	1 (0.9)	0
鉄欠乏	4 (3.3)	0	4 (0.7)
ラクトース不耐性	0	0	2 (0.3)
栄養障害	0	0	0
代謝性アシドーシス	0	0	0
代謝症候群	0	0	0
肥満	0	0	0
2型糖尿病	1 (0.8)	0	0
過少体重	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
低蛋白血症	1 (4.2)	1 (0.3)	0	0	2 (0.1)
食欲亢進	0	1 (0.3)	0	0	2 (0.1)
鉄欠乏	0	2 (0.6)	1 (0.2)	2 (0.5)	8 (0.4)
ラクトース不耐性	0	0	0	0	2 (0.1)
栄養障害	0	0	0	1 (0.2)	1 (<0.1)
代謝性アシドーシス	0	0	1 (0.2)	0	1 (<0.1)
代謝症候群	0	0	0	1 (0.2)	1 (<0.1)
肥満	0	0	1 (0.2)	1 (0.2)	2 (0.1)
2型糖尿病	0	1 (0.3)	0	0	0
過少体重	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
ビタミンB群欠乏	0	0	0
ビタミンB1欠乏	1 (0.8)	0	0
ビタミンB12欠乏	0	0	1 (0.2)
ビタミンD欠乏	1 (0.8)	2 (1.8)	3 (0.5)
筋骨格系および結合組織障害	65 (54.0)	38 (35.1)	160 (27.3)
強直性脊椎炎	0	0	0
関節痛	14 (11.6)	7 (6.5)	44 (7.5)
関節炎	1 (0.8)	3 (2.8)	4 (0.7)
腸炎性関節炎	0	0	0
関節障害	8 (6.6)	1 (0.9)	10 (1.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
ビタミンB群欠乏	0	0	1 (0.2)	0	1 (<0.1)
ビタミンB1欠乏	0	0	0	0	0
ビタミンB12欠乏	0	0	1 (0.2)	0	2 (0.1)
ビタミンD欠乏	0	4 (1.1)	3 (0.6)	6 (1.4)	16 (0.9)
筋骨格系および結合組織障害	13 (54.0)	145 (40.4)	112 (24.0)	88 (19.8)	471 (25.9)
強直性脊椎炎	0	1 (0.3)	0	0	0
関節痛	3 (12.5)	33 (9.2)	36 (7.7)	20 (4.5)	118 (6.5)
関節炎	2 (8.3)	1 (0.3)	2 (0.4)	0	10 (0.5)
腸炎性関節炎	0	3 (0.8)	0	1 (0.2)	1 (<0.1)
関節障害	2 (8.3)	10 (2.8)	7 (1.5)	3 (0.7)	26 (1.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
腋窩腫瘤	0	0	1 (0.2)
背部痛	6 (5.0)	6 (5.5)	18 (3.1)
骨痛	0	0	0
滑液包炎	1 (0.8)	0	3 (0.5)
軟骨萎縮	0	0	0
頚部脊柱管狭窄症	0	0	0
軟骨軟化症	0	0	0
尾骨痛	0	0	0
コンパートメント症候群	0	0	1 (0.2)
肋軟骨炎	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
腋窩腫瘤	0	0	0	0	1 (<0.1)
背部痛	0	18 (5.0)	16 (3.4)	11 (2.5)	56 (3.1)
骨痛	0	0	0	1 (0.2)	1 (<0.1)
滑液包炎	0	1 (0.3)	0	2 (0.5)	6 (0.3)
軟骨萎縮	0	0	1 (0.2)	0	1 (<0.1)
頚部脊柱管狭窄症	0	1 (0.3)	0	1 (0.2)	2 (0.1)
軟骨軟化症	0	0	0	2 (0.5)	2 (0.1)
尾骨痛	0	3 (0.8)	0	0	2 (0.1)
コンパートメント症候群	0	0	0	0	1 (<0.1)
肋軟骨炎	0	2 (0.6)	0	2 (0.5)	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
指炎	0	0	0
腱付着部症	0	0	1 (0.2)
外骨腫	0	0	1 (0.2)
側腹部痛	1 (0.8)	0	1 (0.2)
単径部痛	0	0	2 (0.3)
出血性関節症	0	0	0
椎間板変性症	0	0	1 (0.2)
椎間板障害	0	1 (0.9)	0
椎間板突出	0	1 (0.9)	5 (0.9)
関節滲出液	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
指炎	0	1 (0.3)	0	0	1 (<0.1)
腱付着部症	0	0	0	0	1 (<0.1)
外骨腫	0	0	1 (0.2)	0	2 (0.1)
側腹部痛	0	3 (0.8)	1 (0.2)	1 (0.2)	5 (0.3)
尺骨部痛	0	0	0	0	2 (0.1)
出血性関節症	0	1 (0.3)	0	0	0
椎間板変性症	0	1 (0.3)	0	0	1 (<0.1)
椎間板障害	0	0	0	0	1 (<0.1)
椎間板突出	0	1 (0.3)	1 (0.2)	2 (0.5)	10 (0.5)
関節滲出液	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
関節弛緩	0	0	0
関節ロック	0	0	0
関節雑音	0	0	1 (0.2)
関節硬直	1 (0.8)	0	2 (0.3)
関節腫脹	2 (1.7)	0	2 (0.3)
腰部脊柱管狭窄症	0	0	1 (0.2)
脛骨内側過労性症候群	0	0	1 (0.2)
筋拘縮	0	0	0
筋不快感	1 (0.8)	0	0
筋障害	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
関節弛緩	0	0	0	1 (0.2)	1 (<0.1)
関節ロック	0	0	0	2 (0.5)	2 (0.1)
関節雑音	0	0	0	0	1 (<0.1)
関節硬直	0	0	1 (0.2)	0	3 (0.2)
関節腫脹	0	1 (0.3)	2 (0.4)	1 (0.2)	6 (0.3)
腰部脊柱管狭窄症	0	1 (0.3)	0	1 (0.2)	3 (0.2)
脛骨内側過労性症候群	0	0	0	0	1 (<0.1)
筋拘縮	0	0	1 (0.2)	1 (0.2)	2 (0.1)
筋不快感	0	0	0	0	0
筋障害	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
筋痙縮	5 (4.2)	0	6 (1.0)
筋緊張	0	0	0
筋力低下	0	0	0
筋骨格系胸痛	1 (0.8)	2 (1.8)	4 (0.7)
筋骨格不快感	0	0	0
筋骨格痛	1 (0.8)	2 (1.8)	4 (0.7)
筋骨格硬直	0	1 (0.9)	3 (0.5)
筋肉痛	5 (4.2)	0	11 (1.9)
筋膜疼痛症候群	0	1 (0.9)	0
ミオパチー	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
筋痙縮	2 (8.3)	3 (0.8)	3 (0.6)	4 (0.9)	18 (1.0)
筋緊張	1 (4.2)	0	0	0	1 (<0.1)
筋力低下	0	1 (0.3)	0	0	0
筋骨格系胸痛	0	6 (1.7)	1 (0.2)	0	10 (0.5)
筋骨格不快感	0	0	1 (0.2)	0	1 (<0.1)
筋骨格痛	0	5 (1.4)	4 (0.9)	3 (0.7)	15 (0.8)
筋骨格硬直	0	0	1 (0.2)	1 (0.2)	6 (0.3)
筋肉痛	1 (4.2)	5 (1.4)	8 (1.7)	6 (1.4)	29 (1.6)
筋膜疼痛症候群	0	0	0	0	1 (<0.1)
ミオパチー	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
筋炎	1 (0.8)	0	0
頚部痛	1 (0.8)	5 (4.6)	2 (0.3)
骨炎	0	0	0
変形性関節症	1 (0.8)	0	1 (0.2)
骨端症	0	0	0
骨壊死	0	0	2 (0.3)
骨減少症	1 (0.8)	0	1 (0.2)
骨粗鬆症	0	0	1 (0.2)
四肢痛	6 (5.0)	2 (1.8)	9 (1.5)
顎痛	0	0	2 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
筋炎	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
頚部痛	0	1 (0.3)	2 (0.4)	3 (0.7)	10 (0.5)
骨炎	0	0	0	1 (0.2)	1 (<0.1)
変形性関節症	0	5 (1.4)	1 (0.2)	0	5 (0.3)
骨端症	0	1 (0.3)	0	0	1 (<0.1)
骨壊死	0	0	2 (0.4)	0	4 (0.2)
骨減少症	0	2 (0.6)	1 (0.2)	2 (0.5)	6 (0.3)
骨粗鬆症	0	3 (0.8)	4 (0.9)	2 (0.5)	9 (0.5)
四肢痛	1 (4.2)	14 (3.9)	3 (0.6)	7 (1.6)	33 (1.8)
顎痛	0	0	0	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
膝蓋大腿関節痛症候群	0	0	1 (0.2)
病的骨折	0	1 (0.9)	0
関節周囲炎	0	0	0
足底筋膜炎	0	0	2 (0.3)
多発性関節炎	1 (0.8)	0	0
横紋筋融解症	0	0	1 (0.2)
関節リウマチ	0	1 (0.9)	0
肩回旋筋腱板症候群	0	0	1 (0.2)
仙腸骨炎	1 (0.8)	0	0
軟部組織腫瘤	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
膝蓋大腿関節痛症候群	0	0	0	0	1 (<0.1)
病的骨折	0	0	0	1 (0.2)	1 (<0.1)
関節周囲炎	0	2 (0.6)	0	1 (0.2)	3 (0.2)
足底筋膜炎	0	2 (0.6)	1 (0.2)	2 (0.5)	7 (0.4)
多発性関節炎	0	0	0	0	0
横紋筋融解症	0	0	1 (0.2)	0	2 (0.1)
関節リウマチ	0	0	0	0	0
肩回旋筋腱板症候群	0	2 (0.6)	2 (0.4)	0	3 (0.2)
仙腸骨炎	0	0	0	0	0
軟部組織腫瘤	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
脊柱変形	0	1 (0.9)	0
変形性脊椎症	0	0	2 (0.3)
脊椎痛	1 (0.8)	0	0
脊椎炎	0	0	1 (0.2)
脊椎関節障害	4 (3.3)	1 (0.9)	0
軟骨下機能不全骨折	0	0	0
滑液嚢腫	1 (0.8)	0	0
滑膜炎	0	0	2 (0.3)
顎関節症候群	0	0	0
腱痛	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
脊柱変形	0	0	0	0	1 (<0.1)
変形性脊椎症	0	2 (0.6)	0	0	4 (0.2)
脊椎痛	0	1 (0.3)	0	0	1 (<0.1)
脊椎炎	0	0	0	0	1 (<0.1)
脊椎関節障害	0	1 (0.3)	4 (0.9)	0	5 (0.3)
軟骨下機能不全骨折	0	0	1 (0.2)	0	1 (<0.1)
滑液嚢腫	0	0	0	0	0
滑膜炎	0	0	0	0	2 (0.1)
顎関節症候群	0	1 (0.3)	0	1 (0.2)	2 (0.1)
腱痛	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
腱炎	0	1 (0.9)	3 (0.5)
腱鞘炎	0	0	0
弾発指	0	0	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.8)	9 (8.3)	18 (3.1)
アクロコルドン	0	0	1 (0.2)
結腸腺癌	0	1 (0.9)	0
膵腺癌	0	0	1 (0.2)
基底細胞癌	0	3 (2.8)	0
肺の良性新生物	0	0	0
精巣の良性新生物	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
腱炎	0	2 (0.6)	0	2 (0.5)	6 (0.3)
腱鞘炎	0	1 (0.3)	0	0	0
弾発指	1 (4.2)	0	1 (0.2)	0	3 (0.2)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)	1 (4.2)	9 (2.5)	14 (3.0)	22 (5.0)	68 (3.7)
アクロコルドン	0	0	0	0	1 (<0.1)
結腸腺癌	0	0	0	1 (0.2)	2 (0.1)
膵腺癌	0	0	0	0	1 (<0.1)
基底細胞癌	0	1 (0.3)	0	5 (1.1)	9 (0.5)
肺の良性新生物	0	0	1 (0.2)	0	1 (<0.1)
精巣の良性新生物	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
良性脾腫瘍	0	0	0
ボーエン病	0	0	1 (0.2)
気管支の良性新生物	0	0	0
大腸腺腫	0	2 (1.8)	2 (0.3)
線維腫	0	0	0
線維性組織球腫	0	0	1 (0.2)
神経節腫	0	0	0
皮膚血管腫	0	0	0
浸潤性乳癌	0	0	0
喉頭扁平上皮癌	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
良性脾腫瘍	0	0	0	1 (0.2)	1 (<0.1)
ボーエン病	0	0	0	1 (0.2)	2 (0.1)
気管支の良性新生物	0	0	1 (0.2)	0	1 (<0.1)
大腸腺腫	0	2 (0.6)	1 (0.2)	0	5 (0.3)
線維腫	0	0	0	1 (0.2)	1 (<0.1)
線維性組織球腫	0	0	0	1 (0.2)	2 (0.1)
神経節腫	1 (4.2)	0	0	0	1 (<0.1)
皮膚血管腫	0	0	1 (0.2)	0	1 (<0.1)
浸潤性乳癌	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
喉頭扁平上皮癌	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
脂肪腫	0	0	0
悪性黒色腫	0	0	1 (0.2)
メラノサイト性母斑	0	0	4 (0.7)
口腔線維腫	0	1 (0.9)	0
卵巣胚細胞良性奇形腫	0	0	0
前立腺癌	0	0	0
脂漏性角化症	1 (0.8)	0	0
皮膚乳頭腫	0	1 (0.9)	4 (0.7)
小細胞癌	0	0	0
扁平上皮癌	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
脂肪腫	0	0	1 (0.2)	1 (0.2)	2 (0.1)
悪性黒色腫	0	0	0	0	1 (<0.1)
メラノサイト性母斑	0	0	1 (0.2)	0	5 (0.3)
口腔線維腫	0	0	0	0	0
卵巣胚細胞良性奇形腫	0	0	1 (0.2)	0	1 (<0.1)
前立腺癌	0	1 (0.3)	0	0	1 (<0.1)
脂漏性角化症	0	1 (0.3)	1 (0.2)	2 (0.5)	3 (0.2)
皮膚乳頭腫	0	1 (0.3)	1 (0.2)	6 (1.4)	13 (0.7)
小細胞癌	0	0	0	1 (0.2)	1 (<0.1)
扁平上皮癌	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
皮膚有棘細胞癌	0	0	1 (0.2)
子宮頚部扁平上皮癌	0	0	0
精巣（純粋）セミノーマ	0	0	0
精巣癌	0	0	0
甲状腺腺腫	0	0	0
子宮平滑筋腫	0	0	1 (0.2)
神経系障害	32 (26.6)	24 (22.2)	87 (14.8)
健忘	0	0	1 (0.2)
脳損傷	0	0	0
灼熱感	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
皮膚有棘細胞癌	0	1 (0.3)	0	0	2 (0.1)
子宮頚部扁平上皮癌	0	0	0	1 (0.2)	1 (<0.1)
精巣（純粋）セミノーマ	0	0	1 (0.2)	0	1 (<0.1)
精巣癌	0	0	0	1 (0.2)	1 (<0.1)
甲状腺腺腫	0	0	1 (0.2)	0	1 (<0.1)
子宮平滑筋腫	0	1 (0.3)	1 (0.2)	0	3 (0.2)
神経系障害	11 (45.7)	62 (17.3)	56 (12.0)	76 (17.1)	279 (15.3)
健忘	0	0	0	0	1 (<0.1)
脳損傷	0	0	1 (0.2)	0	1 (<0.1)
灼熱感	1 (4.2)	0	1 (0.2)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
神経系障害 (Cont.)			
手根管症候群	2 (1.7)	0	3 (0.5)
脳虚血	0	0	0
脳血管発作	0	0	0
頚髄神経根障害	0	0	1 (0.2)
注意力障害	0	0	2 (0.3)
浮動性めまい	1 (0.8)	4 (3.7)	11 (1.9)
異常感覚	0	0	1 (0.2)
構語障害	0	0	1 (0.2)
味覚不全	0	0	0
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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)					
手根管症候群	0	1 (0.3)	2 (0.4)	2 (0.5)	7 (0.4)
脳虚血	0	0	2 (0.4)	0	2 (0.1)
脳血管発作	0	0	0	1 (0.2)	1 (<0.1)
頚髄神経根障害	0	1 (0.3)	0	0	1 (<0.1)
注意力障害	0	0	0	0	2 (0.1)
浮動性めまい	0	5 (1.4)	7 (1.5)	13 (2.9)	36 (2.0)
異常感覚	0	0	0	0	1 (<0.1)
構語障害	0	0	0	0	1 (<0.1)
味覚不全	0	1 (0.3)	0	0	0
てんかん	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
神経系障害 (Cont.)			
本態性振戦	0	0	0
頭痛	20 (16.6)	10 (9.2)	35 (6.0)
知覚過敏	0	0	2 (0.3)
感覚鈍麻	0	1 (0.9)	3 (0.5)
頭蓋内動脈瘤	0	0	1 (0.2)
ラクナ梗塞	0	0	0
腰仙部神経根障害	0	0	0
記憶障害	0	0	1 (0.2)
片頭痛	3 (2.5)	0	8 (1.4)
神経圧迫	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)					
本態性振戦	0	1 (0.3)	0	0	0
頭痛	6 (24.9)	31 (8.6)	29 (6.2)	32 (7.2)	128 (7.0)
知覚過敏	0	1 (0.3)	0	0	2 (0.1)
感覚鈍麻	0	2 (0.6)	4 (0.9)	2 (0.5)	11 (0.6)
頭蓋内動脈瘤	0	0	0	0	1 (<0.1)
ラクナ梗塞	0	0	0	1 (0.2)	1 (<0.1)
腰仙部神経根障害	0	0	1 (0.2)	0	1 (<0.1)
記憶障害	0	0	0	1 (0.2)	2 (0.1)
片頭痛	2 (8.3)	8 (2.2)	4 (0.9)	4 (0.9)	22 (1.2)
神経圧迫	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
神経系障害 (Cont.)			
神経痛	0	0	1 (0.2)
神経炎	0	0	0
末梢性ニューロパチー	0	0	0
後頭神経痛	0	0	0
起立不耐性	0	1 (0.9)	0
錯感覚	2 (1.7)	2 (1.8)	4 (0.7)
末梢性感覚ニューロパチー	0	1 (0.9)	0
睡眠の質低下	0	0	0
ヘルペス後神経痛	0	0	0
失神寸前の状態	1 (0.8)	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)					
神経痛	0	1 (0.3)	0	1 (0.2)	3 (0.2)
神経炎	0	0	0	1 (0.2)	1 (<0.1)
末梢性ニューロパチー	1 (4.2)	1 (0.3)	0	1 (0.2)	2 (0.1)
後頭神経痛	0	0	1 (0.2)	0	1 (<0.1)
起立不耐性	0	0	0	0	1 (<0.1)
錯感覚	0	3 (0.8)	1 (0.2)	2 (0.5)	10 (0.5)
末梢性感覚ニューロパチー	0	0	0	0	0
睡眠の質低下	0	0	0	1 (0.2)	1 (<0.1)
ヘルペス後神経痛	1 (4.2)	0	0	1 (0.2)	2 (0.1)
失神寸前の状態	0	1 (0.3)	0	1 (0.2)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
神経系障害 (Cont.)			
回内筋症候群	0	0	1 (0.2)
橈骨神経麻痺	0	0	1 (0.2)
神経根痛	0	0	1 (0.2)
下肢静止不能症候群	0	0	1 (0.2)
坐骨神経痛	0	2 (1.8)	2 (0.3)
発作様現象	0	0	1 (0.2)
副鼻腔炎に伴う頭痛	0	0	1 (0.2)
傾眠	0	0	0
脊椎炎性脊髄症	0	0	0
くも膜下出血	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)					
回内筋症候群	0	0	0	0	1 (<0.1)
橈骨神経麻痺	0	0	0	0	1 (<0.1)
神経根痛	0	0	0	0	1 (<0.1)
下肢静止不能症候群	0	0	0	1 (0.2)	2 (0.1)
坐骨神経痛	0	1 (0.3)	1 (0.2)	1 (0.2)	5 (0.3)
発作様現象	0	0	0	0	1 (<0.1)
副鼻腔炎に伴う頭痛	0	0	0	0	1 (<0.1)
傾眠	0	0	0	1 (0.2)	1 (<0.1)
脊椎炎性脊髄症	0	0	0	1 (0.2)	1 (<0.1)
くも膜下出血	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
神経系障害 (Cont.)			
硬膜下滲出液	0	0	0
失神	1 (0.8)	1 (0.9)	2 (0.3)
味覚障害	0	0	0
緊張性頭痛	2 (1.7)	1 (0.9)	0
振戦	0	1 (0.9)	1 (0.2)
視野欠損	0	0	0
精神障害	19 (15.8)	9 (8.3)	36 (6.1)
異常な夢	0	0	1 (0.2)
急性精神病	0	0	0
急性ストレス反応	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

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)					
硬膜下滲出液	0	0	1 (0.2)	0	1 (<0.1)
失神	0	2 (0.6)	0	2 (0.5)	6 (0.3)
味覚障害	0	0	0	1 (0.2)	1 (<0.1)
緊張性頭痛	0	0	0	1 (0.2)	2 (0.1)
振戦	0	1 (0.3)	1 (0.2)	1 (0.2)	5 (0.3)
視野欠損	0	0	0	1 (0.2)	1 (<0.1)
精神障害	3 (12.5)	36 (10.0)	21 (4.5)	29 (6.5)	114 (6.3)
異常な夢	0	0	0	0	1 (<0.1)
急性精神病	0	0	1 (0.2)	0	1 (<0.1)
急性ストレス反応	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
精神障害 (Cont.)			
感情障害	0	0	0
激越	0	0	1 (0.2)
不安	8 (6.6)	6 (5.5)	2 (0.3)
不安障害	0	0	0
注意欠如・多動性障害	0	0	1 (0.2)
自閉症スペクトラム障害	0	0	1 (0.2)
抑うつ気分	0	0	1 (0.2)
うつ病	3 (2.5)	1 (0.9)	9 (1.5)
全般性不安障害	0	0	1 (0.2)
初期不眠症	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害 (Cont.)					
感情障害	0	1 (0.3)	0	0	1 (<0.1)
激越	0	0	0	0	1 (<0.1)
不安	1 (4.2)	8 (2.2)	6 (1.3)	4 (0.9)	20 (1.1)
不安障害	0	0	2 (0.4)	0	2 (0.1)
注意欠如・多動性障害	0	0	0	0	1 (<0.1)
自閉症スペクトラム障害	0	0	0	0	1 (<0.1)
抑うつ気分	0	0	0	1 (0.2)	2 (0.1)
うつ病	0	5 (1.4)	3 (0.6)	9 (2.0)	25 (1.4)
全般性不安障害	0	0	0	0	1 (<0.1)
初期不眠症	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
精神障害 (Cont.)			
不眠症	6 (5.0)	1 (0.9)	11 (1.9)
故意の自傷行為	0	0	0
易刺激性	0	1 (0.9)	2 (0.3)
リビドー減退	0	0	0
精神障害	0	0	0
気分変化	0	0	1 (0.2)
悪夢	0	0	0
パニック発作	1 (0.8)	0	0
心的外傷後ストレス障害	0	0	0
落ち着きのなさ	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害 (Cont.)					
不眠症	2 (8.3)	13 (3.6)	3 (0.6)	12 (2.7)	36 (2.0)
故意の自傷行為	0	0	0	1 (0.2)	1 (<0.1)
易刺激性	0	1 (0.3)	0	0	2 (0.1)
リビドー減退	0	1 (0.3)	0	0	1 (<0.1)
精神障害	0	1 (0.3)	0	0	0
気分変化	0	0	0	0	1 (<0.1)
悪夢	0	0	0	1 (0.2)	1 (<0.1)
パニック発作	0	0	1 (0.2)	0	1 (<0.1)
心的外傷後ストレス障害	0	0	1 (0.2)	0	1 (<0.1)
落ち着きのなさ	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
精神障害 (Cont.)			
睡眠障害	1 (0.8)	0	2 (0.3)
社交不安障害	0	0	1 (0.2)
ストレス	0	0	0
自殺念慮	0	0	0
自殺企図	0	0	1 (0.2)
腎および尿路障害	11 (9.1)	5 (4.6)	38 (6.5)
急性腎障害	0	0	0
膀胱痛	1 (0.8)	0	0
膀胱タンポナーデ	0	0	1 (0.2)
尿路結石	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害 (Cont.)					
睡眠障害	0	2 (0.6)	3 (0.6)	0	6 (0.3)
社交不安障害	0	0	0	0	1 (<0.1)
ストレス	0	0	0	1 (0.2)	1 (<0.1)
自殺念慮	0	2 (0.6)	0	0	1 (<0.1)
自殺企図	0	1 (0.3)	0	0	2 (0.1)
腎および尿路障害	3 (12.5)	26 (7.2)	17 (3.6)	28 (6.3)	103 (5.7)
急性腎障害	0	1 (0.3)	1 (0.2)	1 (0.2)	2 (0.1)
膀胱痛	0	0	0	0	0
膀胱タンポナーデ	0	0	0	0	1 (<0.1)
尿路結石	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
慢性腎臓病	0	0	0
肋骨脊柱角圧痛	0	0	1 (0.2)
出血性膀胱炎	0	0	1 (0.2)
非感染性膀胱炎	0	0	2 (0.3)
排尿困難	2 (1.7)	0	7 (1.2)
糖尿	0	0	0
血尿	1 (0.8)	0	1 (0.2)
水腎症	0	0	0
緊張性膀胱	0	0	0
ケトン尿	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
慢性腎臓病	1 (4.2)	0	0	1 (0.2)	2 (0.1)
肋骨脊柱角圧痛	0	0	0	0	1 (<0.1)
出血性膀胱炎	0	0	0	0	1 (<0.1)
非感染性膀胱炎	0	0	0	0	2 (0.1)
排尿困難	1 (4.2)	5 (1.4)	3 (0.6)	3 (0.7)	18 (1.0)
糖尿	0	1 (0.3)	0	0	0
血尿	0	3 (0.8)	2 (0.4)	5 (1.1)	9 (0.5)
水腎症	0	1 (0.3)	0	0	0
緊張性膀胱	0	1 (0.3)	0	1 (0.2)	2 (0.1)
ケトン尿	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
白血球尿	0	0	0
排尿異常	0	0	0
尿意切迫	0	0	2 (0.3)
腎石灰沈着症	0	0	0
腎結石症	1 (0.8)	3 (2.8)	4 (0.7)
夜間頻尿	0	0	3 (0.5)
頻尿	2 (1.7)	1 (0.9)	1 (0.2)
多尿	0	0	1 (0.2)
蛋白尿	4 (3.3)	0	7 (1.2)
腎萎縮	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
白血球尿	1 (4.2)	1 (0.3)	0	0	1 (<0.1)
排尿異常	0	0	0	1 (0.2)	1 (<0.1)
尿意切迫	0	0	0	0	2 (0.1)
腎石灰沈着症	0	1 (0.3)	0	0	0
腎結石症	0	5 (1.4)	5 (1.1)	4 (0.9)	19 (1.0)
夜間頻尿	0	0	0	0	3 (0.2)
頻尿	0	1 (0.3)	0	1 (0.2)	3 (0.2)
多尿	0	0	0	0	1 (<0.1)
蛋白尿	0	4 (1.1)	1 (0.2)	3 (0.7)	13 (0.7)
腎萎縮	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
腎仙痛	0	0	1 (0.2)
腎機能障害	0	0	1 (0.2)
腎臓痛	0	0	1 (0.2)
腎尿細管機能障害	0	0	0
尿管閉塞	0	0	1 (0.2)
尿管結石症	0	0	3 (0.5)
尿閉	0	0	0
生殖系および乳房障害	0	5 (4.6)	18 (3.1)
無月経	0	0	0
萎縮性外陰腟炎	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
腎仙痛	0	0	0	6 (1.4)	7 (0.4)
腎機能障害	0	0	2 (0.4)	0	3 (0.2)
腎臓痛	0	1 (0.3)	0	0	2 (0.1)
腎尿細管機能障害	0	0	0	1 (0.2)	1 (<0.1)
尿管閉塞	0	0	0	0	1 (<0.1)
尿管結石症	0	0	1 (0.2)	1 (0.2)	5 (0.3)
尿閉	0	0	1 (0.2)	0	1 (<0.1)
生殖系および乳房障害	0	19 (5.3)	18 (3.9)	16 (3.6)	68 (3.7)
無月経	0	2 (0.6)	1 (0.2)	1 (0.2)	4 (0.2)
萎縮性外陰腟炎	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
バルトリン嚢腫	0	0	0
良性前立腺肥大症	0	0	2 (0.3)
乳房嚢胞	0	0	0
乳房障害	0	0	0
乳房腫大	0	0	1 (0.2)
乳房腫瘤	0	0	0
乳房痛	0	0	0
子宮頚部上皮異形成	0	0	1 (0.2)
子宮頚管ポリープ	0	0	1 (0.2)
子宮頚部障害	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
バルトリン嚢腫	0	1 (0.3)	0	0	0
良性前立腺肥大症	0	0	3 (0.6)	2 (0.5)	7 (0.4)
乳房嚢胞	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
乳房障害	0	1 (0.3)	0	0	1 (<0.1)
乳房腫大	0	0	0	0	1 (<0.1)
乳房腫瘤	0	1 (0.3)	0	0	1 (<0.1)
乳房痛	0	0	1 (0.2)	0	1 (<0.1)
子宮頚部上皮異形成	0	1 (0.3)	0	2 (0.5)	4 (0.2)
子宮頚管ポリープ	0	0	0	0	1 (<0.1)
子宮頚部障害	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
子宮頚部の炎症	0	0	0
性交出血	0	0	1 (0.2)
月経困難症	0	0	0
勃起不全	0	1 (0.9)	1 (0.2)
性器びらん	0	0	1 (0.2)
閉経期症状	0	0	0
不規則月経	0	0	1 (0.2)
不正子宮出血	0	0	0
卵巣嚢胞	0	0	1 (0.2)
卵巣静脈血栓症	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
子宮頚部の炎症	0	0	1 (0.2)	0	1 (<0.1)
性交出血	0	0	0	0	1 (<0.1)
月経困難症	0	0	1 (0.2)	2 (0.5)	3 (0.2)
勃起不全	0	0	1 (0.2)	1 (0.2)	4 (0.2)
性器びらん	0	0	0	0	1 (<0.1)
閉経期症状	0	2 (0.6)	0	0	1 (<0.1)
不規則月経	0	2 (0.6)	1 (0.2)	1 (0.2)	4 (0.2)
不正子宮出血	0	0	2 (0.4)	1 (0.2)	3 (0.2)
卵巣嚢胞	0	1 (0.3)	0	0	2 (0.1)
卵巣静脈血栓症	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
多嚢胞性卵巣	0	0	0
閉経後出血	0	0	0
月経前頭痛	0	0	0
月経前症候群	0	1 (0.9)	0
前立腺炎	0	1 (0.9)	2 (0.3)
精液変色	0	0	0
精嚢腺炎	0	0	0
子宮ポリープ	0	0	1 (0.2)
子宮脱	0	1 (0.9)	0
腟分泌物	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
多嚢胞性卵巣	0	0	1 (0.2)	0	1 (<0.1)
閉経後出血	0	0	0	1 (0.2)	1 (<0.1)
月経前頭痛	0	0	0	1 (0.2)	1 (<0.1)
月経前症候群	0	0	0	0	1 (<0.1)
前立腺炎	0	2 (0.6)	1 (0.2)	1 (0.2)	6 (0.3)
精液変色	0	1 (0.3)	0	2 (0.5)	3 (0.2)
精嚢腺炎	0	0	1 (0.2)	0	1 (<0.1)
子宮ポリープ	0	0	0	0	1 (<0.1)
子宮脱	0	0	0	0	1 (<0.1)
腟分泌物	0	0	1 (0.2)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
腟出血	0	0	0
精索静脈瘤	0	0	0
外陰腟不快感	0	0	1 (0.2)
外陰腟の炎症	0	0	1 (0.2)
外陰腟痛	0	0	1 (0.2)
外陰腟そう痒症	0	0	0
呼吸器、胸郭および縦隔障害	31 (25.7)	8 (7.4)	110 (18.8)
急性呼吸不全	0	0	0
胞隔炎	0	0	0
失声症	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
腟出血	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
精索静脈瘤	0	0	1 (0.2)	0	1 (<0.1)
外陰腟不快感	0	0	0	1 (0.2)	2 (0.1)
外陰腟の炎症	0	0	0	0	1 (<0.1)
外陰腟痛	0	0	0	0	1 (<0.1)
外陰腟そう痒症	0	2 (0.6)	0	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	14 (58.1)	56 (15.6)	48 (10.3)	58 (13.1)	268 (14.7)
急性呼吸不全	0	1 (0.3)	0	1 (0.2)	1 (<0.1)
胞隔炎	1 (4.2)	0	0	0	1 (<0.1)
失声症	0	0	0	2 (0.5)	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
喘息	0	0	7 (1.2)
無気肺	0	0	1 (0.2)
気管支反応性亢進	0	0	0
気管支拡張症	0	0	0
カタル	1 (0.8)	0	0
慢性閉塞性肺疾患	1 (0.8)	0	1 (0.2)
咳嗽	7 (5.8)	2 (1.8)	25 (4.3)
嚢胞性肺疾患	0	0	0
横隔膜痛	1 (0.8)	0	0
咽喉乾燥	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
喘息	0	1 (0.3)	1 (0.2)	1 (0.2)	10 (0.5)
無気肺	0	1 (0.3)	0	0	2 (0.1)
気管支反応性亢進	0	0	0	1 (0.2)	1 (<0.1)
気管支拡張症	0	1 (0.3)	0	0	0
カタル	0	0	0	0	0
慢性閉塞性肺疾患	0	0	3 (0.6)	0	4 (0.2)
咳嗽	4 (16.6)	12 (3.3)	11 (2.4)	9 (2.0)	59 (3.2)
嚢胞性肺疾患	0	0	1 (0.2)	0	1 (<0.1)
横隔膜痛	0	0	0	0	0
咽喉乾燥	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
発声障害	0	0	1 (0.2)
呼吸困難	0	0	10 (1.7)
労作性呼吸困難	0	0	1 (0.2)
肺気腫	0	0	0
鼻出血	0	1 (0.9)	8 (1.4)
喀血	0	0	0
しゃっくり	0	0	0
上気道分泌増加	0	0	0
間質性肺疾患	0	0	0
肺過膨脹	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
発声障害	0	1 (0.3)	0	0	2 (0.1)
呼吸困難	2 (8.3)	1 (0.3)	2 (0.4)	2 (0.5)	17 (0.9)
労作性呼吸困難	0	0	0	1 (0.2)	2 (0.1)
肺気腫	0	0	0	1 (0.2)	1 (<0.1)
鼻出血	0	1 (0.3)	1 (0.2)	4 (0.9)	15 (0.8)
喀血	0	1 (0.3)	0	0	0
しゃっくり	0	1 (0.3)	0	1 (0.2)	1 (<0.1)
上気道分泌増加	0	1 (0.3)	0	0	1 (<0.1)
間質性肺疾患	0	1 (0.3)	0	0	0
肺過膨脹	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
肺浸潤	0	0	1 (0.2)
鼻閉	1 (0.8)	1 (0.9)	6 (1.0)
鼻中隔弯曲	0	0	0
鼻中隔障害	0	0	0
鼻甲介肥大	0	0	0
鼻潰瘍	0	0	0
非感染性気管支炎	0	0	0
口腔咽頭不快感	0	0	0
口腔咽頭痛	3 (2.5)	2 (1.8)	22 (3.8)
呼吸時疼痛	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
肺浸潤	0	0	0	0	1 (<0.1)
鼻閉	1 (4.2)	3 (0.8)	1 (0.2)	4 (0.9)	13 (0.7)
鼻中隔弯曲	0	0	1 (0.2)	0	1 (<0.1)
鼻中隔障害	0	0	0	1 (0.2)	1 (<0.1)
鼻甲介肥大	0	0	1 (0.2)	0	1 (<0.1)
鼻潰瘍	0	0	3 (0.6)	0	3 (0.2)
非感染性気管支炎	0	0	0	1 (0.2)	1 (<0.1)
口腔咽頭不快感	0	1 (0.3)	0	0	1 (<0.1)
口腔咽頭痛	3 (12.5)	9 (2.5)	10 (2.1)	10 (2.3)	51 (2.8)
呼吸時疼痛	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
副鼻腔不快感	1 (0.8)	0	0
副鼻腔分泌過多	0	0	1 (0.2)
咽頭紅斑	0	0	0
咽頭病変	0	0	1 (0.2)
胸膜障害	1 (0.8)	0	0
胸水	0	0	2 (0.3)
胸膜痛	0	0	1 (0.2)
肺臓炎	2 (1.7)	0	0
気胸	1 (0.8)	0	0
湿性咳嗽	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
副鼻腔不快感	0	0	0	0	0
副鼻腔分泌過多	0	0	0	0	1 (<0.1)
咽頭紅斑	0	0	0	1 (0.2)	1 (<0.1)
咽頭病変	0	0	0	0	1 (<0.1)
胸膜障害	0	0	0	0	0
胸水	0	0	1 (0.2)	0	3 (0.2)
胸膜痛	0	0	0	0	1 (<0.1)
肺臓炎	0	0	0	0	0
気胸	0	0	0	0	0
湿性咳嗽	0	3 (0.8)	2 (0.4)	3 (0.7)	8 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
肺塞栓症	1 (0.8)	0	3 (0.5)
肺出血	0	0	0
肺腫瘤	2 (1.7)	0	3 (0.5)
気道うっ血	0	0	2 (0.3)
鼻痛	0	0	1 (0.2)
アレルギー性鼻炎	1 (0.8)	0	1 (0.2)
鼻漏	2 (1.7)	1 (0.9)	1 (0.2)
低音性連続性ラ音	0	0	0
副鼻腔うっ血	2 (1.7)	0	2 (0.3)
副鼻腔障害	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
肺塞栓症	1 (4.2)	0	2 (0.4)	0	6 (0.3)
肺出血	0	1 (0.3)	0	0	0
肺腫瘤	1 (4.2)	0	0	1 (0.2)	5 (0.3)
気道うっ血	0	1 (0.3)	0	0	3 (0.2)
鼻痛	1 (4.2)	0	0	0	2 (0.1)
アレルギー性鼻炎	0	4 (1.1)	2 (0.4)	1 (0.2)	7 (0.4)
鼻漏	0	0	0	2 (0.5)	4 (0.2)
低音性連続性ラ音	0	0	1 (0.2)	0	1 (<0.1)
副鼻腔うっ血	0	3 (0.8)	2 (0.4)	4 (0.9)	8 (0.4)
副鼻腔障害	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
副鼻腔痛	0	0	0
睡眠時無呼吸症候群	0	0	3 (0.5)
咽喉刺激感	0	0	1 (0.2)
扁桃肥大	0	0	1 (0.2)
上気道うっ血	0	0	1 (0.2)
上気道の炎症	2 (1.7)	0	0
上気道咳症候群	2 (1.7)	0	1 (0.2)
声帯ポリープ	0	1 (0.9)	0
喘鳴	0	0	0
皮膚および皮下組織障害	48 (39.8)	26 (24.0)	126 (21.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
副鼻腔痛	0	1 (0.3)	0	0	1 (<0.1)
睡眠時無呼吸症候群	0	0	1 (0.2)	1 (0.2)	5 (0.3)
咽喉刺激感	0	0	0	1 (0.2)	2 (0.1)
扁桃肥大	0	0	0	0	1 (<0.1)
上気道うっ血	0	0	0	0	1 (<0.1)
上気道の炎症	0	4 (1.1)	1 (0.2)	1 (0.2)	4 (0.2)
上気道咳症候群	0	1 (0.3)	0	2 (0.5)	4 (0.2)
声帯ポリープ	0	0	0	0	0
喘鳴	0	2 (0.6)	0	0	2 (0.1)
皮膚および皮下組織障害	19 (78.9)	149 (41.5)	113 (24.2)	141 (31.8)	487 (26.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
ざ瘡	3 (2.5)	3 (2.8)	18 (3.1)
嚢胞性ざ瘡	0	0	0
光線角化症	0	0	1 (0.2)
脱毛症	2 (1.7)	1 (0.9)	11 (1.9)
アンドロゲン性脱毛症	0	0	0
皮脂欠乏症	0	0	0
水疱	0	0	0
皮膚嚢腫	1 (0.8)	0	1 (0.2)
皮膚炎	2 (1.7)	1 (0.9)	3 (0.5)
ざ瘡様皮膚炎	1 (0.8)	0	5 (0.9)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
ざ瘡	5 (20.8)	25 (7.0)	28 (6.0)	38 (8.6)	109 (6.0)
嚢胞性ざ瘡	0	0	1 (0.2)	0	1 (<0.1)
光線角化症	0	1 (0.3)	0	0	2 (0.1)
脱毛症	2 (8.3)	4 (1.1)	5 (1.1)	9 (2.0)	32 (1.8)
アンドロゲン性脱毛症	0	0	0	1 (0.2)	1 (<0.1)
皮脂欠乏症	0	0	0	1 (0.2)	1 (<0.1)
水疱	0	1 (0.3)	0	1 (0.2)	2 (0.1)
皮膚嚢腫	0	0	1 (0.2)	0	2 (0.1)
皮膚炎	0	4 (1.1)	3 (0.6)	4 (0.9)	11 (0.6)
ざ瘡様皮膚炎	1 (4.2)	2 (0.6)	3 (0.6)	1 (0.2)	12 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
アレルギー性皮膚炎	1 (0.8)	0	0
アトピー性皮膚炎	1 (0.8)	0	0
接触皮膚炎	3 (2.5)	0	2 (0.3)
剥脱性皮膚炎	0	0	0
乾癬様皮膚炎	0	1 (0.9)	0
皮膚症	0	0	0
びまん性脱毛症	0	0	0
薬疹	0	0	1 (0.2)
皮膚乾燥	3 (2.5)	1 (0.9)	2 (0.3)
異汗性湿疹	2 (1.7)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
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	3 (0.8)	2 (0.4)	1 (0.2)	3 (0.2)
接触皮膚炎	0	3 (0.8)	2 (0.4)	2 (0.5)	7 (0.4)
剥脱性皮膚炎	0	0	1 (0.2)	0	1 (<0.1)
乾癬様皮膚炎	0	0	0	0	0
皮膚症	0	1 (0.3)	0	0	1 (<0.1)
びまん性脱毛症	0	0	1 (0.2)	0	1 (<0.1)
薬疹	0	0	0	0	1 (<0.1)
皮膚乾燥	0	5 (1.4)	2 (0.4)	2 (0.5)	6 (0.3)
異汗性湿疹	0	2 (0.6)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
斑状出血	0	0	1 (0.2)
湿疹	4 (3.3)	0	9 (1.5)
皮脂欠乏性湿疹	0	0	0
紅斑	1 (0.8)	2 (1.8)	4 (0.7)
環状紅斑	0	0	1 (0.2)
多形紅斑	0	0	0
結節性紅斑	0	1 (0.9)	0
固定疹	0	0	0
多汗症	1 (0.8)	0	0
過角化	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
斑状出血	0	3 (0.8)	0	1 (0.2)	4 (0.2)
湿疹	1 (4.2)	9 (2.5)	7 (1.5)	8 (1.8)	29 (1.6)
皮脂欠乏性湿疹	0	1 (0.3)	0	2 (0.5)	2 (0.1)
紅斑	0	4 (1.1)	4 (0.9)	4 (0.9)	14 (0.8)
環状紅斑	0	0	0	0	1 (<0.1)
多形紅斑	1 (4.2)	0	0	0	1 (<0.1)
結節性紅斑	0	1 (0.3)	0	1 (0.2)	1 (<0.1)
固定疹	0	0	0	1 (0.2)	1 (<0.1)
多汗症	0	0	0	0	0
過角化	0	2 (0.6)	0	1 (0.2)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
多毛症	0	1 (0.9)	0
嵌入爪	0	0	0
内方発育毛	0	0	1 (0.2)
瘢痕そう痒感	0	0	0
毛孔性角化症	0	0	1 (0.2)
黒子	0	0	0
扁平苔癬	0	0	1 (0.2)
機械性蕁麻疹	0	0	1 (0.2)
汗疹	0	0	1 (0.2)
爪肥厚	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
多毛症	0	0	0	0	0
嵌入爪	0	1 (0.3)	1 (0.2)	0	2 (0.1)
内方発育毛	0	0	0	0	1 (<0.1)
瘢痕そう痒感	0	0	0	1 (0.2)	1 (<0.1)
毛孔性角化症	0	0	0	0	1 (<0.1)
黒子	0	0	0	1 (0.2)	1 (<0.1)
扁平苔癬	0	0	0	0	1 (<0.1)
機械性蕁麻疹	0	0	0	1 (0.2)	2 (0.1)
汗疹	0	1 (0.3)	0	1 (0.2)	3 (0.2)
爪肥厚	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
神経皮膚炎	0	0	0
寝汗	1 (0.8)	1 (0.9)	3 (0.5)
爪破損	0	0	1 (0.2)
爪甲剥離症	0	0	1 (0.2)
皮膚疼痛	0	0	0
脂肪織炎	0	0	1 (0.2)
丘疹	1 (0.8)	0	1 (0.2)
口囲皮膚炎	0	0	1 (0.2)
点状出血	0	0	1 (0.2)
光線性皮膚症	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
神経皮膚炎	0	1 (0.3)	0	0	0
寝汗	0	1 (0.3)	3 (0.6)	3 (0.7)	10 (0.5)
爪破損	0	1 (0.3)	0	1 (0.2)	2 (0.1)
爪甲剥離症	0	0	0	1 (0.2)	2 (0.1)
皮膚疼痛	1 (4.2)	0	0	1 (0.2)	2 (0.1)
脂肪織炎	0	0	1 (0.2)	0	2 (0.1)
丘疹	1 (4.2)	1 (0.3)	2 (0.4)	3 (0.7)	8 (0.4)
口囲皮膚炎	0	0	1 (0.2)	0	2 (0.1)
点状出血	0	0	0	0	1 (<0.1)
光線性皮膚症	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
光線過敏性反応	0	0	0
そう痒症	9 (7.5)	3 (2.8)	10 (1.7)
乾癬	0	0	2 (0.3)
壊疽性膿皮症	1 (0.8)	0	0
発疹	5 (4.2)	5 (4.6)	25 (4.3)
紅斑性皮疹	1 (0.8)	0	1 (0.2)
毛孔性皮疹	0	0	0
斑状皮疹	0	0	1 (0.2)
斑状丘疹状皮疹	0	2 (1.8)	0
丘疹性皮疹	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
光線過敏性反応	1 (4.2)	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)
そう痒症	1 (4.2)	12 (3.3)	6 (1.3)	3 (0.7)	26 (1.4)
乾癬	0	1 (0.3)	0	0	3 (0.2)
壊疽性膿皮症	1 (4.2)	1 (0.3)	0	0	1 (<0.1)
発疹	2 (8.3)	25 (7.0)	14 (3.0)	21 (4.7)	81 (4.4)
紅斑性皮疹	0	0	3 (0.6)	0	4 (0.2)
毛孔性皮疹	1 (4.2)	1 (0.3)	2 (0.4)	0	4 (0.2)
斑状皮疹	0	0	2 (0.4)	2 (0.5)	5 (0.3)
斑状丘疹状皮疹	0	1 (0.3)	2 (0.4)	5 (1.1)	7 (0.4)
丘疹性皮疹	0	3 (0.8)	2 (0.4)	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
そう痒性皮疹	0	0	2 (0.3)
酒さ	1 (0.8)	1 (0.9)	6 (1.0)
脂漏性皮膚炎	1 (0.8)	0	0
皮膚灼熱感	0	0	0
皮膚変色	0	0	1 (0.2)
皮膚びらん	0	0	0
皮膚剥脱	0	0	0
皮膚亀裂	0	0	0
皮膚色素過剰	0	0	0
皮膚病変	0	1 (0.9)	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
そう痒性皮疹	0	0	0	2 (0.5)	4 (0.2)
酒さ	0	3 (0.8)	3 (0.6)	1 (0.2)	13 (0.7)
脂漏性皮膚炎	1 (4.2)	9 (2.5)	3 (0.6)	2 (0.5)	8 (0.4)
皮膚灼熱感	0	1 (0.3)	0	0	0
皮膚変色	0	1 (0.3)	0	0	2 (0.1)
皮膚びらん	0	1 (0.3)	0	0	0
皮膚剥脱	0	2 (0.6)	1 (0.2)	0	2 (0.1)
皮膚亀裂	0	2 (0.6)	1 (0.2)	0	2 (0.1)
皮膚色素過剰	0	1 (0.3)	0	0	0
皮膚病変	0	2 (0.6)	2 (0.4)	4 (0.9)	10 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
皮膚腫瘤	0	0	0
皮膚線条	0	0	0
皮膚潰瘍	0	1 (0.9)	0
日光皮膚炎	0	1 (0.9)	0
毛細血管拡張症	0	0	0
蕁麻疹	2 (1.7)	0	2 (0.3)
尋常性白斑	1 (0.8)	0	0
社会環境	0	0	0
閉経	0	0	0
外科および内科処置	0	1 (0.9)	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
皮膚腫瘤	0	0	1 (0.2)	0	1 (<0.1)
皮膚線条	0	0	1 (0.2)	0	1 (<0.1)
皮膚潰瘍	0	0	0	3 (0.7)	3 (0.2)
日光皮膚炎	0	0	0	0	0
毛細血管拡張症	0	0	1 (0.2)	0	1 (<0.1)
蕁麻疹	0	4 (1.1)	0	5 (1.1)	8 (0.4)
尋常性白斑	0	0	0	0	0
社会環境	0	1 (0.3)	0	0	1 (<0.1)
閉経	0	1 (0.3)	0	0	1 (<0.1)
外科および内科処置	0	1 (0.3)	5 (1.1)	1 (0.2)	8 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
外科および内科処置 (Cont.)			
人工流産	0	0	0
植込み型除細動器挿入	0	0	0
抜歯	0	1 (0.9)	0
智歯抜歯	0	0	0
血管障害	11 (9.1)	6 (5.5)	25 (4.3)
大動脈瘤	0	0	0
大動脈硬化症	0	0	0
動脈硬化症	0	0	1 (0.2)
出血性静脈瘤	0	0	0
深部静脈血栓症	0	2 (1.8)	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 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
外科および内科処置 (Cont.)					
人工流産	0	0	2 (0.4)	0	2 (0.1)
植込み型除細動器挿入	0	0	1 (0.2)	0	1 (<0.1)
抜歯	0	0	1 (0.2)	1 (0.2)	3 (0.2)
智歯抜歯	0	1 (0.3)	1 (0.2)	0	2 (0.1)
血管障害	2 (8.3)	18 (5.0)	23 (4.9)	31 (7.0)	100 (5.5)
大動脈瘤	0	0	1 (0.2)	0	1 (<0.1)
大動脈硬化症	0	0	1 (0.2)	1 (0.2)	2 (0.1)
動脈硬化症	0	1 (0.3)	0	0	2 (0.1)
出血性静脈瘤	0	0	1 (0.2)	0	1 (<0.1)
深部静脈血栓症	1 (4.2)	0	0	2 (0.5)	6 (0.3)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
血管障害 (Cont.)			
本態性高血圧症	0	0	0
潮紅	0	0	2 (0.3)
血腫	1 (0.8)	0	1 (0.2)
出血	0	0	1 (0.2)
ほてり	0	0	3 (0.5)
高血圧	6 (5.0)	4 (3.7)	13 (2.2)
高血圧クリーゼ	0	0	1 (0.2)
低血圧	1 (0.8)	0	0
起立性低血圧	0	0	0
蒼白	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血管障害 (Cont.)					
本態性高血圧症	0	0	0	1 (0.2)	1 (<0.1)
潮紅	0	0	1 (0.2)	0	3 (0.2)
血腫	0	0	0	0	1 (<0.1)
出血	0	0	0	0	1 (<0.1)
ほてり	0	1 (0.3)	0	1 (0.2)	5 (0.3)
高血圧	0	11 (3.1)	15 (3.2)	20 (4.5)	61 (3.3)
高血圧クリーゼ	0	0	0	0	1 (<0.1)
低血圧	1 (4.2)	1 (0.3)	0	2 (0.5)	3 (0.2)
起立性低血圧	0	0	0	1 (0.2)	1 (<0.1)
蒼白	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
血管障害 (Cont.)			
骨盤静脈血栓症	1 (0.8)	0	0
末梢冷感	1 (0.8)	0	0
末梢静脈疾患	0	0	0
静脈炎	0	0	0
レイノー現象	0	0	0
血栓性静脈炎	0	0	0
表在性血栓性静脈炎	1 (0.8)	0	0
静脈瘤	0	0	1 (0.2)
静脈血栓症	0	0	0
白衣性高血圧	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Induction Dose = 45 mg QD [C] UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血管障害 (Cont.)					
骨盤静脈血栓症	0	0	0	0	0
末梢冷感	0	0	0	0	0
末梢静脈疾患	0	0	1 (0.2)	0	1 (<0.1)
静脈炎	0	0	0	1 (0.2)	1 (<0.1)
レイノー現象	0	2 (0.6)	1 (0.2)	0	3 (0.2)
血栓性静脈炎	0	1 (0.3)	0	0	1 (<0.1)
表在性血栓性静脈炎	0	0	0	0	0
静脈瘤	0	0	0	0	1 (<0.1)
静脈血栓症	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
白衣性高血圧	0	0	0	2 (0.5)	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).

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表 2.7.4.7-28.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	1468 (516.9)	149 (680.4)	2982 (295.9)	1940 (311.8)	4922 (302.0)	1370 (809.7)	6441 (353.7)
血液およびリンパ系障害	75 (26.4)	3 (13.7)	105 (10.4)	60 (9.6)	165 (10.1)	92 (54.4)	260 (14.3)
貧血	41 (14.4)	2 (9.1)	41 (4.1)	19 (3.1)	60 (3.7)	37 (21.9)	99 (5.4)
大球性貧血	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
失血性貧血	0	0	0	0	0	2 (1.2)	2 (0.1)
周期性好中球減少症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
好酸球増加症	2 (0.7)	0	0	0	0	0	0
内出血発生の増加傾向	1 (0.4)	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)
鉄欠乏性貧血	6 (2.1)	0	4 (0.4)	4 (0.6)	8 (0.5)	6 (3.5)	14 (0.8)
白血球増加症	1 (0.4)	0	2 (0.2)	2 (0.3)	4 (0.2)	1 (0.6)	5 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)							
白血球減少症	5 (1.8)	0	16 (1.6)	9 (1.4)	25 (1.5)	10 (5.9)	35 (1.9)
リンパ節症	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
リンパ球増加症	1 (0.4)	0	0	0	0	0	0
リンパ球減少症	7 (2.5)	1 (4.6)	12 (1.2)	7 (1.1)	19 (1.2)	14 (8.3)	34 (1.9)
小球性貧血	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
好中球減少症	6 (2.1)	0	16 (1.6)	13 (2.1)	29 (1.8)	19 (11.2)	48 (2.6)
正球性貧血	1 (0.4)	0	0	0	0	0	0
汎血球減少症	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
網状赤血球増加症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脾腫	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)							
血小板減少症	2 (0.7)	0	0	0	0	2 (1.2)	2 (0.1)
血小板増加症	1 (0.4)	0	4 (0.4)	0	4 (0.2)	0	4 (0.2)
心臓障害	18 (6.3)	0	22 (2.2)	15 (2.4)	37 (2.3)	5 (3.0)	42 (2.3)
急性心筋梗塞	1 (0.4)	0	0	0	0	0	0
不安定狭心症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
不整脈	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
心房細動	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
第一度房室ブロック	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
二束ブロック	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
徐脈	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
心臓障害 (Cont.)							
左脚ブロック	1 (0.4)	0	0	0	0	0	0
心不全	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
うっ血性心不全	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
心拡大	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
慢性左室不全	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
冠動脈疾患	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
虚血性心筋症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
僧帽弁閉鎖不全症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
心筋梗塞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
動悸	9 (3.2)	0	3 (0.3)	0	3 (0.2)	3 (1.8)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
心臓障害 (Cont.)							
心膜炎	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
洞性不整脈	1 (0.4)	0	0	0	0	0	0
洞性徐脈	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
洞性頻脈	0	0	0	0	0	1 (0.6)	1 (<0.1)
上室性期外収縮	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
上室性頻脈	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
頻脈	2 (0.7)	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
心室性期外収縮	1 (0.4)	0	1 (<0.1)	3 (0.5)	4 (0.2)	0	4 (0.2)
心室性頻脈	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
ウォルフ・パーキンソン・ホワイト症候群	0	0	0	1 (0.2)	1 (<0.1)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
先天性、家族性および遺伝性障害	0	0	4 (0.4)	0	4 (0.2)	0	4 (0.2)
ジルベール症候群	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
魚鱗癬	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
歯原性嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
耳および迷路障害	7 (2.5)	2 (9.1)	18 (1.8)	11 (1.8)	29 (1.8)	9 (5.3)	40 (2.2)
耳垢栓塞	0	1 (4.6)	0	0	0	0	1 (<0.1)
感音性難聴	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
片耳難聴	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
耳不快感	0	0	0	0	0	1 (0.6)	1 (<0.1)
耳痛	1 (0.4)	0	5 (0.5)	1 (0.2)	6 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
耳および迷路障害 (Cont.)							
耳部腫脹	1 (0.4)	0	0	0	0	0	0
外耳道の外骨腫	1 (0.4)	0	0	0	0	0	0
外耳の炎症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
聴力低下	0	0	0	0	0	1 (0.6)	1 (<0.1)
内耳障害	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
メニエール病	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
中耳滲出液	1 (0.4)	0	0	0	0	0	0
突発性難聴	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
耳鳴	0	1 (4.6)	4 (0.4)	3 (0.5)	7 (0.4)	3 (1.8)	11 (0.6)
回転性めまい	2 (0.7)	0	7 (0.7)	3 (0.5)	10 (0.6)	1 (0.6)	11 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
内分泌障害	2 (0.7)	2 (9.1)	6 (0.6)	4 (0.6)	10 (0.6)	1 (0.6)	13 (0.7)
アジソン病	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
副腎機能不全	0	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
急性副腎皮質機能不全	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
クッシング症候群	1 (0.4)	0	0	0	0	0	0
クッシング様症状	0	2 (9.1)	1 (<0.1)	0	1 (<0.1)	1 (0.6)	4 (0.2)
甲状腺腫	0	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
甲状腺機能亢進症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
甲状腺機能低下症	1 (0.4)	0	0	0	0	0	0
甲状腺腫瘤	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害	22 (7.7)	5 (22.8)	35 (3.5)	21 (3.4)	56 (3.4)	24 (14.2)	85 (4.7)
眼精疲労	1 (0.4)	0	0	0	0	1 (0.6)	1 (<0.1)
眼瞼炎	1 (0.4)	0	3 (0.3)	3 (0.5)	6 (0.4)	1 (0.6)	7 (0.4)
眼瞼痙攣	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
白内障	2 (0.7)	2 (9.1)	7 (0.7)	1 (0.2)	8 (0.5)	3 (1.8)	13 (0.7)
霰粒腫	0	0	1 (<0.1)	4 (0.6)	5 (0.3)	1 (0.6)	6 (0.3)
結膜嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
結膜出血	0	1 (4.6)	1 (<0.1)	0	1 (<0.1)	2 (1.2)	4 (0.2)
結膜充血	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
アレルギー性結膜炎	2 (0.7)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)							
結膜弛緩症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
角膜びらん	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
角膜混濁	1 (0.4)	0	0	0	0	0	0
後天性涙道狭窄	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ドライアイ	0	0	5 (0.5)	2 (0.3)	7 (0.4)	4 (2.4)	11 (0.6)
上強膜炎	2 (0.7)	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
眼のアレルギー	1 (0.4)	0	0	0	0	0	0
眼の障害	0	0	0	0	0	2 (1.2)	2 (0.1)
眼出血	0	0	0	0	0	1 (0.6)	1 (<0.1)
眼刺激	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)							
眼痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼そう痒症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼部腫脹	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼瞼嚢胞	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
眼瞼障害	1 (0.4)	0	0	0	0	0	0
眼瞼刺激	0	0	0	0	0	1 (0.6)	1 (<0.1)
眼瞼発疹	1 (0.4)	0	0	0	0	0	0
眼瞼肥厚	0	0	0	0	0	1 (0.6)	1 (<0.1)
緑内障	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
虹彩毛様体炎	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)							
角膜炎	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
流涙増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼部不快感	1 (0.4)	0	0	0	0	0	0
眼充血	0	0	3 (0.3)	1 (0.2)	4 (0.2)	1 (0.6)	5 (0.3)
高眼圧症	0	0	0	0	0	2 (1.2)	2 (0.1)
開放隅角緑内障	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
眼窩周囲腫脹	1 (0.4)	0	0	0	0	1 (0.6)	1 (<0.1)
光視症	0	1 (4.6)	0	0	0	0	1 (<0.1)
翼状片	1 (0.4)	0	0	0	0	0	0
潰瘍性角膜炎	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)							
ぶどう膜炎	2 (0.7)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
霧視	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
視力低下	1 (0.4)	0	0	0	0	0	0
視力障害	0	1 (4.6)	1 (<0.1)	0	1 (<0.1)	0	2 (0.1)
硝子体浮遊物	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
胃腸障害	330 (116.2)	25 (114.2)	474 (47.0)	273 (43.9)	747 (45.8)	201 (118.8)	973 (53.4)
腹部不快感	4 (1.4)	0	3 (0.3)	0	3 (0.2)	1 (0.6)	4 (0.2)
腹部膨満	4 (1.4)	4 (18.3)	8 (0.8)	10 (1.6)	18 (1.1)	9 (5.3)	31 (1.7)
腹部腫瘤	1 (0.4)	0	0	0	0	0	0
腹痛	10 (3.5)	3 (13.7)	29 (2.9)	9 (1.4)	38 (2.3)	19 (11.2)	60 (3.3)

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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
下腹部痛	5 (1.8)	0	6 (0.6)	0	6 (0.4)	4 (2.4)	10 (0.5)
上腹部痛	8 (2.8)	0	15 (1.5)	6 (1.0)	21 (1.3)	5 (3.0)	26 (1.4)
腹部圧痛	1 (0.4)	1 (4.6)	6 (0.6)	4 (0.6)	10 (0.6)	4 (2.4)	15 (0.8)
異常便	1 (0.4)	0	0	0	0	0	0
無酸症	0	0	0	0	0	1 (0.6)	1 (<0.1)
裂肛	2 (0.7)	0	5 (0.5)	1 (0.2)	6 (0.4)	5 (3.0)	11 (0.6)
痔瘻	0	0	2 (0.2)	3 (0.5)	5 (0.3)	0	5 (0.3)
肛門失禁	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肛門の炎症	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
肛門そう痒症	2 (0.7)	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
肛門潰瘍	0	0	0	0	0	1 (0.6)	1 (<0.1)
口角口唇炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肛門直腸不快感	0	0	0	0	0	1 (0.6)	1 (<0.1)
アフタ性潰瘍	6 (2.1)	1 (4.6)	7 (0.7)	5 (0.8)	12 (0.7)	4 (2.4)	17 (0.9)
口唇のひび割れ	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
大腸炎	9 (3.2)	0	2 (0.2)	2 (0.3)	4 (0.2)	0	4 (0.2)
虚血性大腸炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
潰瘍性大腸炎	167 (58.8)	4 (18.3)	157 (15.6)	82 (13.2)	239 (14.7)	27 (16.0)	270 (14.8)
結腸異形成	0	0	3 (0.3)	2 (0.3)	5 (0.3)	1 (0.6)	6 (0.3)
便秘	5 (1.8)	2 (9.1)	12 (1.2)	11 (1.8)	23 (1.4)	15 (8.9)	40 (2.2)

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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
クローン病	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
便意切迫	2 (0.7)	0	3 (0.3)	1 (0.2)	4 (0.2)	0	4 (0.2)
齲歯	2 (0.7)	0	4 (0.4)	3 (0.5)	7 (0.4)	1 (0.6)	8 (0.4)
歯不快感	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
歯組織の壊死	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
横隔膜ヘルニア	1 (0.4)	0	0	0	0	0	0
下痢	4 (1.4)	2 (9.1)	19 (1.9)	4 (0.6)	23 (1.4)	7 (4.1)	32 (1.8)
血性下痢	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
腸憩室	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
口内乾燥	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	2 (1.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
十二指腸炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
排便困難	1 (0.4)	0	0	0	0	0	0
消化不良	6 (2.1)	0	12 (1.2)	10 (1.6)	22 (1.3)	6 (3.5)	28 (1.5)
嚥下障害	2 (0.7)	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)
小腸炎	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
腸炎	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
心窩部不快感	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
おくび	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
糞塊	2 (0.7)	0	0	0	0	0	0
変色便	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
白色便	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
軟便	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
大腿ヘルニア	1 (0.4)	0	0	0	0	0	0
鼓腸	8 (2.8)	2 (9.1)	8 (0.8)	7 (1.1)	15 (0.9)	6 (3.5)	23 (1.3)
食中毒	3 (1.1)	0	0	0	0	2 (1.2)	2 (0.1)
排便回数増加	0	0	4 (0.4)	0	4 (0.2)	1 (0.6)	5 (0.3)
胃障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胃ポリープ	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胃潰瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胃炎	2 (0.7)	0	7 (0.7)	2 (0.3)	9 (0.6)	0	9 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
びらん性胃炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
胃腸障害	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
消化管運動障害	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
消化器痛	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胃食道逆流性疾患	5 (1.8)	0	13 (1.3)	7 (1.1)	20 (1.2)	9 (5.3)	29 (1.6)
歯肉痛	0	0	0	1 (0.2)	1 (<0.1)	2 (1.2)	3 (0.2)
歯肉腫脹	1 (0.4)	0	0	0	0	1 (0.6)	1 (<0.1)
舌痛	1 (0.4)	0	0	0	0	0	0
血便排泄	2 (0.7)	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
痔出血	2 (0.7)	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
痔核	6 (2.1)	0	16 (1.6)	8 (1.3)	24 (1.5)	13 (7.7)	37 (2.0)
血栓性痔核	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
裂孔ヘルニア	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胃酸過多	0	0	0	0	0	1 (0.6)	1 (<0.1)
肛門肥大乳頭	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
回腸潰瘍	1 (0.4)	0	0	0	0	0	0
イレウス	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
鼠径ヘルニア	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
腸閉塞	1 (0.4)	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
腸管ポリープ	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
過敏性腸症候群	0	0	2 (0.2)	2 (0.3)	4 (0.2)	0	4 (0.2)
大腸穿孔	2 (0.7)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
大腸ポリープ	2 (0.7)	0	10 (1.0)	4 (0.6)	14 (0.9)	2 (1.2)	16 (0.9)
口唇水疱	0	0	0	0	0	1 (0.6)	1 (<0.1)
口唇乾燥	0	0	0	0	0	1 (0.6)	1 (<0.1)
口唇腫脹	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
口唇潰瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
口腔嚢胞	1 (0.4)	0	0	0	0	0	0
口腔内潰瘍形成	4 (1.4)	0	5 (0.5)	1 (0.2)	6 (0.4)	2 (1.2)	8 (0.4)
粘液便	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
悪心	18 (6.3)	2 (9.1)	33 (3.3)	26 (4.2)	59 (3.6)	10 (5.9)	71 (3.9)
非感染性歯肉炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
嚥下痛	2 (0.7)	0	0	2 (0.3)	2 (0.1)	1 (0.6)	3 (0.2)
食道運動低下	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
食道痛	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
食道潰瘍	0	0	0	0	0	1 (0.6)	1 (<0.1)
食道炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
口腔障害	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
口腔知覚不全	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
口腔扁平苔癬	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
口腔内痛	0	0	0	0	0	3 (1.8)	3 (0.2)
膵臓障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膵脂肪変性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膵炎	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
肛門周囲紅斑	0	1 (4.6)	0	0	0	0	1 (<0.1)
歯周病	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
肛門周囲痛	0	1 (4.6)	5 (0.5)	1 (0.2)	6 (0.4)	3 (1.8)	10 (0.5)
直腸炎	1 (0.4)	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
偽性ポリポーシス	0	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (0.2)
直腸分泌物	1 (0.4)	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
直腸異形成	0	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (0.2)
直腸出血	2 (0.7)	0	4 (0.4)	5 (0.8)	9 (0.6)	0	9 (0.5)
直腸ポリープ	0	0	0	0	0	1 (0.6)	1 (<0.1)
直腸しぶり	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
口内炎	7 (2.5)	0	5 (0.5)	5 (0.8)	10 (0.6)	9 (5.3)	19 (1.0)
舌障害	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
舌潰瘍	0	0	0	0	0	2 (1.2)	2 (0.1)
歯の障害	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
埋伏歯	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
歯の脱落	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)							
歯痛	0	0	9 (0.9)	9 (1.4)	18 (1.1)	1 (0.6)	19 (1.0)
臍ヘルニア	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
嘔吐	5 (1.8)	2 (9.1)	18 (1.8)	6 (1.0)	24 (1.5)	5 (3.0)	31 (1.7)
一般・全身障害および投与部位の状態	70 (24.6)	11 (50.2)	113 (11.2)	86 (13.8)	199 (12.2)	81 (47.9)	291 (16.0)
医薬品副作用	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
無力症	2 (0.7)	1 (4.6)	4 (0.4)	0	4 (0.2)	6 (3.5)	11 (0.6)
胸部不快感	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	4 (2.4)	5 (0.3)
胸痛	2 (0.7)	0	10 (1.0)	10 (1.6)	20 (1.2)	2 (1.2)	22 (1.2)
悪寒	5 (1.8)	0	6 (0.6)	6 (1.0)	12 (0.7)	3 (1.8)	15 (0.8)
状態悪化	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
医療機器に対する不耐性	1 (0.4)	0	0	0	0	0	0
不快感	0	0	0	0	0	1 (0.6)	1 (<0.1)
薬効欠如	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
異形成	0	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
顔面浮腫	0	0	0	0	0	1 (0.6)	1 (<0.1)
疲労	13 (4.6)	2 (9.1)	22 (2.2)	11 (1.8)	33 (2.0)	11 (6.5)	46 (2.5)
異常感	0	0	0	0	0	1 (0.6)	1 (<0.1)
びくびく感	0	0	0	0	0	1 (0.6)	1 (<0.1)
全身性浮腫	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
宿酔	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
過形成	0	0	0	0	0	1 (0.6)	1 (<0.1)
高体温症	1 (0.4)	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
治癒不良	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
硬結	1 (0.4)	0	0	0	0	0	0
炎症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
インフルエンザ様疾患	3 (1.1)	2 (9.1)	9 (0.9)	7 (1.1)	16 (1.0)	1 (0.6)	19 (1.0)
注入部位反応	0	0	0	0	0	1 (0.6)	1 (<0.1)
医療機器関連損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
倦怠感	2 (0.7)	1 (4.6)	1 (<0.1)	1 (0.2)	2 (0.1)	3 (1.8)	6 (0.3)
腫瘤	0	0	0	2 (0.3)	2 (0.1)	1 (0.6)	3 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
小結節	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
非心臓性胸痛	0	0	0	0	0	1 (0.6)	1 (<0.1)
浮腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
末梢性浮腫	5 (1.8)	0	5 (0.5)	3 (0.5)	8 (0.5)	2 (1.2)	10 (0.5)
疼痛	4 (1.4)	1 (4.6)	5 (0.5)	5 (0.8)	10 (0.6)	2 (1.2)	13 (0.7)
末梢腫脹	2 (0.7)	0	3 (0.3)	2 (0.3)	5 (0.3)	1 (0.6)	6 (0.3)
ポリープ	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
偽ポリープ	0	1 (4.6)	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	4 (0.2)
発熱	22 (7.7)	2 (9.1)	31 (3.1)	29 (4.7)	60 (3.7)	34 (20.1)	96 (5.3)
異物感	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)							
腫脹	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
顔面腫脹	0	1 (4.6)	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	4 (0.2)
ワクチン接種部位紅斑	1 (0.4)	0	0	0	0	0	0
ワクチン接種部位疼痛	1 (0.4)	0	0	0	0	0	0
ワクチン接種部位反応	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乾燥症	1 (0.4)	0	0	0	0	0	0
肝胆道系障害	9 (3.2)	0	33 (3.3)	8 (1.3)	41 (2.5)	6 (3.5)	47 (2.6)
胆道ジスキネジア	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
胆汁性嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
硬化性胆管炎	0	0	5 (0.5)	0	5 (0.3)	0	5 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
肝胆道系障害 (Cont.)							
胆石症	0	0	3 (0.3)	0	3 (0.2)	2 (1.2)	5 (0.3)
胆汁うっ滞	1 (0.4)	0	0	0	0	0	0
薬物性肝障害	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
肝嚢胞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肝機能異常	2 (0.7)	0	8 (0.8)	2 (0.3)	10 (0.6)	2 (1.2)	12 (0.7)
脂肪肝	0	0	6 (0.6)	2 (0.3)	8 (0.5)	0	8 (0.4)
肝炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肝細胞損傷	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
肝腫大	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
高ビリルビン血症	2 (0.7)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) 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	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
肝障害	1 (0.4)	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
肝損傷	2 (0.7)	0	0	0	0	0	0
非アルコール性脂肪性肝炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
非アルコール性脂肪性肝疾患	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
門脈血栓症	1 (0.4)	0	0	0	0	0	0
免疫系障害	6 (2.1)	0	11 (1.1)	13 (2.1)	24 (1.5)	3 (1.8)	27 (1.5)
動物アレルギー	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
アミロイドーシス	1 (0.4)	0	0	0	0	0	0
アナフィラキシー反応	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
免疫系障害 (Cont.)							
薬物過敏症	2 (0.7)	0	0	2 (0.3)	2 (0.1)	1 (0.6)	3 (0.2)
粉塵アレルギー	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
過敏症	0	0	2 (0.2)	1 (0.2)	3 (0.2)	1 (0.6)	4 (0.2)
ダニアレルギー	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
季節性アレルギー	1 (0.4)	0	8 (0.8)	7 (1.1)	15 (0.9)	1 (0.6)	16 (0.9)
感染症および寄生虫症	253 (89.1)	27 (123.3)	737 (73.1)	488 (78.4)	1225 (75.2)	251 (148.4)	1503 (82.5)
腹部膿瘍	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腹壁膿瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膿瘍	1 (0.4)	0	0	0	0	1 (0.6)	1 (<0.1)
頚部膿瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
ダニ皮膚炎	0	0	4 (0.4)	1 (0.2)	5 (0.3)	0	5 (0.3)
急性心内膜炎	1 (0.4)	0	0	0	0	0	0
急性副鼻腔炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
歯槽骨炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肛門膿瘍	1 (0.4)	0	4 (0.4)	3 (0.5)	7 (0.4)	1 (0.6)	8 (0.4)
肛門直腸感染	2 (0.7)	0	0	0	0	0	0
虫垂炎	0	0	0	1 (0.2)	1 (<0.1)	2 (1.2)	3 (0.2)
細菌性関節炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
無症候性COVID-19	1 (0.4)	0	4 (0.4)	2 (0.3)	6 (0.4)	0	6 (0.3)
無症候性細菌尿	0	0	0	0	0	1 (0.6)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
異型肺炎	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
細菌感染	0	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
細菌性膣症	1 (0.4)	0	0	2 (0.3)	2 (0.1)	1 (0.6)	3 (0.2)
細菌尿	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
バルトリン腺炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ブラストシスティス感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
体部白癬	0	0	0	0	0	1 (0.6)	1 (<0.1)
ボレリア感染	0	0	0	0	0	1 (0.6)	1 (<0.1)
乳房膿瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
気管支炎	6 (2.1)	1 (4.6)	32 (3.2)	9 (1.4)	41 (2.5)	3 (1.8)	45 (2.5)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
感染性滑液包炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
COVID-19	13 (4.6)	0	34 (3.4)	28 (4.5)	62 (3.8)	1 (0.6)	63 (3.5)
COVID-19肺炎	1 (0.4)	0	7 (0.7)	7 (1.1)	14 (0.9)	2 (1.2)	16 (0.9)
カンピロバクター胃腸炎	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
カンピロバクター感染	0	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
カンジダ感染	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
蜂巣炎	9 (3.2)	0	9 (0.9)	3 (0.5)	12 (0.7)	0	12 (0.7)
条虫感染	0	0	0	0	0	1 (0.6)	1 (<0.1)
感染性胆嚢炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
慢性副鼻腔炎	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
クロストリジウム・ディフィシレ大腸炎	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
クロストリジウム・ディフィシレ感染	5 (1.8)	0	8 (0.8)	12 (1.9)	20 (1.2)	1 (0.6)	21 (1.2)
結腸膿瘍	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
結膜炎	2 (0.7)	0	4 (0.4)	2 (0.3)	6 (0.4)	0	6 (0.3)
ウイルス性結膜炎	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
コロナウイルス感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
サイクロスポリジウム感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膀胱炎	1 (0.4)	3 (13.7)	17 (1.7)	8 (1.3)	25 (1.5)	2 (1.2)	30 (1.6)
サイトメガロウイルス性大腸炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
サイトメガロウイルス感染	2 (0.7)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
毛嚢虫症	0	0	5 (0.5)	5 (0.8)	10 (0.6)	1 (0.6)	11 (0.6)
デング熱	0	0	0	0	0	1 (0.6)	1 (<0.1)
感染性皮膚炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
皮膚糸状菌症	1 (0.4)	1 (4.6)	0	0	0	0	1 (<0.1)
爪の皮膚糸状菌症	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)
医療機器関連敗血症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
感染性下痢	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
憩室炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
耳感染	2 (0.7)	1 (4.6)	7 (0.7)	6 (1.0)	13 (0.8)	2 (1.2)	16 (0.9)
感染性腸炎	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
蟯虫症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腸球菌感染	1 (0.4)	0	0	0	0	0	0
エンテロウイルス感染	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
丹毒	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
遊走性紅斑	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
大腸菌感染	2 (0.7)	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
大腸菌性敗血症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
大腸菌性尿路感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼瞼感染	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
毛包炎	6 (2.1)	1 (4.6)	6 (0.6)	16 (2.6)	22 (1.3)	20 (11.8)	43 (2.4)
真菌感染	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
皮膚真菌感染	2 (0.7)	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)
せつ	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
胃腸炎	8 (2.8)	1 (4.6)	15 (1.5)	17 (2.7)	32 (2.0)	6 (3.5)	39 (2.1)
ノロウイルス性胃腸炎	1 (0.4)	0	0	0	0	1 (0.6)	1 (<0.1)
ウイルス性胃腸炎	0	0	7 (0.7)	6 (1.0)	13 (0.8)	3 (1.8)	16 (0.9)
消化管内細菌過剰増殖	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
消化管感染	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
性器カンジダ症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
陰部ヘルペス	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	2 (1.2)	4 (0.2)
陰部単純ヘルペス	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	2 (1.2)	4 (0.2)
歯肉膿瘍	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
歯肉炎	1 (0.4)	0	4 (0.4)	1 (0.2)	5 (0.3)	2 (1.2)	7 (0.4)
鼠径部膿瘍	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ヘモフィルス感染	1 (0.4)	0	0	0	0	0	0
ヘリコバクター性胃炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
ヘリコバクター感染	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
伝染性単核症肝炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
単純ヘルペス	0	0	12 (1.2)	4 (0.6)	16 (1.0)	5 (3.0)	21 (1.2)

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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
単純ヘルペス性咽頭炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
帯状疱疹	2 (0.7)	0	39 (3.9)	29 (4.7)	68 (4.2)	13 (7.7)	81 (4.4)
播種性帯状疱疹	0	0	0	0	0	1 (0.6)	1 (<0.1)
神経合併症を伴う帯状疱疹感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
帯状疱疹性髄膜炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
耳帯状疱疹	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
麦粒腫	4 (1.4)	0	4 (0.4)	7 (1.1)	11 (0.7)	4 (2.4)	15 (0.8)
膿痂疹	1 (0.4)	0	2 (0.2)	1 (0.2)	3 (0.2)	1 (0.6)	4 (0.2)
咬傷感染	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
感染性嚢腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
感染性皮膚嚢腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
感染	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
伝染性単核症	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
インフルエンザ	5 (1.8)	2 (9.1)	33 (3.3)	19 (3.1)	52 (3.2)	14 (8.3)	68 (3.7)
クレブシエラ感染	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
大腸感染	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
喉頭炎	1 (0.4)	0	2 (0.2)	3 (0.5)	5 (0.3)	0	5 (0.3)
潜伏結核	0	0	6 (0.6)	5 (0.8)	11 (0.7)	0	11 (0.6)
限局性感染	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
下気道感染	2 (0.7)	0	5 (0.5)	0	5 (0.3)	1 (0.6)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
ライム病	0	0	0	0	0	1 (0.6)	1 (<0.1)
乳腺炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
伝染性軟属腫	1 (0.4)	0	0	0	0	0	0
筋膿瘍	1 (0.4)	0	0	0	0	0	0
上咽頭炎	41 (14.4)	1 (4.6)	112 (11.1)	79 (12.7)	191 (11.7)	43 (25.4)	235 (12.9)
食道カンジダ症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
爪真菌症	2 (0.7)	1 (4.6)	8 (0.8)	1 (0.2)	9 (0.6)	0	10 (0.5)
口腔カンジダ症	2 (0.7)	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)
口腔真菌感染	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
口腔ヘルペス	10 (3.5)	1 (4.6)	42 (4.2)	28 (4.5)	70 (4.3)	13 (7.7)	84 (4.6)

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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
精巣炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
外耳炎	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
真菌性外耳炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
中耳炎	0	0	0	0	0	2 (1.2)	2 (0.1)
急性中耳炎	0	0	0	0	0	1 (0.6)	1 (<0.1)
乳頭腫ウイルス感染	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
爪囲炎	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
歯周炎	0	0	3 (0.3)	3 (0.5)	6 (0.4)	1 (0.6)	7 (0.4)
直腸周囲膿瘍	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
咽頭炎	5 (1.8)	0	6 (0.6)	5 (0.8)	11 (0.7)	8 (4.7)	19 (1.0)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
レンサ球菌性咽頭炎	1 (0.4)	0	2 (0.2)	3 (0.5)	5 (0.3)	1 (0.6)	6 (0.3)
毛巣嚢胞	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)
胸膜感染	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
ニューモシスチス・イロベチイ感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ニューモシスチス・イロベチイ肺炎	1 (0.4)	0	0	0	0	0	0
肺炎	6 (2.1)	0	12 (1.2)	8 (1.3)	20 (1.2)	3 (1.8)	23 (1.3)
細菌性肺炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
クリプトコッカス性肺炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
肺炎球菌性肺炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ウイルス性肺炎	0	0	1 (<0.1)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
処置後感染	2 (0.7)	0	0	0	0	0	0
歯髄炎	1 (0.4)	1 (4.6)	3 (0.3)	1 (0.2)	4 (0.2)	0	5 (0.3)
膿疱	1 (0.4)	2 (9.1)	2 (0.2)	1 (0.2)	3 (0.2)	2 (1.2)	7 (0.4)
腎盂腎炎	1 (0.4)	0	3 (0.3)	0	3 (0.2)	1 (0.6)	4 (0.2)
膿皮症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
膿尿	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
膿疱性皮疹	0	0	0	0	0	2 (1.2)	2 (0.1)
RSウイルス感染	0	0	0	0	0	1 (0.6)	1 (<0.1)
気道感染	1 (0.4)	0	4 (0.4)	2 (0.3)	6 (0.4)	2 (1.2)	8 (0.4)
ウイルス性気道感染	2 (0.7)	1 (4.6)	5 (0.5)	1 (0.2)	6 (0.4)	2 (1.2)	9 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
鼻炎	4 (1.4)	0	3 (0.3)	2 (0.3)	5 (0.3)	0	5 (0.3)
根管感染	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
敗血症	0	0	0	2 (0.3)	2 (0.1)	1 (0.6)	3 (0.2)
セラチア感染	1 (0.4)	0	0	0	0	0	0
副鼻腔炎	12 (4.2)	1 (4.6)	21 (2.1)	14 (2.3)	35 (2.1)	5 (3.0)	41 (2.3)
皮膚カンジダ	0	1 (4.6)	0	0	0	0	1 (<0.1)
皮膚感染	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
ブドウ球菌感染	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
レンサ球菌性尿路感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮下組織膿瘍	0	0	1 (<0.1)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
股部白癬	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
白癬感染	2 (0.7)	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
手白癬	1 (0.4)	0	0	0	0	0	0
足部白癬	3 (1.1)	0	6 (0.6)	2 (0.3)	8 (0.5)	1 (0.6)	9 (0.5)
癜風	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)
扁桃炎	1 (0.4)	0	5 (0.5)	6 (1.0)	11 (0.7)	1 (0.6)	12 (0.7)
歯膿瘍	2 (0.7)	0	3 (0.3)	6 (1.0)	9 (0.6)	1 (0.6)	10 (0.5)
歯感染	3 (1.1)	0	2 (0.2)	6 (1.0)	8 (0.5)	2 (1.2)	10 (0.5)
トリコモナス症	1 (0.4)	0	0	0	0	0	0
結核	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
上気道感染	19 (6.7)	3 (13.7)	89 (8.8)	35 (5.6)	124 (7.6)	27 (16.0)	154 (8.5)
尿路感染	18 (6.3)	3 (13.7)	42 (4.2)	13 (2.1)	55 (3.4)	11 (6.5)	69 (3.8)
尿路性敗血症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
膣膿瘍	1 (0.4)	0	0	0	0	0	0
膣感染	0	1 (4.6)	3 (0.3)	0	3 (0.2)	0	4 (0.2)
水痘	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
水痘帯状疱疹ウイルス感染	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ウイルス血症	1 (0.4)	0	0	0	0	0	0
ウイルス性下痢	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ウイルス感染	1 (0.4)	0	3 (0.3)	3 (0.5)	6 (0.4)	2 (1.2)	8 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)							
ウイルス性心膜炎	1 (0.4)	0	0	0	0	0	0
ウイルス性咽頭炎	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
ウイルス性上気道感染	4 (1.4)	0	2 (0.2)	9 (1.4)	11 (0.7)	2 (1.2)	13 (0.7)
女性外陰部蜂巣炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
外陰部腟カンジダ症	2 (0.7)	1 (4.6)	3 (0.3)	7 (1.1)	10 (0.6)	3 (1.8)	14 (0.8)
外陰腟真菌感染	1 (0.4)	0	2 (0.2)	2 (0.3)	4 (0.2)	1 (0.6)	5 (0.3)
外陰腟炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
創傷感染	1 (0.4)	0	0	0	0	0	0
傷害、中毒および処置合併症	29 (10.2)	3 (13.7)	105 (10.4)	61 (9.8)	166 (10.2)	36 (21.3)	205 (11.3)
偶発的過量投与	3 (1.1)	0	2 (0.2)	5 (0.8)	7 (0.4)	3 (1.8)	10 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
吻合部漏出	1 (0.4)	0	0	0	0	0	0
動物咬傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
動物による引っかき傷	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
足関節部骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
節足動物咬傷	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
節足動物刺傷	0	0	0	0	0	1 (0.6)	1 (<0.1)
骨挫傷	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
第2度熱傷	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
挫傷	3 (1.1)	0	7 (0.7)	3 (0.5)	10 (0.6)	6 (3.5)	16 (0.9)
上顎炎	0	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
毒性物質曝露	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
眼外傷	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
転倒	0	1 (4.6)	8 (0.8)	6 (1.0)	14 (0.9)	1 (0.6)	16 (0.9)
腓骨骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
足骨折	0	0	2 (0.2)	3 (0.5)	5 (0.3)	0	5 (0.3)
骨折	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
仙骨骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
消化管ストーマ壊死	1 (0.4)	0	0	0	0	0	0
手骨折	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
頭部損傷	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
熱疲労	0	0	0	0	0	1 (0.6)	1 (<0.1)
熱中症	1 (0.4)	0	0	0	0	0	0
熱射病	1 (0.4)	0	0	0	0	0	0
股関節部骨折	1 (0.4)	0	0	0	0	0	0
損傷	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.2)
企図的過量投与	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
関節脱臼	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
関節損傷	1 (0.4)	0	4 (0.4)	1 (0.2)	5 (0.3)	0	5 (0.3)
靱帯断裂	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
靱帯捻挫	4 (1.4)	0	1 (<0.1)	3 (0.5)	4 (0.2)	4 (2.4)	8 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
四肢損傷	1 (0.4)	0	2 (0.2)	2 (0.3)	4 (0.2)	0	4 (0.2)
四肢外傷性切断	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
腰椎骨折	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
つち指	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
半月板損傷	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
筋断裂	0	0	2 (0.2)	4 (0.6)	6 (0.4)	0	6 (0.3)
肉離れ	1 (0.4)	0	7 (0.7)	2 (0.3)	9 (0.6)	2 (1.2)	11 (0.6)
筋骨格内異物	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
過量投与	0	1 (4.6)	3 (0.3)	0	3 (0.2)	1 (0.6)	5 (0.3)
膝蓋骨骨折	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
骨盤骨折	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
処置後血尿	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
処置後出血	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
外傷後頚部症候群	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
外傷後疼痛	0	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
術後イレウス	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
処置による腸管穿孔	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
処置による疼痛	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
肺挫傷	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
橈骨骨折	0	0	1 (<0.1)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
肋骨骨折	1 (0.4)	0	5 (0.5)	2 (0.3)	7 (0.4)	1 (0.6)	8 (0.4)
交通事故	1 (0.4)	0	2 (0.2)	3 (0.5)	5 (0.3)	0	5 (0.3)
瘢痕	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
陰嚢血腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
皮膚擦過傷	1 (0.4)	0	4 (0.4)	0	4 (0.2)	2 (1.2)	6 (0.3)
皮膚裂傷	1 (0.4)	0	6 (0.6)	0	6 (0.4)	2 (1.2)	8 (0.4)
軟部組織損傷	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
脊柱損傷	0	0	0	0	0	1 (0.6)	1 (<0.1)
脊椎圧迫骨折	1 (0.4)	1 (4.6)	0	0	0	0	1 (<0.1)
スポーツ損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
ストレス骨折	0	0	3 (0.3)	2 (0.3)	5 (0.3)	0	5 (0.3)
皮下血腫	1 (0.4)	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
腱損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腱断裂	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
熱傷	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
胸椎骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脛骨骨折	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
歯牙破折	1 (0.4)	0	1 (<0.1)	3 (0.5)	4 (0.2)	0	4 (0.2)
子宮穿孔	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ワクチン接種合併症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)							
創傷	0	0	2 (0.2)	0	2 (0.1)	4 (2.4)	6 (0.3)
創合併症	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
手首関節骨折	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
臨床検査	93 (32.7)	9 (41.1)	341 (33.8)	234 (37.6)	575 (35.3)	230 (135.9)	814 (44.7)
アラニンアミノトランスフェラーゼ増加	8 (2.8)	3 (13.7)	21 (2.1)	10 (1.6)	31 (1.9)	10 (5.9)	44 (2.4)
αヒドロキシ酪酸脱水素酵素増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
アミラーゼ増加	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.2)
抗好中球細胞質抗体陽性	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
抗核抗体増加	1 (0.4)	0	0	0	0	0	0
大動脈雑音	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
関節鏡検査	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
アスパラギン酸アミノトランスフェラーゼ増加	9 (3.2)	2 (9.1)	20 (2.0)	9 (1.4)	29 (1.8)	17 (10.0)	48 (2.6)
細菌検査陽性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
好塩基球数増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血中アルブミン減少	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
血中アルブミン増加	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
血中アルカリホスファターゼ減少	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中アルカリホスファターゼ増加	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
血中重炭酸塩減少	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
血中ビリルビン増加	0	0	4 (0.4)	8 (1.3)	12 (0.7)	5 (3.0)	17 (0.9)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
血中非抱合ビリルビン増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中カルシウム増加	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
血中クロール減少	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中コレステロール減少	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
血中コレステロール増加	0	0	8 (0.8)	9 (1.4)	17 (1.0)	4 (2.4)	21 (1.2)
血中クレアチン増加	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
血中クレアチンホスホキナーゼMB増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血中クレアチンホスホキナーゼ増加	13 (4.6)	0	59 (5.9)	57 (9.2)	116 (7.1)	62 (36.6)	178 (9.8)
血中クレアチニン増加	3 (1.1)	0	1 (<0.1)	5 (0.8)	6 (0.4)	5 (3.0)	11 (0.6)
血中葉酸減少	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
血中ブドウ糖	1 (0.4)	0	0	0	0	0	0
血中ブドウ糖減少	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
血中ブドウ糖増加	3 (1.1)	0	5 (0.5)	1 (0.2)	6 (0.4)	0	6 (0.3)
血中鉄減少	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
血中乳酸脱水素酵素増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中マグネシウム減少	0	0	0	0	0	1 (0.6)	1 (<0.1)
血中リン減少	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	3 (1.8)	6 (0.3)
血中カリウム減少	0	0	4 (0.4)	0	4 (0.2)	0	4 (0.2)
血中カリウム増加	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
血圧上昇	0	0	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
血中ナトリウム増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血中トリグリセリド異常	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血中トリグリセリド減少	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
血中トリグリセリド増加	0	0	4 (0.4)	1 (0.2)	5 (0.3)	1 (0.6)	6 (0.3)
血中尿素増加	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
血中尿酸増加	0	0	0	0	0	1 (0.6)	1 (<0.1)
尿中血陽性	0	0	1 (<0.1)	4 (0.6)	5 (0.3)	2 (1.2)	7 (0.4)
体温上昇	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
骨密度減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
心雑音	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
クロストリジウム検査陽性	0	0	2 (0.2)	0	2 (0.1)	3 (1.8)	5 (0.3)
凝固時間延長	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
尿中結晶陽性	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
心電図QT延長	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
心電図異常	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
心電図再分極異常	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
便中カルプロテクチン増加	0	0	4 (0.4)	0	4 (0.2)	0	4 (0.2)
γ-グルタミルトランスフェラーゼ増加	8 (2.8)	0	15 (1.5)	4 (0.6)	19 (1.2)	2 (1.2)	21 (1.2)
糸球体濾過率減少	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.2)
尿中ブドウ糖陽性	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
顆粒球数減少	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
握力低下	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ヘマトクリット減少	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
ヘモグロビン減少	5 (1.8)	2 (9.1)	6 (0.6)	7 (1.1)	13 (0.8)	5 (3.0)	20 (1.1)
尿中ヘモグロビン陽性	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
肝酵素上昇	0	0	9 (0.9)	8 (1.3)	17 (1.0)	5 (3.0)	22 (1.2)
B型肝炎DNA測定陽性	1 (0.4)	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
高比重リポ蛋白増加	0	0	6 (0.6)	2 (0.3)	8 (0.5)	1 (0.6)	9 (0.5)
ヒト乳頭腫ウイルス検査陽性	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
眼圧上昇	0	0	0	1 (0.2)	1 (<0.1)	2 (1.2)	3 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
臨床検査異常	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
リパーゼ増加	0	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (0.2)
肝機能検査異常	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
肝機能検査値上昇	1 (0.4)	0	3 (0.3)	2 (0.3)	5 (0.3)	0	5 (0.3)
低比重リポ蛋白減少	0	0	3 (0.3)	0	3 (0.2)	1 (0.6)	4 (0.2)
低比重リポ蛋白増加	0	0	2 (0.2)	6 (1.0)	8 (0.5)	1 (0.6)	9 (0.5)
リンパ球数減少	3 (1.1)	1 (4.6)	16 (1.6)	12 (1.9)	28 (1.7)	9 (5.3)	38 (2.1)
リンパ球数増加	1 (0.4)	1 (4.6)	1 (<0.1)	2 (0.3)	3 (0.2)	4 (2.4)	8 (0.4)
リンパ球百分率減少	0	0	1 (<0.1)	3 (0.5)	4 (0.2)	4 (2.4)	8 (0.4)
リンパ球百分率増加	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
平均赤血球容積異常	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
平均赤血球容積増加	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
単球数増加	0	0	4 (0.4)	0	4 (0.2)	0	4 (0.2)
結核菌群検査陽性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
好中球数減少	4 (1.4)	0	19 (1.9)	18 (2.9)	37 (2.3)	30 (17.7)	67 (3.7)
好中球数増加	3 (1.1)	0	12 (1.2)	3 (0.5)	15 (0.9)	2 (1.2)	17 (0.9)
好中球百分率増加	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
血小板数減少	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
血小板数増加	0	0	2 (0.2)	3 (0.5)	5 (0.3)	1 (0.6)	6 (0.3)
プレアルブミン減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
前立腺特異性抗原増加	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
総蛋白減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
総蛋白増加	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
尿中蛋白陽性	6 (2.1)	0	7 (0.7)	1 (0.2)	8 (0.5)	1 (0.6)	9 (0.5)
赤血球数減少	0	0	6 (0.6)	4 (0.6)	10 (0.6)	0	10 (0.5)
赤血球数増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
血沈亢進	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
網状赤血球数減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
網状赤血球数増加	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
血清フェリチン減少	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
尿比重増加	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ブドウ球菌検査陽性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
トランスアミナーゼ上昇	0	0	2 (0.2)	2 (0.3)	4 (0.2)	1 (0.6)	5 (0.3)
尿検査異常	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
尿中ケトン体陽性	1 (0.4)	0	3 (0.3)	1 (0.2)	4 (0.2)	0	4 (0.2)
尿中白血球エステラーゼ陽性	0	0	4 (0.4)	1 (0.2)	5 (0.3)	0	5 (0.3)
尿量減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ビタミンB12減少	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ビタミンD減少	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
体重減少	2 (0.7)	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)							
体重増加	2 (0.7)	0	6 (0.6)	4 (0.6)	10 (0.6)	2 (1.2)	12 (0.7)
白血球数減少	7 (2.5)	0	17 (1.7)	12 (1.9)	29 (1.8)	20 (11.8)	49 (2.7)
白血球数増加	1 (0.4)	0	4 (0.4)	3 (0.5)	7 (0.4)	3 (1.8)	10 (0.5)
尿中白血球陽性	0	0	3 (0.3)	3 (0.5)	6 (0.4)	0	6 (0.3)
代謝および栄養障害	49 (17.3)	6 (27.4)	91 (9.0)	48 (7.7)	139 (8.5)	25 (14.8)	170 (9.3)
食欲減退	5 (1.8)	1 (4.6)	5 (0.5)	0	5 (0.3)	1 (0.6)	7 (0.4)
脱水	2 (0.7)	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
糖尿病	1 (0.4)	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
糖尿病性代謝代償不全	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脂質異常症	0	0	8 (0.8)	2 (0.3)	10 (0.6)	0	10 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
体液貯留	0	1 (4.6)	0	0	0	0	1 (<0.1)
葉酸欠乏	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
耐糖能障害	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
痛風	0	0	3 (0.3)	1 (0.2)	4 (0.2)	1 (0.6)	5 (0.3)
ヒスタミン不耐性	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
高カルシウム血症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
高コレステロール血症	4 (1.4)	0	14 (1.4)	9 (1.4)	23 (1.4)	1 (0.6)	24 (1.3)
高血糖	7 (2.5)	1 (4.6)	12 (1.2)	1 (0.2)	13 (0.8)	4 (2.4)	18 (1.0)
高ホモシステイン血症	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
高カリウム血症	0	0	0	0	0	1 (0.6)	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
高リパーゼ血症	1 (0.4)	0	0	0	0	0	0
高脂血症	2 (0.7)	0	8 (0.8)	4 (0.6)	12 (0.7)	2 (1.2)	14 (0.8)
高ナトリウム血症	0	0	0	0	0	1 (0.6)	1 (<0.1)
高トリグリセリド血症	2 (0.7)	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (0.2)
高尿酸血症	1 (0.4)	0	1 (<0.1)	2 (0.3)	3 (0.2)	1 (0.6)	4 (0.2)
低アルブミン血症	1 (0.4)	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (0.2)
低カリウム血症	5 (1.8)	2 (9.1)	6 (0.6)	1 (0.2)	7 (0.4)	1 (0.6)	10 (0.5)
低マグネシウム血症	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
低ナトリウム血症	3 (1.1)	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
低リン酸血症	3 (1.1)	0	3 (0.3)	6 (1.0)	9 (0.6)	2 (1.2)	11 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
低蛋白血症	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
食欲亢進	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
鉄欠乏	5 (1.8)	1 (4.6)	4 (0.4)	2 (0.3)	6 (0.4)	1 (0.6)	8 (0.4)
ラクトース不耐性	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
栄養障害	0	0	0	0	0	1 (0.6)	1 (<0.1)
代謝性アシドーシス	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
代謝症候群	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
肥満	0	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
2型糖尿病	2 (0.7)	0	0	0	0	0	0
過少体重	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
ビタミンB群欠乏	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ビタミンB1欠乏	1 (0.4)	0	0	0	0	0	0
ビタミンB12欠乏	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
ビタミンD欠乏	3 (1.1)	0	8 (0.8)	7 (1.1)	15 (0.9)	1 (0.6)	16 (0.9)
筋骨格系および結合組織障害	150 (52.8)	14 (63.9)	242 (24.0)	145 (23.3)	387 (23.7)	70 (41.4)	471 (25.9)
強直性脊椎炎	1 (0.4)	0	0	0	0	0	0
関節痛	39 (13.7)	7 (32.0)	58 (5.8)	35 (5.6)	93 (5.7)	18 (10.6)	118 (6.5)
関節炎	3 (1.1)	0	5 (0.5)	2 (0.3)	7 (0.4)	3 (1.8)	10 (0.5)
腸炎性関節炎	3 (1.1)	0	0	0	0	1 (0.6)	1 (<0.1)
関節障害	15 (5.3)	1 (4.6)	13 (1.3)	9 (1.4)	22 (1.3)	3 (1.8)	26 (1.4)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
腋窩腫瘤	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
背部痛	19 (6.7)	1 (4.6)	33 (3.3)	15 (2.4)	48 (2.9)	7 (4.1)	56 (3.1)
骨痛	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
滑液包炎	1 (0.4)	1 (4.6)	3 (0.3)	2 (0.3)	5 (0.3)	0	6 (0.3)
軟骨萎縮	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
頚部脊柱管狭窄症	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
軟骨軟化症	0	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
尾骨痛	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
コンパートメント症候群	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
肋軟骨炎	2 (0.7)	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
指炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腱付着部症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
外骨腫	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
側腹部痛	2 (0.7)	0	2 (0.2)	1 (0.2)	3 (0.2)	2 (1.2)	5 (0.3)
単径部痛	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
出血性関節症	1 (0.4)	0	0	0	0	0	0
椎間板変性症	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
椎間板障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
椎間板突出	0	0	7 (0.7)	3 (0.5)	10 (0.6)	0	10 (0.5)
関節滲出液	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
関節弛緩	0	0	0	0	0	1 (0.6)	1 (<0.1)
関節ロック	0	0	0	0	0	2 (1.2)	2 (0.1)
関節雑音	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
関節硬直	1 (0.4)	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
関節腫脹	2 (0.7)	0	5 (0.5)	1 (0.2)	6 (0.4)	0	6 (0.3)
腰部脊柱管狭窄症	0	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
脛骨内側過労性症候群	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
筋拘縮	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
筋不快感	1 (0.4)	0	0	0	0	0	0
筋障害	0	0	0	0	0	1 (0.6)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
筋痙縮	5 (1.8)	1 (4.6)	6 (0.6)	5 (0.8)	11 (0.7)	6 (3.5)	18 (1.0)
筋緊張	0	0	0	0	0	1 (0.6)	1 (<0.1)
筋力低下	1 (0.4)	0	0	0	0	0	0
筋骨格系胸痛	4 (1.4)	0	6 (0.6)	3 (0.5)	9 (0.6)	1 (0.6)	10 (0.5)
筋骨格不快感	0	0	0	0	0	1 (0.6)	1 (<0.1)
筋骨格痛	4 (1.4)	1 (4.6)	7 (0.7)	6 (1.0)	13 (0.8)	1 (0.6)	15 (0.8)
筋骨格硬直	0	0	3 (0.3)	1 (0.2)	4 (0.2)	2 (1.2)	6 (0.3)
筋肉痛	7 (2.5)	0	17 (1.7)	8 (1.3)	25 (1.5)	4 (2.4)	29 (1.6)
筋膜疼痛症候群	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ミオパチー	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
筋炎	2 (0.7)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
頚部痛	4 (1.4)	0	4 (0.4)	6 (1.0)	10 (0.6)	0	10 (0.5)
骨炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
変形性関節症	3 (1.1)	0	4 (0.4)	1 (0.2)	5 (0.3)	0	5 (0.3)
骨端症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
骨壊死	0	0	3 (0.3)	1 (0.2)	4 (0.2)	0	4 (0.2)
骨減少症	1 (0.4)	1 (4.6)	3 (0.3)	2 (0.3)	5 (0.3)	0	6 (0.3)
骨粗鬆症	1 (0.4)	1 (4.6)	2 (0.2)	4 (0.6)	6 (0.4)	2 (1.2)	9 (0.5)
四肢痛	9 (3.2)	0	12 (1.2)	16 (2.6)	28 (1.7)	5 (3.0)	33 (1.8)
顎痛	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
膝蓋大腿関節痛症候群	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
病的骨折	1 (0.4)	0	0	0	0	1 (0.6)	1 (<0.1)
関節周囲炎	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
足底筋膜炎	0	0	5 (0.5)	2 (0.3)	7 (0.4)	0	7 (0.4)
多発性関節炎	1 (0.4)	0	0	0	0	0	0
横紋筋融解症	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
関節リウマチ	1 (0.4)	0	0	0	0	0	0
肩回旋筋腱板症候群	2 (0.7)	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
仙腸骨炎	1 (0.4)	0	0	0	0	0	0
軟部組織腫瘤	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
脊柱変形	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
変形性脊椎症	0	0	2 (0.2)	2 (0.3)	4 (0.2)	0	4 (0.2)
脊椎痛	1 (0.4)	0	0	0	0	1 (0.6)	1 (<0.1)
脊椎炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脊椎関節障害	5 (1.8)	0	3 (0.3)	1 (0.2)	4 (0.2)	1 (0.6)	5 (0.3)
軟骨下機能不全骨折	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
滑液嚢腫	1 (0.4)	0	0	0	0	0	0
滑膜炎	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
顎関節症候群	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
腱痛	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)							
腱炎	2 (0.7)	0	4 (0.4)	1 (0.2)	5 (0.3)	1 (0.6)	6 (0.3)
腱鞘炎	1 (0.4)	0	0	0	0	0	0
弾発指	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	6 (2.1)	4 (18.3)	29 (2.9)	30 (4.8)	59 (3.6)	5 (3.0)	68 (3.7)
アクロコルドン	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
結腸腺癌	0	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
膵腺癌	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
基底細胞癌	0	0	1 (<0.1)	8 (1.3)	9 (0.6)	0	9 (0.5)
肺の良性新生物	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
精巣の良性新生物	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)							
良性脾腫瘍	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
ボーエン病	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
気管支の良性新生物	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
大腸腺腫	2 (0.7)	0	4 (0.4)	1 (0.2)	5 (0.3)	0	5 (0.3)
線維腫	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
線維性組織球腫	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
神経節腫	0	0	0	0	0	1 (0.6)	1 (<0.1)
皮膚血管腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
浸潤性乳癌	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
喉頭扁平上皮癌	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)							
脂肪腫	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
悪性黒色腫	0	1 (4.6)	0	0	0	0	1 (<0.1)
メラノサイト性母斑	0	2 (9.1)	2 (0.2)	1 (0.2)	3 (0.2)	0	5 (0.3)
口腔線維腫	1 (0.4)	0	0	0	0	0	0
卵巣胚細胞良性奇形腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
前立腺癌	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
脂漏性角化症	2 (0.7)	0	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
皮膚乳頭腫	0	1 (4.6)	5 (0.5)	5 (0.8)	10 (0.6)	2 (1.2)	13 (0.7)
小細胞癌	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
扁平上皮癌	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)							
皮膚有棘細胞癌	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
子宮頚部扁平上皮癌	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
精巣（純粋）セミノーマ	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
精巣癌	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
甲状腺腺腫	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
子宮平滑筋腫	0	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (0.2)
神経系障害	69 (24.3)	7 (32.0)	114 (11.3)	81 (13.0)	195 (12.0)	77 (45.5)	279 (15.3)
健忘	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
脳損傷	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
灼熱感	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)							
手根管症候群	3 (1.1)	0	2 (0.2)	5 (0.8)	7 (0.4)	0	7 (0.4)
脳虚血	0	0	0	0	0	2 (1.2)	2 (0.1)
脳血管発作	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
頚髄神経根障害	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
注意力障害	0	1 (4.6)	1 (<0.1)	0	1 (<0.1)	0	2 (0.1)
浮動性めまい	5 (1.8)	1 (4.6)	14 (1.4)	11 (1.8)	25 (1.5)	10 (5.9)	36 (2.0)
異常感覚	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
構語障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
味覚不全	1 (0.4)	0	0	0	0	0	0
てんかん	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)							
本態性振戦	1 (0.4)	0	0	0	0	0	0
頭痛	35 (12.3)	4 (18.3)	48 (4.8)	30 (4.8)	78 (4.8)	46 (27.2)	128 (7.0)
知覚過敏	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
感覚鈍麻	1 (0.4)	0	7 (0.7)	3 (0.5)	10 (0.6)	1 (0.6)	11 (0.6)
頭蓋内動脈瘤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ラクナ梗塞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
腰仙部神経根障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
記憶障害	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
片頭痛	7 (2.5)	0	12 (1.2)	7 (1.1)	19 (1.2)	3 (1.8)	22 (1.2)
神経圧迫	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)							
神経痛	0	0	1 (<0.1)	0	1 (<0.1)	2 (1.2)	3 (0.2)
神経炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
末梢性ニューロパチー	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
後頭神経痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
起立不耐性	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
錯感覚	4 (1.4)	0	5 (0.5)	4 (0.6)	9 (0.6)	1 (0.6)	10 (0.5)
末梢性感覚ニューロパチー	1 (0.4)	0	0	0	0	0	0
睡眠の質低下	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
ヘルペス後神経痛	0	0	0	1 (0.2)	1 (<0.1)	1 (0.6)	2 (0.1)
失神寸前の状態	1 (0.4)	0	0	2 (0.3)	2 (0.1)	1 (0.6)	3 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)							
回内筋症候群	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
橈骨神経麻痺	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
神経根痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
下肢静止不能症候群	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
坐骨神経痛	2 (0.7)	0	3 (0.3)	1 (0.2)	4 (0.2)	1 (0.6)	5 (0.3)
発作様現象	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
副鼻腔炎に伴う頭痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
傾眠	0	0	0	0	0	1 (0.6)	1 (<0.1)
脊椎炎性脊髄症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
くも膜下出血	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)							
硬膜下滲出液	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
失神	2 (0.7)	0	3 (0.3)	2 (0.3)	5 (0.3)	1 (0.6)	6 (0.3)
味覚障害	0	0	0	0	0	1 (0.6)	1 (<0.1)
緊張性頭痛	2 (0.7)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
振戦	0	1 (4.6)	1 (<0.1)	0	1 (<0.1)	3 (1.8)	5 (0.3)
視野欠損	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
精神障害	39 (13.7)	5 (22.8)	55 (5.5)	35 (5.6)	90 (5.5)	19 (11.2)	114 (6.3)
異常な夢	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
急性精神病	0	0	0	0	0	1 (0.6)	1 (<0.1)
急性ストレス反応	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害 (Cont.)							
感情障害	0	0	0	0	0	1 (0.6)	1 (<0.1)
激越	0	1 (4.6)	0	0	0	0	1 (<0.1)
不安	15 (5.3)	0	11 (1.1)	5 (0.8)	16 (1.0)	4 (2.4)	20 (1.1)
不安障害	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
注意欠如・多動性障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
自閉症スペクトラム障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
抑うつ気分	0	1 (4.6)	0	1 (0.2)	1 (<0.1)	0	2 (0.1)
うつ病	5 (1.8)	1 (4.6)	15 (1.5)	7 (1.1)	22 (1.3)	2 (1.2)	25 (1.4)
全般性不安障害	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
初期不眠症	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害 (Cont.)							
不眠症	12 (4.2)	1 (4.6)	13 (1.3)	16 (2.6)	29 (1.8)	6 (3.5)	36 (2.0)
故意の自傷行為	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
易刺激性	2 (0.7)	1 (4.6)	1 (<0.1)	0	1 (<0.1)	0	2 (0.1)
リビドー減退	0	0	0	0	0	1 (0.6)	1 (<0.1)
精神障害	1 (0.4)	0	0	0	0	0	0
気分変化	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
悪夢	0	0	0	0	0	1 (0.6)	1 (<0.1)
パニック発作	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
心的外傷後ストレス障害	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
落ち着きのなさ	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害 (Cont.)							
睡眠障害	2 (0.7)	0	4 (0.4)	0	4 (0.2)	2 (1.2)	6 (0.3)
社交不安障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ストレス	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
自殺念慮	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
自殺企図	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
腎および尿路障害	25 (8.8)	2 (9.1)	44 (4.4)	42 (6.8)	86 (5.3)	15 (8.9)	103 (5.7)
急性腎障害	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
膀胱痛	1 (0.4)	0	0	0	0	0	0
膀胱タンポナーデ	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
尿路結石	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)							
慢性腎臓病	0	0	0	0	0	2 (1.2)	2 (0.1)
肋骨脊柱角圧痛	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
出血性膀胱炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
非感染性膀胱炎	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
排尿困難	3 (1.1)	0	9 (0.9)	6 (1.0)	15 (0.9)	3 (1.8)	18 (1.0)
糖尿	1 (0.4)	0	0	0	0	0	0
血尿	3 (1.1)	0	3 (0.3)	5 (0.8)	8 (0.5)	1 (0.6)	9 (0.5)
水腎症	1 (0.4)	0	0	0	0	0	0
緊張性膀胱	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
ケトン尿	1 (0.4)	0	0	0	0	0	0

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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.

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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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)							
白血球尿	1 (0.4)	0	0	0	0	1 (0.6)	1 (<0.1)
排尿異常	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
尿意切迫	0	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
腎石灰沈着症	1 (0.4)	0	0	0	0	0	0
腎結石症	3 (1.1)	0	8 (0.8)	9 (1.4)	17 (1.0)	2 (1.2)	19 (1.0)
夜間頻尿	0	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
頻尿	3 (1.1)	1 (4.6)	0	1 (0.2)	1 (<0.1)	1 (0.6)	3 (0.2)
多尿	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
蛋白尿	6 (2.1)	0	8 (0.8)	4 (0.6)	12 (0.7)	1 (0.6)	13 (0.7)
腎萎縮	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.
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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.

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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
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MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)							
腎仙痛	0	0	1 (<0.1)	4 (0.6)	5 (0.3)	2 (1.2)	7 (0.4)
腎機能障害	0	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
腎臓痛	0	1 (4.6)	0	0	0	1 (0.6)	2 (0.1)
腎尿細管機能障害	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
尿管閉塞	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
尿管結石症	0	0	1 (<0.1)	3 (0.5)	4 (0.2)	1 (0.6)	5 (0.3)
尿閉	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
生殖系および乳房障害	8 (2.8)	1 (4.6)	37 (3.7)	20 (3.2)	57 (3.5)	10 (5.9)	68 (3.7)
無月経	0	0	2 (0.2)	1 (0.2)	3 (0.2)	1 (0.6)	4 (0.2)
萎縮性外陰膣炎	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

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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.

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TABLE 2.4 5.3.1

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
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MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)							
バルトリン嚢腫	1 (0.4)	0	0	0	0	0	0
良性前立腺肥大症	0	0	5 (0.5)	1 (0.2)	6 (0.4)	1 (0.6)	7 (0.4)
乳房嚢胞	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乳房障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乳房腫大	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乳房腫瘤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
乳房痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
子宮頚部上皮異形成	0	0	1 (<0.1)	3 (0.5)	4 (0.2)	0	4 (0.2)
子宮頚管ポリープ	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
子宮頚部障害	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all 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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)							
子宮頚部の炎症	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
性交出血	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
月経困難症	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
勃起不全	0	0	3 (0.3)	1 (0.2)	4 (0.2)	0	4 (0.2)
性器びらん	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
閉経期症状	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
不規則月経	1 (0.4)	0	2 (0.2)	0	2 (0.1)	2 (1.2)	4 (0.2)
不正子宮出血	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
卵巣嚢胞	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
卵巣静脈血栓症	1 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)							
多嚢胞性卵巣	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
閉経後出血	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
月経前頭痛	0	0	0	0	0	1 (0.6)	1 (<0.1)
月経前症候群	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
前立腺炎	1 (0.4)	0	2 (0.2)	4 (0.6)	6 (0.4)	0	6 (0.3)
精液変色	0	0	0	2 (0.3)	2 (0.1)	1 (0.6)	3 (0.2)
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)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)							
腟出血	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<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 (0.2)	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 (4.6)	0	0	0	0	1 (<0.1)
外陰腟そう痒症	1 (0.4)	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 (20.1)	12 (54.8)	133 (13.2)	76 (12.2)	209 (12.8)	47 (27.8)	268 (14.7)
急性呼吸不全	1 (0.4)	0	0	1 (0.2)	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 (0.3)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
喘息	0	2 (9.1)	7 (0.7)	1 (0.2)	8 (0.5)	0	10 (0.5)
無気肺	0	0	1 (<0.1)	1 (0.2)	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 (0.4)	0	0	0	0	0	0
カタル	1 (0.4)	0	0	0	0	0	0
慢性閉塞性肺疾患	1 (0.4)	0	2 (0.2)	0	2 (0.1)	2 (1.2)	4 (0.2)
咳嗽	11 (3.9)	3 (13.7)	28 (2.8)	12 (1.9)	40 (2.5)	16 (9.5)	59 (3.2)
嚢胞性肺疾患	0	0	0	0	0	1 (0.6)	1 (<0.1)
横隔膜痛	1 (0.4)	0	0	0	0	0	0
咽喉乾燥	0	0	0	0	0	1 (0.6)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
発声障害	0	0	2 (0.2)	0	2 (0.1)	0	2 (0.1)
呼吸困難	0	0	10 (1.0)	4 (0.6)	14 (0.9)	3 (1.8)	17 (0.9)
労作性呼吸困難	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
肺気腫	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
鼻出血	0	0	8 (0.8)	7 (1.1)	15 (0.9)	0	15 (0.8)
喀血	1 (0.4)	0	0	0	0	0	0
しゃっくり	1 (0.4)	0	0	1 (0.2)	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 (0.4)	0	0	0	0	0	0
肺過膨脹	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
肺浸潤	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
鼻閉	4 (1.4)	1 (4.6)	3 (0.3)	8 (1.3)	11 (0.7)	1 (0.6)	13 (0.7)
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 (0.2)	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 (0.2)
非感染性気管支炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
口腔咽頭不快感	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
口腔咽頭痛	8 (2.8)	2 (9.1)	27 (2.7)	14 (2.3)	41 (2.5)	8 (4.7)	51 (2.8)
呼吸時疼痛	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
副鼻腔不快感	1 (0.4)	0	0	0	0	0	0
副鼻腔分泌過多	0	1 (4.6)	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 (4.6)	0	0	0	0	1 (<0.1)
胸膜障害	1 (0.4)	0	0	0	0	0	0
胸水	0	0	3 (0.3)	0	3 (0.2)	0	3 (0.2)
胸膜痛	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
肺臓炎	2 (0.7)	0	0	0	0	0	0
気胸	1 (0.4)	0	0	0	0	0	0
湿性咳嗽	1 (0.4)	0	4 (0.4)	2 (0.3)	6 (0.4)	2 (1.2)	8 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
肺塞栓症	1 (0.4)	0	5 (0.5)	0	5 (0.3)	1 (0.6)	6 (0.3)
肺出血	1 (0.4)	0	0	0	0	0	0
肺腫瘤	2 (0.7)	2 (9.1)	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	5 (0.3)
気道うっ血	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	1 (0.6)	3 (0.2)
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 (0.7)	0	3 (0.3)	2 (0.3)	5 (0.3)	2 (1.2)	7 (0.4)
鼻漏	2 (0.7)	0	2 (0.2)	2 (0.3)	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 (1.8)	0	4 (0.4)	3 (0.5)	7 (0.4)	1 (0.6)	8 (0.4)
副鼻腔障害	0	0	0	0	0	1 (0.6)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)							
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	4 (0.4)	1 (0.2)	5 (0.3)	0	5 (0.3)
咽喉刺激感	0	0	1 (<0.1)	1 (0.2)	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 (0.2)	1 (<0.1)	0	1 (<0.1)
上気道の炎症	4 (1.4)	0	3 (0.3)	1 (0.2)	4 (0.2)	0	4 (0.2)
上気道咳症候群	2 (0.7)	0	1 (<0.1)	3 (0.5)	4 (0.2)	0	4 (0.2)
声帯ポリープ	1 (0.4)	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	135 (47.5)	9 (41.1)	178 (17.7)	155 (24.9)	333 (20.4)	145 (85.7)	487 (26.7)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
ざ瘡	11 (3.9)	1 (4.6)	26 (2.6)	28 (4.5)	54 (3.3)	54 (31.9)	109 (6.0)
嚢胞性ざ瘡	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
光線角化症	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
脱毛症	2 (0.7)	0	13 (1.3)	7 (1.1)	20 (1.2)	12 (7.1)	32 (1.8)
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 (0.2)	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	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
皮膚炎	6 (2.1)	0	5 (0.5)	4 (0.6)	9 (0.6)	2 (1.2)	11 (0.6)
ざ瘡様皮膚炎	1 (0.4)	1 (4.6)	4 (0.4)	2 (0.3)	6 (0.4)	5 (3.0)	12 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
アレルギー性皮膚炎	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
アトピー性皮膚炎	4 (1.4)	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
接触皮膚炎	5 (1.8)	0	6 (0.6)	1 (0.2)	7 (0.4)	0	7 (0.4)
剥脱性皮膚炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
乾癬様皮膚炎	1 (0.4)	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 (3.2)	0	3 (0.3)	3 (0.5)	6 (0.4)	0	6 (0.3)
異汗性湿疹	4 (1.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
斑状出血	1 (0.4)	0	1 (<0.1)	1 (0.2)	2 (0.1)	2 (1.2)	4 (0.2)
湿疹	9 (3.2)	0	13 (1.3)	12 (1.9)	25 (1.5)	4 (2.4)	29 (1.6)
皮脂欠乏性湿疹	1 (0.4)	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
紅斑	5 (1.8)	0	7 (0.7)	6 (1.0)	13 (0.8)	1 (0.6)	14 (0.8)
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 (0.7)	0	0	1 (0.2)	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 (0.4)	0	0	0	0	0	0
過角化	0	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
多毛症	1 (0.4)	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 (0.2)	1 (<0.1)	0	1 (<0.1)
瘢痕そう痒感	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
毛孔性角化症	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
黒子	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
扁平苔癬	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
機械性蕁麻疹	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
汗疹	0	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (0.2)
爪肥厚	0	0	0	1 (0.2)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
神経皮膚炎	1 (0.4)	0	0	0	0	0	0
寝汗	2 (0.7)	1 (4.6)	6 (0.6)	2 (0.3)	8 (0.5)	1 (0.6)	10 (0.5)
爪破損	1 (0.4)	0	0	2 (0.3)	2 (0.1)	0	2 (0.1)
爪甲剥離症	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
皮膚疼痛	0	0	0	0	0	2 (1.2)	2 (0.1)
脂肪織炎	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
丘疹	1 (0.4)	0	2 (0.2)	1 (0.2)	3 (0.2)	5 (3.0)	8 (0.4)
口囲皮膚炎	0	0	1 (<0.1)	1 (0.2)	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 (0.4)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
光線過敏性反応	1 (0.4)	0	0	1 (0.2)	1 (<0.1)	2 (1.2)	3 (0.2)
そう痒症	18 (6.3)	2 (9.1)	12 (1.2)	9 (1.4)	21 (1.3)	3 (1.8)	26 (1.4)
乾癬	0	0	2 (0.2)	1 (0.2)	3 (0.2)	0	3 (0.2)
壊疽性膿皮症	2 (0.7)	0	0	0	0	1 (0.6)	1 (<0.1)
発疹	16 (5.6)	3 (13.7)	26 (2.6)	31 (5.0)	57 (3.5)	21 (12.4)	81 (4.4)
紅斑性皮疹	1 (0.4)	0	3 (0.3)	1 (0.2)	4 (0.2)	0	4 (0.2)
毛孔性皮疹	0	0	3 (0.3)	0	3 (0.2)	1 (0.6)	4 (0.2)
斑状皮疹	0	0	1 (<0.1)	3 (0.5)	4 (0.2)	1 (0.6)	5 (0.3)
斑状丘疹状皮疹	3 (1.1)	0	1 (<0.1)	4 (0.6)	5 (0.3)	2 (1.2)	7 (0.4)
丘疹性皮疹	0	0	2 (0.2)	1 (0.2)	3 (0.2)	3 (1.8)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
そう痒性皮疹	0	0	1 (<0.1)	3 (0.5)	4 (0.2)	0	4 (0.2)
酒さ	2 (0.7)	1 (4.6)	8 (0.8)	3 (0.5)	11 (0.7)	1 (0.6)	13 (0.7)
脂漏性皮膚炎	8 (2.8)	0	1 (<0.1)	2 (0.3)	3 (0.2)	5 (3.0)	8 (0.4)
皮膚灼熱感	1 (0.4)	0	0	0	0	0	0
皮膚変色	0	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
皮膚びらん	1 (0.4)	0	0	0	0	0	0
皮膚剥脱	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
皮膚亀裂	1 (0.4)	0	1 (<0.1)	0	1 (<0.1)	1 (0.6)	2 (0.1)
皮膚色素過剰	1 (0.4)	0	0	0	0	0	0
皮膚病変	0	0	5 (0.5)	3 (0.5)	8 (0.5)	2 (1.2)	10 (0.5)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)							
皮膚腫瘤	0	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 (0.4)	0	0	1 (0.2)	1 (<0.1)	2 (1.2)	3 (0.2)
日光皮膚炎	1 (0.4)	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 (1.8)	0	2 (0.2)	6 (1.0)	8 (0.5)	0	8 (0.4)
尋常性白斑	1 (0.4)	0	0	0	0	0	0
社会環境	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
閉経	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
外科および内科処置	0	0	5 (0.5)	3 (0.5)	8 (0.5)	0	8 (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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
外科および内科処置 (Cont.)							
人工流産	0	0	2 (0.2)	0	2 (0.1)	0	2 (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	1 (<0.1)	2 (0.3)	3 (0.2)	0	3 (0.2)
智歯抜歯	0	0	1 (<0.1)	1 (0.2)	2 (0.1)	0	2 (0.1)
血管障害	16 (5.6)	2 (9.1)	50 (5.0)	30 (4.8)	80 (4.9)	18 (10.6)	100 (5.5)
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 (0.2)	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)
深部静脈血栓症	1 (0.4)	0	2 (0.2)	3 (0.5)	5 (0.3)	1 (0.6)	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=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血管障害 (Cont.)							
本態性高血圧症	0	0	0	0	0	1 (0.6)	1 (<0.1)
潮紅	0	1 (4.6)	1 (<0.1)	0	1 (<0.1)	1 (0.6)	3 (0.2)
血腫	1 (0.4)	1 (4.6)	0	0	0	0	1 (<0.1)
出血	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
ほてり	0	0	4 (0.4)	0	4 (0.2)	1 (0.6)	5 (0.3)
高血圧	8 (2.8)	0	32 (3.2)	20 (3.2)	52 (3.2)	9 (5.3)	61 (3.3)
高血圧クリーゼ	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
低血圧	2 (0.7)	0	0	2 (0.3)	2 (0.1)	1 (0.6)	3 (0.2)
起立性低血圧	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
蒼白	0	0	0	0	0	1 (0.6)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 5.3.1

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

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=608) (PYs=284.0) Events (E/100 PYs)	UPA 7.5 mg QD (N=47) (PYs=21.9) Events (E/100 PYs)	UPA 15 mg QD (N=822) (PYs=1007.8) Events (E/100 PYs)	UPA 30 mg QD (N=610) (PYs=622.2) Events (E/100 PYs)	UPA 15/30 mg QD (N=1089) (PYs=1630.0) Events (E/100 PYs)	UPA 45 mg QD (N=987) (PYs=169.2) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血管障害 (Cont.)							
骨盤静脈血栓症	1 (0.4)	0	0	0	0	0	0
末梢冷感	1 (0.4)	0	0	0	0	0	0
末梢静脈疾患	0	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
静脈炎	0	0	0	1 (0.2)	1 (<0.1)	0	1 (<0.1)
レイノー現象	0	0	2 (0.2)	0	2 (0.1)	1 (0.6)	3 (0.2)
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 (0.4)	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 (0.4)	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
白衣性高血圧	0	0	0	2 (0.3)	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 2.7.4.7-29.

[redacted]20[redacted] 16:56 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
Any adverse event	71 (424.0)	19 (244.4)	179 (270.8)
血液およびリンパ系障害	5 (29.9)	1 (12.9)	5 (7.6)
貧血	4 (23.9)	1 (12.9)	1 (1.5)
鉄欠乏性貧血	0	0	0
白血球減少症	0	0	2 (3.0)
リンパ節症	0	0	0
リンパ球減少症	1 (6.0)	0	1 (1.5)
小球性貧血	0	0	0
好中球減少症	0	0	1 (1.5)
血小板減少症	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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
Any adverse event	49 (1999.7)	260 (423.7)	236 (282.5)	300 (399.1)	926 (340.8)
血液およびリンパ系障害	3 (122.4)	20 (32.6)	12 (14.4)	16 (21.3)	47 (17.3)
貧血	1 (40.8)	4 (6.5)	3 (3.6)	3 (4.0)	10 (3.7)
鉄欠乏性貧血	0	4 (6.5)	2 (2.4)	0	3 (1.1)
白血球減少症	0	4 (6.5)	3 (3.6)	2 (2.7)	10 (3.7)
リンパ節症	0	1 (1.6)	0	0	1 (0.4)
リンパ球減少症	1 (40.8)	2 (3.3)	1 (1.2)	1 (1.3)	5 (1.8)
小球性貧血	0	0	0	1 (1.3)	1 (0.4)
好中球減少症	1 (40.8)	4 (6.5)	3 (3.6)	9 (12.0)	17 (6.3)
血小板減少症	0	1 (1.6)	0	0	0

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

Program Source Code: [redacted]

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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
心臓障害	0	0	0
不整脈	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
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

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
心臓障害	0	0	2 (2.4)	3 (4.0)	5 (1.8)
不整脈	0	0	1 (1.2)	0	1 (0.4)
僧帽弁閉鎖不全症	0	0	0	1 (1.3)	1 (0.4)
上室性期外収縮	0	0	1 (1.2)	0	1 (0.4)
心室性期外収縮	0	0	0	2 (2.7)	2 (0.7)
先天性、家族性および遺伝性障害	0	1 (1.6)	0	0	1 (0.4)
歯原性嚢胞	0	1 (1.6)	0	0	1 (0.4)
耳および迷路障害	0	0	5 (6.0)	4 (5.3)	9 (3.3)
感音性難聴	0	0	1 (1.2)	0	1 (0.4)
片耳難聴	0	0	0	1 (1.3)	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
耳および迷路障害 (Cont.)			
メニエール病	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 (3.0)
副腎機能不全	0	0	1 (1.5)
甲状腺腫	0	0	1 (1.5)
甲状腺腫瘤	0	0	0
眼障害	2 (11.9)	1 (12.9)	1 (1.5)
眼瞼炎	0	0	0
白内障	0	1 (12.9)	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=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
耳および迷路障害 (Cont.)					
メニエール病	0	0	0	2 (2.7)	2 (0.7)
耳鳴	0	0	1 (1.2)	0	1 (0.4)
回転性めまい	0	0	3 (3.6)	1 (1.3)	4 (1.5)
内分泌障害	0	0	0	1 (1.3)	3 (1.1)
副腎機能不全	0	0	0	0	1 (0.4)
甲状腺腫	0	0	0	0	1 (0.4)
甲状腺腫瘤	0	0	0	1 (1.3)	1 (0.4)
眼障害	0	6 (9.8)	2 (2.4)	7 (9.3)	14 (5.2)
眼瞼炎	0	1 (1.6)	0	0	0
白内障	0	0	1 (1.2)	0	2 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
眼障害 (Cont.)			
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 (6.0)	0	0
ドライアイ	0	0	0
角膜炎	0	0	0
眼充血	0	0	1 (1.5)
翼状片	1 (6.0)	0	0
潰瘍性角膜炎	0	0	0
硝子体浮遊物	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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
眼障害 (Cont.)					
霰粒腫	0	0	0	1 (1.3)	1 (0.4)
結膜嚢胞	0	1 (1.6)	0	0	1 (0.4)
結膜出血	0	0	0	2 (2.7)	2 (0.7)
アレルギー性結膜炎	0	2 (3.3)	0	1 (1.3)	2 (0.7)
ドライアイ	0	1 (1.6)	0	2 (2.7)	3 (1.1)
角膜炎	0	0	0	1 (1.3)	1 (0.4)
眼充血	0	0	0	0	1 (0.4)
翼状片	0	0	0	0	0
潰瘍性角膜炎	0	1 (1.6)	0	0	0
硝子体浮遊物	0	0	1 (1.2)	0	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
胃腸障害	17 (101.5)	5 (64.3)	22 (33.3)
腹部膨満	0	0	2 (3.0)
腹痛	0	0	2 (3.0)
下腹部痛	0	0	0
上腹部痛	0	0	0
肛門の炎症	1 (6.0)	0	0
肛門そう痒症	0	0	0
口角口唇炎	0	0	1 (1.5)
アフタ性潰瘍	0	0	1 (1.5)
虚血性大腸炎	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
胃腸障害	7 (285.7)	47 (76.6)	18 (21.5)	29 (38.6)	99 (36.4)
腹部膨満	1 (40.8)	1 (1.6)	0	0	3 (1.1)
腹痛	0	0	1 (1.2)	0	3 (1.1)
下腹部痛	0	0	1 (1.2)	0	1 (0.4)
上腹部痛	0	2 (3.3)	1 (1.2)	0	2 (0.7)
肛門の炎症	0	0	0	0	0
肛門そう痒症	0	1 (1.6)	0	0	0
口角口唇炎	0	0	0	0	1 (0.4)
アフタ性潰瘍	0	1 (1.6)	0	0	1 (0.4)
虚血性大腸炎	0	0	1 (1.2)	0	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
胃腸障害 (Cont.)			
潰瘍性大腸炎	11 (65.7)	0	5 (7.6)
便秘	1 (6.0)	0	0
齲歯	1 (6.0)	0	1 (1.5)
下痢	0	0	0
消化不良	0	0	0
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	0
歯肉痛	0	0	1 (1.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
胃腸障害 (Cont.)					
潰瘍性大腸炎	3 (122.4)	13 (21.2)	1 (1.2)	2 (2.7)	11 (4.0)
便秘	1 (40.8)	1 (1.6)	1 (1.2)	7 (9.3)	10 (3.7)
齲歯	0	2 (3.3)	1 (1.2)	1 (1.3)	5 (1.8)
下痢	0	0	1 (1.2)	0	1 (0.4)
消化不良	0	4 (6.5)	1 (1.2)	0	5 (1.8)
腸炎	0	1 (1.6)	0	1 (1.3)	2 (0.7)
胃ポリープ	0	1 (1.6)	0	0	1 (0.4)
胃炎	0	2 (3.3)	0	0	2 (0.7)
胃食道逆流性疾患	0	1 (1.6)	1 (1.2)	1 (1.3)	2 (0.7)
歯肉痛	0	0	0	0	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
胃腸障害 (Cont.)			
歯肉腫脹	0	0	0
舌痛	0	0	0
痔出血	0	0	0
痔核	0	0	0
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 (1.5)
大腸ポリープ	0	5 (64.3)	1 (1.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
胃腸障害 (Cont.)					
歯肉腫脹	0	1 (1.6)	1 (1.2)	0	1 (0.4)
舌痛	0	1 (1.6)	0	0	0
痔出血	0	1 (1.6)	0	0	0
痔核	0	2 (3.3)	3 (3.6)	1 (1.3)	5 (1.8)
血栓性痔核	0	1 (1.6)	0	0	0
胃酸過多	0	0	0	1 (1.3)	1 (0.4)
単径ヘルニア	0	0	1 (1.2)	0	1 (0.4)
腸管ポリープ	0	0	1 (1.2)	0	1 (0.4)
過敏性腸症候群	0	0	0	0	1 (0.4)
大腸ポリープ	0	0	0	0	6 (2.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
胃腸障害 (Cont.)			
口唇乾燥	0	0	0
口腔嚢胞	0	0	0
悪心	1 (6.0)	0	1 (1.5)
口腔扁平苔癬	0	0	1 (1.5)
膵炎	0	0	0
歯周病	0	0	0
肛門周囲痛	0	0	0
直腸炎	0	0	2 (3.0)
口内炎	2 (11.9)	0	1 (1.5)
歯の脱落	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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
胃腸障害 (Cont.)					
口唇乾燥	1 (40.8)	0	0	0	1 (0.4)
口腔嚢胞	0	1 (1.6)	0	0	0
悪心	0	1 (1.6)	1 (1.2)	0	2 (0.7)
口腔扁平苔癬	0	0	0	0	1 (0.4)
膵炎	1 (40.8)	1 (1.6)	0	0	1 (0.4)
歯周病	0	0	0	2 (2.7)	2 (0.7)
肛門周囲痛	0	1 (1.6)	0	0	1 (0.4)
直腸炎	0	1 (1.6)	0	0	2 (0.7)
口内炎	0	6 (9.8)	1 (1.2)	9 (12.0)	15 (5.5)
歯の脱落	0	0	0	1 (1.3)	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
胃腸障害 (Cont.)			
歯痛	0	0	2 (3.0)
嘔吐	0	0	0
一般・全身障害および投与部位の状態	4 (23.9)	0	4 (6.1)
医薬品副作用	0	0	0
胸痛	0	0	1 (1.5)
炎症	0	0	0
倦怠感	0	0	0
末梢性浮腫	1 (6.0)	0	0
発熱	3 (17.9)	0	3 (4.5)
肝胆道系障害	1 (6.0)	0	4 (6.1)

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 Dose = 45 mg QD [C] UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	 UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
胃腸障害 (Cont.)					
歯痛	0	0	0	1 (1.3)	3 (1.1)
嘔吐	0	0	0	2 (2.7)	2 (0.7)
一般・全身障害および投与部位の状態	4 (163.2)	5 (8.1)	3 (3.6)	12 (16.0)	26 (9.6)
医薬品副作用	0	0	1 (1.2)	0	1 (0.4)
胸痛	0	0	0	3 (4.0)	4 (1.5)
炎症	0	0	0	1 (1.3)	1 (0.4)
倦怠感	1 (40.8)	1 (1.6)	0	0	1 (0.4)
末梢性浮腫	0	1 (1.6)	0	2 (2.7)	2 (0.7)
発熱	3 (122.4)	3 (4.9)	2 (2.4)	6 (8.0)	17 (6.3)
肝胆道系障害	0	2 (3.3)	5 (6.0)	3 (4.0)	13 (4.8)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
薬物性肝障害	0	0	0
肝機能異常	0	0	3 (4.5)
脂肪肝	0	0	1 (1.5)
肝障害	0	0	0
肝損傷	0	0	0
門脈血栓症	1 (6.0)	0	0
免疫系障害	0	0	1 (1.5)
アナフィラキシー反応	0	0	0
季節性アレルギー	0	0	1 (1.5)
感染症および寄生虫症	8 (47.8)	4 (51.4)	75 (113.5)

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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
肝胆道系障害 (Cont.)					
薬物性肝障害	0	1 (1.6)	0	0	1 (0.4)
肝機能異常	0	0	4 (4.8)	3 (4.0)	10 (3.7)
脂肪肝	0	0	0	0	1 (0.4)
肝障害	0	0	1 (1.2)	0	1 (0.4)
肝損傷	0	1 (1.6)	0	0	0
門脈血栓症	0	0	0	0	0
免疫系障害	0	0	1 (1.2)	3 (4.0)	5 (1.8)
アナフィラキシー反応	0	0	0	1 (1.3)	1 (0.4)
季節性アレルギー	0	0	1 (1.2)	2 (2.7)	4 (1.5)
感染症および寄生虫症	8 (326.5)	62 (101.0)	64 (76.6)	79 (105.1)	274 (100.8)

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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
膿瘍	1 (6.0)	0	0
ダニ皮膚炎	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
バルトリン腺炎	0	0	0
気管支炎	0	0	2 (3.0)
カンピロバクター胃腸炎	0	0	1 (1.5)
カンジダ感染	0	0	0
蜂巣炎	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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
膿瘍	0	0	0	0	0
ダニ皮膚炎	0	0	2 (2.4)	0	2 (0.7)
虫垂炎	0	0	1 (1.2)	0	1 (0.4)
細菌性関節炎	0	0	1 (1.2)	0	1 (0.4)
無症候性細菌尿	0	0	1 (1.2)	0	1 (0.4)
バルトリン腺炎	0	1 (1.6)	0	0	1 (0.4)
気管支炎	0	0	0	2 (2.7)	4 (1.5)
カンピロバクター胃腸炎	0	0	1 (1.2)	1 (1.3)	3 (1.1)
カンジダ感染	0	0	0	1 (1.3)	1 (0.4)
蜂巣炎	0	0	1 (1.2)	0	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
クロストリジウム・ディフィシレ感染	0	1 (12.9)	5 (7.6)
結膜炎	1 (6.0)	0	0
ウイルス性結膜炎	0	0	0
膀胱炎	0	0	3 (4.5)
サイトメガロウイルス性大腸炎	0	0	0
感染性皮膚炎	0	0	0
爪の皮膚糸状菌症	0	0	1 (1.5)
感染性腸炎	0	0	1 (1.5)
毛包炎	0	0	2 (3.0)
胃腸炎	0	0	1 (1.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
クロストリジウム・ディフィシレ感染	0	0	0	0	6 (2.2)
結膜炎	0	0	1 (1.2)	1 (1.3)	2 (0.7)
ウイルス性結膜炎	0	1 (1.6)	0	0	1 (0.4)
膀胱炎	0	2 (3.3)	1 (1.2)	2 (2.7)	8 (2.9)
サイトメガロウイルス性大腸炎	0	0	0	1 (1.3)	1 (0.4)
感染性皮膚炎	0	1 (1.6)	0	0	1 (0.4)
爪の皮膚糸状菌症	0	0	0	1 (1.3)	2 (0.7)
感染性腸炎	0	0	0	1 (1.3)	2 (0.7)
毛包炎	1 (40.8)	1 (1.6)	2 (2.4)	5 (6.7)	10 (3.7)
胃腸炎	0	2 (3.3)	3 (3.6)	0	5 (1.8)

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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
ウイルス性胃腸炎	0	0	2 (3.0)
歯肉炎	0	0	0
ヘリコバクター感染	0	0	0
単純ヘルペス	0	0	0
帯状疱疹	0	2 (25.7)	4 (6.1)
帯状疱疹性髄膜炎	0	0	0
麦粒腫	0	0	2 (3.0)
インフルエンザ	0	0	3 (4.5)
クレブシエラ感染	0	0	1 (1.5)
大腸感染	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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
ウイルス性胃腸炎	0	0	0	0	2 (0.7)
歯肉炎	0	2 (3.3)	1 (1.2)	1 (1.3)	4 (1.5)
ヘリコバクター感染	0	0	1 (1.2)	0	1 (0.4)
単純ヘルペス	0	3 (4.9)	1 (1.2)	0	4 (1.5)
帯状疱疹	3 (122.4)	2 (3.3)	6 (7.2)	6 (8.0)	21 (7.7)
帯状疱疹性髄膜炎	0	0	0	1 (1.3)	1 (0.4)
麦粒腫	0	3 (4.9)	2 (2.4)	1 (1.3)	6 (2.2)
インフルエンザ	1 (40.8)	2 (3.3)	4 (4.8)	3 (4.0)	13 (4.8)
クレブシエラ感染	0	0	0	0	1 (0.4)
大腸感染	0	0	1 (1.2)	1 (1.3)	2 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
潜伏結核	0	0	1 (1.5)
伝染性軟属腫	0	0	0
上咽頭炎	4 (23.9)	0	23 (34.8)
口腔カンジダ症	0	0	0
口腔ヘルペス	0	0	10 (15.1)
外耳炎	0	0	0
歯周炎	0	0	1 (1.5)
咽頭炎	0	0	2 (3.0)
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

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

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=16) (PYs=2.5) Events (E/100 PYs)	UPA 45 mg/ PBO (N=41) (PYs=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
潜伏結核	0	0	0	2 (2.7)	3 (1.1)
伝染性軟属腫	0	1 (1.6)	0	0	0
上咽頭炎	0	18 (29.3)	22 (26.3)	25 (33.3)	83 (30.5)
口腔カンジダ症	0	1 (1.6)	0	0	0
口腔ヘルペス	0	7 (11.4)	6 (7.2)	10 (13.3)	33 (12.1)
外耳炎	0	1 (1.6)	0	0	0
歯周炎	0	3 (4.9)	0	1 (1.3)	5 (1.8)
咽頭炎	0	0	1 (1.2)	4 (5.3)	7 (2.6)
胸膜感染	0	0	0	1 (1.3)	1 (0.4)
ニューモシスチス・イロベチイ肺炎	0	1 (1.6)	0	0	0

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
肺炎	0	0	2 (3.0)
歯髄炎	0	0	0
腎盂腎炎	0	1 (12.9)	0
鼻炎	0	0	1 (1.5)
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
扁桃炎	0	0	3 (4.5)
上気道感染	1 (6.0)	0	3 (4.5)

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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
肺炎	1 (40.8)	1 (1.6)	0	1 (1.3)	4 (1.5)
歯髄炎	0	1 (1.6)	0	0	1 (0.4)
腎盂腎炎	0	1 (1.6)	0	0	2 (0.7)
鼻炎	0	0	0	0	1 (0.4)
副鼻腔炎	0	1 (1.6)	0	0	1 (0.4)
皮膚感染	0	0	0	3 (4.0)	3 (1.1)
白癬感染	1 (40.8)	1 (1.6)	0	0	1 (0.4)
足部白癬	0	1 (1.6)	1 (1.2)	1 (1.3)	2 (0.7)
扁桃炎	0	0	0	1 (1.3)	4 (1.5)
上気道感染	0	4 (6.5)	3 (3.6)	2 (2.7)	12 (4.4)

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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
水痘	0	0	1 (1.5)
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 (6.0)	0	0
傷害、中毒および処置合併症	1 (6.0)	0	5 (7.6)
吻合部漏出	1 (6.0)	0	0
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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any part 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
水痘	0	0	0	0	1 (0.4)
ウイルス感染	1 (40.8)	0	0	0	1 (0.4)
外陰部腟カンジダ症	0	0	1 (1.2)	0	1 (0.4)
創傷感染	0	0	0	0	0
傷害、中毒および処置合併症	1 (40.8)	5 (8.1)	6 (7.2)	4 (5.3)	17 (6.3)
吻合部漏出	0	0	0	0	0
動物咬傷	0	0	0	1 (1.3)	1 (0.4)
節足動物刺傷	0	0	1 (1.2)	0	1 (0.4)
骨挫傷	0	1 (1.6)	0	0	0
挫傷	0	0	0	1 (1.3)	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
上顎炎	0	0	2 (3.0)
足骨折	0	0	0
熱中症	0	0	0
関節損傷	0	0	0
靭帯捻挫	0	0	1 (1.5)
過量投与	0	0	0
処置後出血	0	0	1 (1.5)
肺挫傷	0	0	0
肋骨骨折	0	0	0
皮膚裂傷	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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
上顎炎	0	0	0	0	2 (0.7)
足骨折	0	0	1 (1.2)	1 (1.3)	2 (0.7)
熱中症	0	1 (1.6)	0	0	0
関節損傷	0	0	1 (1.2)	0	1 (0.4)
靭帯捻挫	0	0	0	0	1 (0.4)
過量投与	0	0	1 (1.2)	0	1 (0.4)
処置後出血	0	0	0	0	1 (0.4)
肺挫傷	0	0	1 (1.2)	0	1 (0.4)
肋骨骨折	0	1 (1.6)	0	1 (1.3)	1 (0.4)
皮膚裂傷	1 (40.8)	0	0	0	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
皮下血腫	0	0	0
胸椎骨折	0	0	0
脛骨骨折	0	0	1 (1.5)
臨床検査	6 (35.8)	3 (38.6)	12 (18.2)
アラニンアミノトランスフェラーゼ増加	1 (6.0)	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	1 (6.0)	0	0
血中アルカリホスファターゼ増加	1 (6.0)	0	0
血中ビリルビン増加	0	0	1 (1.5)
血中コレステロール増加	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
皮下血腫	0	2 (3.3)	0	0	1 (0.4)
胸椎骨折	0	0	1 (1.2)	0	1 (0.4)
脛骨骨折	0	0	0	0	1 (0.4)
臨床検査	11 (448.9)	20 (32.6)	47 (56.3)	51 (67.8)	137 (50.4)
アラニンアミノトランスフェラーゼ増加	0	1 (1.6)	3 (3.6)	4 (5.3)	8 (2.9)
アミラーゼ増加	1 (40.8)	1 (1.6)	2 (2.4)	0	3 (1.1)
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 (1.6)	4 (4.8)	3 (4.0)	9 (3.3)
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 (0.4)
血中コレステロール増加	0	0	0	1 (1.3)	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
臨床検査 (Cont.)			
血中クレアチンホスホキナーゼ増加	0	3 (38.6)	3 (4.5)
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
心電図異常	0	0	0
γ-グルタミルトランスフェラーゼ増加	1 (6.0)	0	1 (1.5)
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 (1.5)
リンパ球数増加	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 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
臨床検査 (Cont.)					
血中クレアチンホスホキナーゼ増加	2 (81.6)	5 (8.1)	12 (14.4)	14 (18.6)	38 (14.0)
血中クレアチニン増加	0	1 (1.6)	0	2 (2.7)	2 (0.7)
血中尿酸増加	0	1 (1.6)	0	0	1 (0.4)
尿中血陽性	0	0	0	1 (1.3)	1 (0.4)
心電図異常	0	0	1 (1.2)	0	1 (0.4)
γ-グルタミルトランスフェラーゼ増加	0	1 (1.6)	5 (6.0)	1 (1.3)	8 (2.9)
高比重リポ蛋白増加	0	0	3 (3.6)	0	3 (1.1)
リパーゼ増加	1 (40.8)	0	1 (1.2)	0	2 (0.7)
リンパ球数減少	0	1 (1.6)	1 (1.2)	4 (5.3)	7 (2.6)
リンパ球数増加	1 (40.8)	1 (1.6)	0	1 (1.3)	2 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
臨床検査 (Cont.)			
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 (1.5)
好中球数増加	0	0	1 (1.5)
前立腺特異性抗原増加	0	0	0
尿中蛋白陽性	1 (6.0)	0	0
尿中白血球エステラーゼ陽性	0	0	0
体重減少	1 (6.0)	0	0
体重増加	0	0	0
白血球数減少	0	0	3 (4.5)

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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
臨床検査 (Cont.)					
リンパ球百分率減少	0	0	1 (1.2)	0	1 (0.4)
リンパ球百分率増加	0	0	2 (2.4)	0	2 (0.7)
好中球数減少	2 (81.6)	4 (6.5)	5 (6.0)	13 (17.3)	23 (8.5)
好中球数増加	0	0	0	1 (1.3)	2 (0.7)
前立腺特異性抗原増加	1 (40.8)	0	0	0	1 (0.4)
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 (2.4)	0	2 (0.7)
体重減少	0	0	0	0	0
体重増加	0	0	1 (1.2)	1 (1.3)	2 (0.7)
白血球数減少	1 (40.8)	3 (4.9)	4 (4.8)	5 (6.7)	15 (5.5)

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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
臨床検査 (Cont.)			
白血球数増加	0	0	1 (1.5)
代謝および栄養障害	3 (17.9)	1 (12.9)	4 (6.1)
食欲減退	1 (6.0)	0	0
糖尿病	0	0	0
脂質異常症	0	0	1 (1.5)
高コレステロール血症	0	1 (12.9)	2 (3.0)
高リパーゼ血症	0	0	0
高脂血症	0	0	1 (1.5)
高尿酸血症	1 (6.0)	0	0
低アルブミン血症	1 (6.0)	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
臨床検査 (Cont.)					
白血球数増加	1 (40.8)	0	0	0	2 (0.7)
代謝および栄養障害	0	6 (9.8)	5 (6.0)	5 (6.7)	19 (7.0)
食欲減退	0	0	0	0	0
糖尿病	0	0	0	1 (1.3)	1 (0.4)
脂質異常症	0	1 (1.6)	3 (3.6)	0	5 (1.8)
高コレステロール血症	0	1 (1.6)	1 (1.2)	2 (2.7)	7 (2.6)
高リパーゼ血症	0	1 (1.6)	0	0	0
高脂血症	0	0	1 (1.2)	0	2 (0.7)
高尿酸血症	0	1 (1.6)	0	1 (1.3)	2 (0.7)
低アルブミン血症	0	0	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
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	4 (23.9)	0	11 (16.6)
関節痛	1 (6.0)	0	2 (3.0)
関節炎	0	0	1 (1.5)
関節障害	2 (11.9)	0	0
背部痛	0	0	1 (1.5)
頚部脊柱管狭窄症	0	0	0
側腹部痛	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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
低ナトリウム血症	0	1 (1.6)	0	0	0
低蛋白血症	0	1 (1.6)	0	0	1 (0.4)
栄養障害	0	0	0	1 (1.3)	1 (0.4)
筋骨格系および結合組織障害	3 (122.4)	30 (48.9)	21 (25.1)	14 (18.6)	65 (23.9)
関節痛	0	4 (6.5)	6 (7.2)	2 (2.7)	10 (3.7)
関節炎	1 (40.8)	1 (1.6)	1 (1.2)	0	4 (1.5)
関節障害	1 (40.8)	2 (3.3)	0	0	2 (0.7)
背部痛	0	4 (6.5)	4 (4.8)	4 (5.3)	10 (3.7)
頚部脊柱管狭窄症	0	1 (1.6)	0	0	1 (0.4)
側腹部痛	0	2 (3.3)	0	0	2 (0.7)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
椎間板突出	0	0	3 (4.5)
腰部脊柱管狭窄症	0	0	0
筋痙縮	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	0
筋肉痛	0	0	2 (3.0)
変形性関節症	1 (6.0)	0	0
骨端症	0	0	0
骨壊死	0	0	1 (1.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
椎間板突出	0	1 (1.6)	0	2 (2.7)	6 (2.2)
腰部脊柱管狭窄症	0	1 (1.6)	0	1 (1.3)	2 (0.7)
筋痙縮	0	0	1 (1.2)	1 (1.3)	2 (0.7)
筋骨格系胸痛	0	4 (6.5)	0	0	2 (0.7)
筋骨格痛	0	0	1 (1.2)	1 (1.3)	2 (0.7)
筋骨格硬直	0	0	1 (1.2)	0	1 (0.4)
筋肉痛	0	0	2 (2.4)	1 (1.3)	5 (1.8)
変形性関節症	0	3 (4.9)	1 (1.2)	0	3 (1.1)
骨端症	0	1 (1.6)	0	0	1 (0.4)
骨壊死	0	0	2 (2.4)	0	3 (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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
骨粗鬆症	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 (1.5)
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）	1 (6.0)	0	2 (3.0)
結腸腺癌	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
骨粗鬆症	0	0	1 (1.2)	0	1 (0.4)
四肢痛	0	1 (1.6)	0	1 (1.3)	1 (0.4)
関節周囲炎	0	2 (3.3)	0	1 (1.3)	3 (1.1)
横紋筋融解症	0	0	0	0	1 (0.4)
肩回旋筋腱板症候群	0	1 (1.6)	0	0	0
変形性脊椎症	0	1 (1.6)	0	0	1 (0.4)
腱鞘炎	0	1 (1.6)	0	0	0
弾発指	1 (40.8)	0	1 (1.2)	0	2 (0.7)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)	0	2 (3.3)	2 (2.4)	4 (5.3)	9 (3.3)
結腸腺癌	0	0	0	1 (1.3)	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
大腸腺腫	0	0	1 (1.5)
線維腫	0	0	0
脂漏性角化症	1 (6.0)	0	0
皮膚乳頭腫	0	0	1 (1.5)
子宮平滑筋腫	0	0	0
神経系障害	3 (17.9)	0	7 (10.6)
手根管症候群	2 (11.9)	0	0
浮動性めまい	0	0	1 (1.5)
異常感覚	0	0	1 (1.5)
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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
大腸腺腫	0	1 (1.6)	1 (1.2)	0	2 (0.7)
線維腫	0	0	0	1 (1.3)	1 (0.4)
脂漏性角化症	0	0	0	0	0
皮膚乳頭腫	0	1 (1.6)	0	2 (2.7)	4 (1.5)
子宮平滑筋腫	0	0	1 (1.2)	0	1 (0.4)
神経系障害	5 (204.1)	7 (11.4)	6 (7.2)	10 (13.3)	32 (11.8)
手根管症候群	0	0	0	0	0
浮動性めまい	0	0	1 (1.2)	2 (2.7)	4 (1.5)
異常感覚	0	0	0	0	1 (0.4)
てんかん	0	1 (1.6)	0	0	0

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

Program Source Code: [redacted]

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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
神経系障害 (Cont.)			
頭痛	0	0	3 (4.5)
感覚鈍麻	0	0	1 (1.5)
頭蓋内動脈瘤	0	0	1 (1.5)
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 (6.0)	0	0
くも膜下出血	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
神経系障害 (Cont.)					
頭痛	3 (122.4)	1 (1.6)	3 (3.6)	3 (4.0)	13 (4.8)
感覚鈍麻	0	0	1 (1.2)	1 (1.3)	3 (1.1)
頭蓋内動脈瘤	0	0	0	0	1 (0.4)
片頭痛	0	2 (3.3)	0	0	1 (0.4)
神経痛	0	1 (1.6)	0	0	1 (0.4)
末梢性ニューロパチー	1 (40.8)	1 (1.6)	0	0	1 (0.4)
後頭神経痛	0	0	1 (1.2)	0	1 (0.4)
ヘルペス後神経痛	1 (40.8)	0	0	1 (1.3)	2 (0.7)
失神寸前の状態	0	1 (1.6)	0	0	1 (0.4)
くも膜下出血	0	0	0	1 (1.3)	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
神経系障害 (Cont.)			
失神	0	0	0
味覚障害	0	0	0
精神障害	2 (11.9)	0	3 (4.5)
不安	0	0	0
不安障害	0	0	0
抑うつ気分	0	0	0
不眠症	2 (11.9)	0	3 (4.5)
腎および尿路障害	0	2 (25.7)	6 (9.1)
急性腎障害	0	0	0
慢性腎臓病	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
神経系障害 (Cont.)					
失神	0	0	0	1 (1.3)	1 (0.4)
味覚障害	0	0	0	1 (1.3)	1 (0.4)
精神障害	0	5 (8.1)	1 (1.2)	4 (5.3)	10 (3.7)
不安	0	0	0	1 (1.3)	1 (0.4)
不安障害	0	0	1 (1.2)	0	1 (0.4)
抑うつ気分	0	0	0	1 (1.3)	1 (0.4)
不眠症	0	5 (8.1)	0	2 (2.7)	7 (2.6)
腎および尿路障害	1 (40.8)	0	1 (1.2)	3 (4.0)	13 (4.8)
急性腎障害	0	0	0	1 (1.3)	1 (0.4)
慢性腎臓病	1 (40.8)	0	0	0	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
排尿困難	0	0	1 (1.5)
腎結石症	0	2 (25.7)	0
蛋白尿	0	0	2 (3.0)
腎機能障害	0	0	1 (1.5)
尿管結石症	0	0	2 (3.0)
生殖系および乳房障害	0	0	1 (1.5)
無月経	0	0	0
子宮頚管ポリープ	0	0	1 (1.5)
月経困難症	0	0	0
閉経期症状	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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
排尿困難	0	0	0	0	1 (0.4)
腎結石症	0	0	0	0	2 (0.7)
蛋白尿	0	0	0	1 (1.3)	3 (1.1)
腎機能障害	0	0	1 (1.2)	0	2 (0.7)
尿管結石症	0	0	0	1 (1.3)	3 (1.1)
生殖系および乳房障害	0	3 (4.9)	2 (2.4)	0	5 (1.8)
無月経	0	1 (1.6)	0	0	1 (0.4)
子宮頚管ポリープ	0	0	0	0	1 (0.4)
月経困難症	0	0	1 (1.2)	0	1 (0.4)
閉経期症状	0	1 (1.6)	0	0	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
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 (17.9)	0	1 (1.5)
喘息	0	0	0
咳嗽	0	0	0
発声障害	0	0	0
しゃっくり	0	0	0
口腔咽頭不快感	0	0	0
口腔咽頭痛	0	0	0
咽頭病変	0	0	1 (1.5)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
不規則月経	0	1 (1.6)	0	0	0
前立腺炎	0	0	1 (1.2)	0	1 (0.4)
呼吸器、胸郭および縦隔障害	3 (122.4)	8 (13.0)	7 (8.4)	6 (8.0)	22 (8.1)
喘息	0	1 (1.6)	0	0	1 (0.4)
咳嗽	1 (40.8)	0	3 (3.6)	0	4 (1.5)
発声障害	0	1 (1.6)	0	0	1 (0.4)
しゃっくり	0	1 (1.6)	0	1 (1.3)	1 (0.4)
口腔咽頭不快感	0	1 (1.6)	0	0	1 (0.4)
口腔咽頭痛	2 (81.6)	0	1 (1.2)	4 (5.3)	7 (2.6)
咽頭病変	0	0	0	0	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
気胸	1 (6.0)	0	0
アレルギー性鼻炎	0	0	0
上気道の炎症	2 (11.9)	0	0
皮膚および皮下組織障害	9 (53.7)	1 (12.9)	12 (18.2)
ざ瘡	0	0	1 (1.5)
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 (6.0)	0	0
ざ瘡様皮膚炎	0	0	2 (3.0)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
気胸	0	0	0	0	0
アレルギー性鼻炎	0	0	2 (2.4)	0	2 (0.7)
上気道の炎症	0	4 (6.5)	1 (1.2)	1 (1.3)	4 (1.5)
皮膚および皮下組織障害	3 (122.4)	27 (44.0)	23 (27.5)	34 (45.2)	85 (31.3)
ざ瘡	0	7 (11.4)	7 (8.4)	11 (14.6)	23 (8.5)
脱毛症	0	0	0	2 (2.7)	2 (0.7)
皮脂欠乏症	0	0	0	1 (1.3)	1 (0.4)
皮膚嚢腫	0	0	1 (1.2)	0	1 (0.4)
皮膚炎	0	0	1 (1.2)	0	1 (0.4)
ざ瘡様皮膚炎	0	0	1 (1.2)	1 (1.3)	4 (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 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
皮膚および皮下組織障害 (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 (1.5)
皮膚乾燥	1 (6.0)	0	1 (1.5)
異汗性湿疹	1 (6.0)	0	0
湿疹	3 (17.9)	0	2 (3.0)
皮脂欠乏性湿疹	0	0	0
紅斑	0	0	1 (1.5)
多形紅斑	0	0	0
瘢痕そう痒感	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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
アトピー性皮膚炎	0	0	1 (1.2)	0	1 (0.4)
接触皮膚炎	0	2 (3.3)	0	0	1 (0.4)
薬疹	0	0	0	0	1 (0.4)
皮膚乾燥	0	0	0	0	1 (0.4)
異汗性湿疹	0	0	0	0	0
湿疹	1 (40.8)	3 (4.9)	5 (6.0)	4 (5.3)	14 (5.2)
皮脂欠乏性湿疹	0	1 (1.6)	0	2 (2.7)	2 (0.7)
紅斑	0	0	0	0	1 (0.4)
多形紅斑	1 (40.8)	0	0	0	1 (0.4)
瘢痕そう痒感	0	0	0	1 (1.3)	1 (0.4)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.1 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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
汗疹	0	0	0
皮膚疼痛	0	0	0
脂肪織炎	0	0	0
丘疹	0	0	1 (1.5)
光線過敏性反応	0	0	0
そう痒症	2 (11.9)	0	1 (1.5)
壊疽性膿皮症	1 (6.0)	0	0
発疹	0	1 (12.9)	1 (1.5)
斑状丘疹状皮疹	0	0	0
脂漏性皮膚炎	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 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
汗疹	0	1 (1.6)	0	0	1 (0.4)
皮膚疼痛	1 (40.8)	0	0	1 (1.3)	2 (0.7)
脂肪織炎	0	0	1 (1.2)	0	1 (0.4)
丘疹	0	0	0	0	1 (0.4)
光線過敏性反応	0	1 (1.6)	0	1 (1.3)	1 (0.4)
そう痒症	0	0	2 (2.4)	0	3 (1.1)
壊疽性膿皮症	0	1 (1.6)	0	0	0
発疹	0	4 (6.5)	2 (2.4)	1 (1.3)	6 (2.2)
斑状丘疹状皮疹	0	0	0	4 (5.3)	4 (1.5)
脂漏性皮膚炎	0	6 (9.8)	2 (2.4)	1 (1.3)	5 (1.8)

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=16.7) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=3) (PYs=7.8) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=29) (PYs=66.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
蕁麻疹	0	0	1 (1.5)
血管障害	2 (11.9)	1 (12.9)	1 (1.5)
大動脈瘤	0	0	0
本態性高血圧症	0	0	0
ほてり	0	0	0
高血圧	0	1 (12.9)	1 (1.5)
低血圧	1 (6.0)	0	0
末梢冷感	1 (6.0)	0	0
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 4.3.1 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=61.4) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=49) (PYs=83.5) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=54) (PYs=75.2) Events (E/100 PYs)	 Any UPA (N=192) (PYs=271.7) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
蕁麻疹	0	1 (1.6)	0	4 (5.3)	6 (2.2)
血管障害	0	4 (6.5)	3 (3.6)	8 (10.6)	16 (5.9)
大動脈瘤	0	0	1 (1.2)	0	1 (0.4)
本態性高血圧症	0	0	0	1 (1.3)	1 (0.4)
ほてり	0	0	0	1 (1.3)	1 (0.4)
高血圧	0	3 (4.9)	2 (2.4)	5 (6.7)	12 (4.4)
低血圧	0	0	0	0	0
末梢冷感	0	0	0	0	0
静脈炎	0	0	0	1 (1.3)	1 (0.4)
静脈血栓症	0	1 (1.6)	0	0	0

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

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表 2.7.4.7-30.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 13

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
Any adverse event	65 (17.2) [16.7]	189 (26.3) [26.4]
血液およびリンパ系障害	6 (1.6) [1.5]	26 (3.6) [3.6]
貧血	3 (0.8) [0.7]	3 (0.4) [0.4]
好酸球増加症	1 (0.3) [0.2]	0
白血球増加症	0	1 (0.1) [0.1]
白血球減少症	0	5 (0.7) [0.7]
リンパ節痛	0	1 (0.1) [0.1]
リンパ球減少症	1 (0.3) [0.3]	6 (0.8) [0.8]
好中球減少症	1 (0.3) [0.3]	13 (1.8) [1.8]
心臓障害	1 (0.3) [0.3]	0
頻脈	1 (0.3) [0.3]	0
耳および迷路障害	1 (0.3) [0.3]	2 (0.3) [0.3]
耳痛	1 (0.3) [0.3]	0
聴力低下	0	1 (0.1) [0.1]
突発性難聴	0	1 (0.1) [0.1]
耳鳴	0	2 (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 and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
眼障害	1 (0.3) [0.3]	5 (0.7) [0.7]
眼瞼炎	0	1 (0.1) [0.1]
ドライアイ	0	1 (0.1) [0.1]
角膜炎	0	1 (0.1) [0.1]
眼部不快感	1 (0.3) [0.3]	0
霧視	0	2 (0.3) [0.3]
胃腸障害	20 (5.3) [5.2]	28 (3.9) [3.9]
腹部膨満	0	2 (0.3) [0.3]
腹痛	1 (0.3) [0.2]	3 (0.4) [0.4]
下腹部痛	0	1 (0.1) [0.1]
上腹部痛	2 (0.5) [0.5]	2 (0.3) [0.3]
肛門潰瘍	0	1 (0.1) [0.2]
肛門直腸不快感	0	1 (0.1) [0.2]
アフタ性潰瘍	0	3 (0.4) [0.4]
大腸炎	1 (0.3) [0.2]	0
潰瘍性大腸炎	12 (3.2) [3.3]	3 (0.4) [0.5]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
胃腸障害 (Cont.)		
便秘	0	5 (0.7) [0.7]
便意切迫	1 (0.3) [0.3]	0
下痢	0	2 (0.3) [0.3]
血性下痢	0	1 (0.1) [0.1]
消化不良	1 (0.3) [0.3]	1 (0.1) [0.1]
おくび	0	1 (0.1) [0.1]
鼓腸	2 (0.5) [0.5]	1 (0.1) [0.1]
胃食道逆流性疾患	0	2 (0.3) [0.3]
歯肉痛	0	1 (0.1) [0.1]
痔核	0	1 (0.1) [0.1]
悪心	1 (0.3) [0.3]	3 (0.4) [0.4]
口腔内痛	0	1 (0.1) [0.1]
肛門周囲痛	0	1 (0.1) [0.2]
直腸分泌物	1 (0.3) [0.2]	0
直腸しぶり	0	1 (0.1) [0.2]
口内炎	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
一般・全身障害および投与部位の状態	2 (0.5) [0.5]	19 (2.6) [2.7]
無力症	1 (0.3) [0.3]	3 (0.4) [0.4]
胸部不快感	0	2 (0.3) [0.3]
胸痛	1 (0.3) [0.3]	0
疲労	1 (0.3) [0.3]	5 (0.7) [0.7]
異常感	0	1 (0.1) [0.2]
過形成	0	1 (0.1) [0.1]
倦怠感	0	3 (0.4) [0.4]
腫瘤	0	1 (0.1) [0.2]
末梢性浮腫	0	1 (0.1) [0.1]
発熱	0	5 (0.7) [0.7]
感染症および寄生虫症	11 (2.9) [2.7]	49 (6.8) [6.8]
膿瘍	1 (0.3) [0.2]	1 (0.1) [0.1]
虫垂炎	0	1 (0.1) [0.1]
無症候性細菌尿	0	1 (0.1) [0.1]
蜂巣炎	1 (0.3) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
感染症および寄生虫症 (Cont.)		
条虫感染	0	1 (0.1) [0.1]
クロストリジウム・ディフィシレ感染	1 (0.3) [0.2]	0
膀胱炎	0	1 (0.1) [0.1]
爪の皮膚糸状菌症	0	1 (0.1) [0.1]
毛包炎	0	7 (1.0) [1.0]
真菌感染	1 (0.3) [0.3]	0
陰部ヘルペス	0	1 (0.1) [0.1]
歯肉炎	1 (0.3) [0.3]	0
単純ヘルペス	0	2 (0.3) [0.3]
帯状疱疹	0	2 (0.3) [0.3]
播種性帯状疱疹	0	1 (0.1) [0.2]
インフルエンザ	0	1 (0.1) [0.1]
上咽頭炎	2 (0.5) [0.5]	4 (0.6) [0.5]
口腔ヘルペス	0	5 (0.7) [0.7]
真菌性外耳炎	0	1 (0.1) [0.1]
爪囲炎	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
感染症および寄生虫症 (Cont.)		
咽頭炎	1 (0.3) [0.2]	1 (0.1) [0.1]
肺炎	0	3 (0.4) [0.4]
膿疱	0	1 (0.1) [0.1]
膿疱性皮疹	0	1 (0.1) [0.1]
RSウイルス感染	0	1 (0.1) [0.2]
気道感染	0	1 (0.1) [0.1]
敗血症	0	1 (0.1) [0.2]
副鼻腔炎	0	2 (0.3) [0.3]
足部白癬	0	1 (0.1) [0.1]
癜風	0	1 (0.1) [0.1]
上気道感染	2 (0.5) [0.6]	7 (1.0) [1.0]
尿路感染	1 (0.3) [0.3]	0
ウイルス感染	0	1 (0.1) [0.1]
ウイルス性上気道感染	0	2 (0.3) [0.3]
外陰部腟カンジダ症	0	2 (0.3) [0.3]
創傷感染	1 (0.3) [0.2]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
傷害、中毒および処置合併症	3 (0.8) [0.6]	2 (0.3) [0.3]
偶発的過量投与	3 (0.8) [0.6]	1 (0.1) [0.2]
挫傷	0	1 (0.1) [0.1]
創傷	0	1 (0.1) [0.1]
臨床検査	8 (2.1) [2.1]	62 (8.6) [8.6]
アラニンアミノトランスフェラーゼ増加	2 (0.5) [0.5]	5 (0.7) [0.7]
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.1) [0.1]
アミラーゼ増加	0	1 (0.1) [0.1]
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.5) [0.5]	6 (0.8) [0.8]
血中アルカリホスファターゼ増加	1 (0.3) [0.2]	0
血中ビリルビン増加	0	2 (0.3) [0.3]
血中クロール減少	0	1 (0.1) [0.1]
血中コレステロール増加	0	1 (0.1) [0.1]
血中クレアチンホスホキナーゼ増加	1 (0.3) [0.3]	26 (3.6) [3.6]
血中クレアチニン増加	1 (0.3) [0.3]	2 (0.3) [0.3]
血中乳酸脱水素酵素増加	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
臨床検査 (Cont.)		
尿中結晶陽性	1 (0.3) [0.3]	0
γ-グルタミルトランスフェラーゼ増加	1 (0.3) [0.2]	1 (0.1) [0.1]
肝酵素上昇	0	1 (0.1) [0.1]
高比重リポ蛋白増加	0	1 (0.1) [0.1]
眼圧上昇	0	1 (0.1) [0.1]
肝機能検査値上昇	1 (0.3) [0.3]	0
低比重リポ蛋白増加	0	1 (0.1) [0.1]
リンパ球数減少	0	4 (0.6) [0.5]
リンパ球数増加	0	2 (0.3) [0.3]
リンパ球百分率減少	0	4 (0.6) [0.6]
好中球数減少	0	20 (2.8) [2.8]
好中球数増加	0	1 (0.1) [0.1]
好中球百分率増加	0	1 (0.1) [0.1]
血小板数減少	0	1 (0.1) [0.1]
尿中蛋白陽性	1 (0.3) [0.3]	0
トランスアミナーゼ上昇	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
臨床検査 (Cont.)		
白血球数減少	1 (0.3) [0.3]	12 (1.7) [1.6]
代謝および栄養障害	2 (0.5) [0.5]	4 (0.6) [0.5]
食欲減退	0	1 (0.1) [0.1]
高血糖	1 (0.3) [0.3]	0
高脂血症	0	1 (0.1) [0.1]
低ナトリウム血症	0	1 (0.1) [0.1]
低リン酸血症	1 (0.3) [0.2]	0
食欲亢進	0	1 (0.1) [0.1]
筋骨格系および結合組織障害	7 (1.9) [1.8]	9 (1.3) [1.3]
関節痛	1 (0.3) [0.3]	3 (0.4) [0.4]
筋痙縮	4 (1.1) [1.0]	1 (0.1) [0.1]
筋緊張	0	1 (0.1) [0.1]
筋骨格系胸痛	0	1 (0.1) [0.1]
筋骨格硬直	0	1 (0.1) [0.2]
筋肉痛	1 (0.3) [0.3]	1 (0.1) [0.1]
四肢痛	1 (0.3) [0.3]	1 (0.1) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)		
顎関節症候群	0	1 (0.1) [0.2]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (0.1) [0.1]
皮膚乳頭腫	0	1 (0.1) [0.1]
神経系障害	9 (2.4) [2.2]	19 (2.6) [2.7]
灼熱感	0	1 (0.1) [0.1]
脳虚血	0	1 (0.1) [0.1]
浮動性めまい	0	4 (0.6) [0.5]
頭痛	8 (2.1) [1.9]	11 (1.5) [1.6]
感覚鈍麻	0	1 (0.1) [0.1]
片頭痛	1 (0.3) [0.3]	1 (0.1) [0.1]
末梢性ニューロパチー	0	1 (0.1) [0.1]
錯感覚	0	1 (0.1) [0.1]
ヘルペス後神経痛	0	1 (0.1) [0.1]
精神障害	2 (0.5) [0.5]	2 (0.3) [0.3]
不眠症	1 (0.3) [0.2]	1 (0.1) [0.1]
リビドー減退	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
精神障害 (Cont.)		
睡眠障害	1 (0.3) [0.3]	0
腎および尿路障害	2 (0.5) [0.6]	5 (0.7) [0.7]
慢性腎臓病	0	2 (0.3) [0.3]
排尿困難	0	2 (0.3) [0.3]
頻尿	0	1 (0.1) [0.2]
蛋白尿	2 (0.5) [0.6]	0
生殖系および乳房障害	0	4 (0.6) [0.5]
不規則月経	0	2 (0.3) [0.3]
精液変色	0	2 (0.3) [0.3]
呼吸器、胸郭および縦隔障害	2 (0.5) [0.5]	5 (0.7) [0.7]
咳嗽	0	1 (0.1) [0.1]
横隔膜痛	1 (0.3) [0.3]	0
呼吸困難	0	1 (0.1) [0.1]
鼻閉	1 (0.3) [0.3]	0
口腔咽頭痛	0	1 (0.1) [0.1]
肺塞栓症	1 (0.3) [0.3]	1 (0.1) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)		
気道うっ血	0	1 (0.1) [0.1]
副鼻腔障害	0	1 (0.1) [0.1]
皮膚および皮下組織障害	6 (1.6) [1.6]	48 (6.7) [6.6]
ざ瘡	2 (0.5) [0.5]	23 (3.2) [3.2]
脱毛症	0	3 (0.4) [0.4]
ざ瘡様皮膚炎	0	1 (0.1) [0.1]
湿疹	0	1 (0.1) [0.1]
過角化	0	1 (0.1) [0.1]
皮膚疼痛	0	2 (0.3) [0.3]
丘疹	0	3 (0.4) [0.4]
光線過敏性反応	0	1 (0.1) [0.1]
そう痒症	4 (1.1) [1.0]	1 (0.1) [0.1]
壊疽性膿皮症	0	1 (0.1) [0.1]
発疹	2 (0.5) [0.5]	8 (1.1) [1.1]
紅斑性皮疹	1 (0.3) [0.3]	0
毛孔性皮疹	0	1 (0.1) [0.2]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.7

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
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)		
斑状皮疹	0	1 (0.1) [0.1]
斑状丘疹状皮疹	0	1 (0.1) [0.1]
丘疹性皮疹	0	4 (0.6) [0.5]
脂漏性皮膚炎	0	1 (0.1) [0.1]
皮膚剥脱	0	1 (0.1) [0.1]
皮膚病変	0	1 (0.1) [0.1]
皮膚線条	0	1 (0.1) [0.1]
血管障害	2 (0.5) [0.5]	2 (0.3) [0.3]
深部静脈血栓症	0	1 (0.1) [0.2]
高血圧	1 (0.3) [0.3]	1 (0.1) [0.1]
骨盤静脈血栓症	1 (0.3) [0.3]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表 2.7.4.7-31.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - 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	83 (33.9) [33.4]	82 (32.8) [32.9]	92 (36.7) [36.7]	108 (37.9) [38.0]	112 (38.5) [38.4]
血液およびリンパ系障害	14 (5.7) [5.6]	6 (2.4) [2.5]	8 (3.2) [3.2]	12 (4.2) [4.2]	11 (3.8) [3.7]
貧血	6 (2.4) [2.4]	1 (0.4) [0.4]	3 (1.2) [1.2]	2 (0.7) [0.7]	4 (1.4) [1.4]
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]	5 (1.8) [1.7]	3 (1.0) [1.0]
リンパ球増加症	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%]
血液およびリンパ系障害 (Cont.)					
リンパ球減少症	2 (0.8) [0.8]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]
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]	2 (0.8) [0.8]	5 (2.0) [2.0]	2 (0.7) [0.7]	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
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]

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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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 (Cont.)					
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
胃腸障害	30 (12.2) [12.0]	9 (3.6) [3.6]	13 (5.2) [5.2]	16 (5.6) [5.6]	15 (5.2) [5.2]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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]
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]	5 (2.0) [2.0]	3 (1.2) [1.2]	10 (3.5) [3.5]	3 (1.0) [1.0]
結腸異形成	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
消化不良	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.3) [0.3]
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	3 (1.0) [1.0]
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]	0
嘔吐	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%]
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
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]

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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.8) [0.8]	2 (0.7) [0.7]	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	1 (0.4) [0.4]	0	0	0	0
高トランスアミナーゼ血症	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
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	28 (11.4) [11.2]	32 (12.8) [12.8]	35 (13.9) [14.0]	46 (16.1) [16.2]	47 (16.2) [16.1]
腹壁膿瘍	0	0	0	1 (0.4) [0.3]	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.10

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.)					
細菌性関節炎	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	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]
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]
結膜炎	0	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
COVID-19	2 (0.8) [0.9]	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.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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
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
帯状疱疹	0	8 (3.2) [3.1]	9 (3.6) [3.6]	14 (4.9) [4.9]	14 (4.8) [4.8]

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

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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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	1 (0.4) [0.4]	0	1 (0.3) [0.3]
歯髄炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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	0	0
鼻炎	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.)					
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]
ブドウ球菌感染	1 (0.4) [0.4]	0	0	0	0
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
扁桃炎	0	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.10

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.)					
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]	3 (1.2) [1.2]	3 (1.1) [1.0]	3 (1.0) [1.0]
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
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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	0	0	0
肋骨骨折	1 (0.4) [0.4]	0	0	0	0
臨床検査	12 (4.9) [4.9]	28 (11.2) [11.2]	37 (14.7) [14.7]	35 (12.3) [12.3]	45 (15.5) [15.4]
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]	6 (2.1) [2.1]	6 (2.1) [2.1]
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]	7 (2.5) [2.5]	5 (1.7) [1.7]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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]
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]	9 (3.6) [3.6]	12 (4.8) [4.8]	14 (4.9) [4.9]	18 (6.2) [6.1]
血中クレアチニン増加	0	0	3 (1.2) [1.2]	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 3.3.10

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.)					
血中カリウム減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
血圧上昇	0	0	0	1 (0.4) [0.3]	0
血中トリグリセリド異常	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
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	1 (0.3) [0.3]
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]	1 (0.3) [0.3]
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]	1 (0.4) [0.4]	1 (0.3) [0.3]
B型肝炎DNA測定陽性	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
高比重リポ蛋白増加	0	2 (0.8) [0.8]	1 (0.4) [0.4]	3 (1.1) [1.0]	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%]
臨床検査 (Cont.)					
肝機能検査値上昇	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
低比重リポ蛋白減少	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
低比重リポ蛋白増加	0	1 (0.4) [0.4]	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]	4 (1.4) [1.4]
リンパ球数増加	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.8) [0.8]	1 (0.4) [0.3]	2 (0.7) [0.7]
リンパ球百分率減少	0	1 (0.4) [0.4]	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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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]	8 (2.7) [2.8]
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]
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]	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%]
臨床検査 (Cont.)					
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
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]	5 (1.7) [1.7]
白血球数増加	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%]
臨床検査 (Cont.)					
尿中白血球陽性	0	0	0	0	1 (0.3) [0.4]
代謝および栄養障害	1 (0.4) [0.4]	6 (2.4) [2.5]	5 (2.0) [2.0]	6 (2.1) [2.1]	5 (1.7) [1.7]
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]	2 (0.7) [0.7]
高血糖	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	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]	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%]
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]	2 (0.8) [0.8]	5 (2.0) [2.0]	3 (1.1) [1.1]	6 (2.1) [2.1]
関節痛	3 (1.2) [1.3]	1 (0.4) [0.4]	3 (1.2) [1.2]	1 (0.4) [0.3]	3 (1.0) [1.1]
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	0	0
骨痛	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
筋拘縮	0	0	0	1 (0.4) [0.4]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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	1 (0.3) [0.4]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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%]
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.)					
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
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]	5 (1.7) [1.7]
灼熱感	0	0	0	1 (0.4) [0.3]	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]	2 (0.7) [0.7]
感覚鈍麻	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%]
神経系障害 (Cont.)					
片頭痛	0	0	0	1 (0.4) [0.3]	0
ヘルペス後神経痛	0	0	0	0	1 (0.3) [0.3]
視野欠損	0	0	0	0	1 (0.3) [0.3]
精神障害	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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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	1 (0.4) [0.4]	2 (0.8) [0.8]	2 (0.8) [0.8]	2 (0.7) [0.7]	3 (1.0) [1.0]
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
水腎症	1 (0.4) [0.4]	0	0	0	0
蛋白尿	1 (0.4) [0.4]	0	0	0	1 (0.3) [0.3]
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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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	2 (0.8) [0.9]	1 (0.4) [0.4]	1 (0.4) [0.4]	2 (0.7) [0.7]	1 (0.3) [0.3]
バルトリン嚢腫	1 (0.4) [0.4]	0	0	0	0
勃起不全	0	0	0	1 (0.4) [0.3]	0
精液変色	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
膣分泌物	0	1 (0.4) [0.4]	0	1 (0.4) [0.4]	0
外陰膣そう痒症	1 (0.4) [0.4]	0	0	0	0
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]	4 (1.4) [1.4]	8 (2.7) [2.7]
気管支拡張症	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 (Cont.)					
咳嗽	0	0	1 (0.4) [0.4]	0	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
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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]	0
副鼻腔うっ血	0	0	0	1 (0.4) [0.3]	0
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]	24 (8.4) [8.4]	22 (7.6) [7.5]
ざ瘡	2 (0.8) [0.8]	3 (1.2) [1.2]	2 (0.8) [0.8]	4 (1.4) [1.4]	3 (1.0) [1.0]

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

Program Source Code: [redacted]

TABLE 2.4 3.3.10

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.)					
嚢胞性ざ瘡	0	0	0	1 (0.4) [0.3]	0
脱毛症	0	1 (0.4) [0.4]	1 (0.4) [0.4]	1 (0.4) [0.3]	1 (0.3) [0.3]
皮膚炎	1 (0.4) [0.4]	0	0	0	0
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
皮膚乾燥	2 (0.8) [0.8]	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.)					
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
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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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]
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]	11 (3.8) [3.8]
紅斑性皮疹	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]	0

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

Program Source Code: [redacted]

TABLE 2.4 3.3.10

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.)					
毛孔性皮疹	0	0	0	1 (0.4) [0.3]	0
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]	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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]	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
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 2.7.4.7-32.

[redacted]20[redacted] 10:46 [redacted]
UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	150 (124.5)	96 (88.7)	432 (73.7)
血液およびリンパ系障害	10 (8.3)	3 (2.8)	23 (3.9)
貧血	4 (3.3)	2 (1.8)	4 (0.7)
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
鉄欠乏性貧血	0	0	0
白血球増加症	0	0	2 (0.3)
白血球減少症	0	0	3 (0.5)
リンパ節症	0	1 (0.9)	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	88 (365.5)	456 (127.1)	507 (108.8)	531 (119.8)	1876 (103.0)
血液およびリンパ系障害	5 (20.8)	42 (11.7)	44 (9.4)	31 (7.0)	125 (6.9)
貧血	2 (8.3)	12 (3.3)	4 (0.9)	6 (1.4)	21 (1.2)
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 (0.3)	0	0	1 (<0.1)
好酸球増加症	0	1 (0.3)	0	0	0
鉄欠乏性貧血	0	0	2 (0.4)	1 (0.2)	3 (0.2)
白血球増加症	0	0	0	1 (0.2)	3 (0.2)
白血球減少症	0	7 (2.0)	18 (3.9)	5 (1.1)	29 (1.6)
リンパ節症	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)			
リンパ球増加症	0	0	0
リンパ球減少症	1 (0.8)	0	7 (1.2)
小球性貧血	0	0	0
好中球減少症	3 (2.5)	0	6 (1.0)
汎血球減少症	0	0	0
網状赤血球増加症	0	0	1 (0.2)
血小板減少症	1 (0.8)	0	0
心臓障害	2 (1.7)	0	2 (0.3)
第一度房室ブロック	0	0	0
動悸	1 (0.8)	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)					
リンパ球増加症	0	1 (0.3)	0	0	0
リンパ球減少症	2 (8.3)	8 (2.2)	6 (1.3)	3 (0.7)	23 (1.3)
小球性貧血	0	0	1 (0.2)	0	1 (<0.1)
好中球減少症	1 (4.2)	11 (3.1)	11 (2.4)	14 (3.2)	40 (2.2)
汎血球減少症	0	0	2 (0.4)	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 (0.3)	0	0	0
心臓障害	0	0	0	2 (0.5)	4 (0.2)
第一度房室ブロック	0	0	0	1 (0.2)	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
心臓障害 (Cont.)			
洞性徐脈	0	0	0
頻脈	1 (0.8)	0	1 (0.2)
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
聴力低下	0	0	0
内耳障害	0	0	1 (0.2)
メニエール病	0	0	0
突発性難聴	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
心臓障害 (Cont.)					
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 (0.8)	3 (0.6)	2 (0.5)	11 (0.6)
耳痛	0	1 (0.3)	0	0	1 (<0.1)
耳部腫脹	0	1 (0.3)	0	0	0
外耳の炎症	0	1 (0.3)	0	0	1 (<0.1)
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
耳および迷路障害 (Cont.)			
耳鳴	0	0	1 (0.2)
回転性めまい	0	0	0
内分泌障害	0	0	1 (0.2)
クッシング様症状	0	0	1 (0.2)
眼障害	1 (0.8)	2 (1.8)	1 (0.2)
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 (0.9)	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
耳および迷路障害 (Cont.)					
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)
眼障害	2 (8.3)	5 (1.4)	4 (0.9)	2 (0.5)	12 (0.7)
眼精疲労	0	1 (0.3)	0	0	0
眼瞼炎	0	2 (0.6)	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 (0.5)	2 (0.1)
上強膜炎	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
眼障害 (Cont.)			
眼部腫脹	0	0	0
眼瞼障害	0	0	0
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
霧視	0	0	0
視力障害	0	0	1 (0.2)
硝子体浮遊物	0	1 (0.9)	0
胃腸障害	34 (28.2)	10 (9.2)	45 (7.7)

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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
眼障害 (Cont.)					
眼部腫脹	0	0	1 (0.2)	0	1 (<0.1)
眼瞼障害	0	1 (0.3)	0	0	0
角膜炎	0	0	1 (0.2)	0	1 (<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 (0.3)	1 (0.2)	0	1 (<0.1)
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)
胃腸障害	16 (66.4)	62 (17.3)	32 (6.9)	47 (10.6)	169 (9.3)

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
腹部不快感	0	2 (1.8)	0
腹部膨満	1 (0.8)	1 (0.9)	1 (0.2)
腹痛	1 (0.8)	0	2 (0.3)
下腹部痛	0	0	1 (0.2)
上腹部痛	2 (1.7)	0	1 (0.2)
腹部圧痛	0	0	0
肛門の炎症	0	0	0
肛門潰瘍	0	0	0
口角口唇炎	0	0	1 (0.2)
肛門直腸不快感	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
腹部不快感	0	0	0	0	1 (<0.1)
腹部膨満	0	1 (0.3)	0	4 (0.9)	5 (0.3)
腹痛	3 (12.5)	1 (0.3)	1 (0.2)	2 (0.5)	9 (0.5)
下腹部痛	0	1 (0.3)	1 (0.2)	0	3 (0.2)
上腹部痛	0	2 (0.6)	1 (0.2)	0	3 (0.2)
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)
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
アフタ性潰瘍	0	0	1 (0.2)
大腸炎	1 (0.8)	0	1 (0.2)
潰瘍性大腸炎	20 (16.6)	2 (1.8)	13 (2.2)
結腸異形成	0	0	1 (0.2)
便秘	0	0	2 (0.3)
便意切迫	1 (0.8)	0	1 (0.2)
下痢	0	1 (0.9)	1 (0.2)
血性下痢	0	0	0
口内乾燥	0	1 (0.9)	0
消化不良	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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
アフタ性潰瘍	0	1 (0.3)	0	4 (0.9)	6 (0.3)
大腸炎	0	1 (0.3)	1 (0.2)	0	2 (0.1)
潰瘍性大腸炎	5 (20.8)	34 (9.5)	16 (3.4)	6 (1.4)	47 (2.6)
結腸異形成	0	0	2 (0.4)	0	3 (0.2)
便秘	2 (8.3)	3 (0.8)	2 (0.4)	4 (0.9)	12 (0.7)
便意切迫	0	0	0	0	1 (<0.1)
下痢	1 (4.2)	1 (0.3)	2 (0.4)	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 (0.3)	1 (0.2)	2 (0.5)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
おくび	0	0	0
鼓腸	2 (1.7)	1 (0.9)	4 (0.7)
排便回数増加	0	0	1 (0.2)
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 (0.2)

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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
おくび	0	0	0	1 (0.2)	1 (<0.1)
鼓腸	0	0	0	5 (1.1)	10 (0.5)
排便回数増加	0	0	0	0	1 (<0.1)
胃炎	0	1 (0.3)	1 (0.2)	0	2 (0.1)
胃食道逆流性疾患	0	2 (0.6)	2 (0.4)	1 (0.2)	5 (0.3)
歯肉痛	0	0	0	1 (0.2)	1 (<0.1)
血便排泄	0	1 (0.3)	0	0	0
痔核	0	1 (0.3)	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
大腸ポリープ	0	0	1 (0.2)
口唇水疱	0	0	0
口腔内潰瘍形成	0	1 (0.9)	1 (0.2)
悪心	2 (1.7)	0	7 (1.2)
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
膵炎	0	0	0
肛門周囲痛	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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
大腸ポリープ	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	7 (2.0)	0	5 (1.1)	17 (0.9)
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)
膵炎	0	1 (0.3)	0	1 (0.2)	1 (<0.1)
肛門周囲痛	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 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
直腸分泌物	1 (0.8)	0	0
直腸出血	0	0	0
直腸しぶり	0	0	0
口内炎	0	0	1 (0.2)
歯痛	0	0	0
嘔吐	1 (0.8)	1 (0.9)	1 (0.2)
一般・全身障害および投与部位の状態	3 (2.5)	3 (2.8)	25 (4.3)
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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
直腸分泌物	0	0	0	1 (0.2)	1 (<0.1)
直腸出血	0	2 (0.6)	0	0	1 (<0.1)
直腸しぶり	1 (4.2)	0	0	0	1 (<0.1)
口内炎	0	1 (0.3)	0	2 (0.5)	3 (0.2)
歯痛	0	0	1 (0.2)	0	1 (<0.1)
嘔吐	0	0	0	1 (0.2)	3 (0.2)
一般・全身障害および投与部位の状態	6 (24.9)	11 (3.1)	16 (3.4)	22 (5.0)	73 (4.0)
無力症	0	0	1 (0.2)	2 (0.5)	5 (0.3)
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
悪寒	0	1 (0.9)	3 (0.5)
不快感	0	0	0
薬効欠如	0	0	1 (0.2)
疲労	1 (0.8)	1 (0.9)	2 (0.3)
異常感	0	0	0
びくびく感	0	0	0
全身性浮腫	0	0	1 (0.2)
過形成	0	0	0
治癒不良	0	0	1 (0.2)
インフルエンザ様疾患	0	0	4 (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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
悪寒	0	1 (0.3)	0	2 (0.5)	6 (0.3)
不快感	0	0	0	1 (0.2)	1 (<0.1)
薬効欠如	0	1 (0.3)	0	0	1 (<0.1)
疲労	1 (4.2)	3 (0.8)	5 (1.1)	3 (0.7)	12 (0.7)
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 (0.3)	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	1 (0.2)	1 (0.2)	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 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
倦怠感	0	0	1 (0.2)
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	0	1 (0.9)	10 (1.7)
異物感	0	0	0
腫脹	0	0	0
肝胆道系障害	1 (0.8)	1 (0.9)	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
倦怠感	1 (4.2)	0	2 (0.4)	1 (0.2)	5 (0.3)
腫瘤	0	0	0	2 (0.5)	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	1 (0.2)	0	1 (<0.1)
末梢腫脹	0	0	0	2 (0.5)	2 (0.1)
発熱	3 (12.5)	4 (1.1)	2 (0.4)	3 (0.7)	19 (1.0)
異物感	0	1 (0.3)	0	0	0
腫脹	0	0	0	1 (0.2)	1 (<0.1)
肝胆道系障害	1 (4.2)	4 (1.1)	2 (0.4)	4 (0.9)	11 (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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
肝胆道系障害 (Cont.)			
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 (0.9)	0
肝炎	0	0	1 (0.2)
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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
肝胆道系障害 (Cont.)					
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	2 (0.6)	0	0	0
脂肪肝	0	0	0	0	1 (<0.1)
肝炎	0	0	0	0	1 (<0.1)
高トランスアミナーゼ血症	1 (4.2)	0	1 (0.2)	0	2 (0.1)
肝障害	0	1 (0.3)	0	1 (0.2)	2 (0.1)
肝損傷	0	0	0	0	0
非アルコール性脂肪性肝疾患	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
免疫系障害	0	0	1 (0.2)
過敏症	0	0	1 (0.2)
感染症および寄生虫症	26 (21.6)	30 (27.7)	138 (23.5)
腹壁膿瘍	0	0	0
膿瘍	1 (0.8)	0	0
肛門膿瘍	1 (0.8)	0	1 (0.2)
虫垂炎	0	0	0
細菌性関節炎	0	0	0
無症候性COVID-19	0	0	1 (0.2)
無症候性細菌尿	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
免疫系障害	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)	105 (29.3)	131 (28.1)	115 (25.9)	487 (26.7)
腹壁膿瘍	0	0	1 (0.2)	0	1 (<0.1)
膿瘍	0	1 (0.3)	0	0	1 (<0.1)
肛門膿瘍	0	1 (0.3)	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)
無症候性細菌尿	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
細菌感染	0	0	0
細菌性膣症	0	0	1 (0.2)
気管支炎	0	0	7 (1.2)
感染性滑液包炎	0	0	0
COVID-19	1 (0.8)	0	0
COVID-19肺炎	0	0	0
カンジダ感染	0	0	0
蜂巣炎	4 (3.3)	0	1 (0.2)
条虫感染	0	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 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
細菌感染	0	1 (0.3)	0	0	1 (<0.1)
細菌性膣症	0	0	0	0	1 (<0.1)
気管支炎	1 (4.2)	4 (1.1)	3 (0.6)	0	14 (0.8)
感染性滑液包炎	0	0	0	1 (0.2)	1 (<0.1)
COVID-19	0	2 (0.6)	1 (0.2)	1 (0.2)	2 (0.1)
COVID-19肺炎	0	2 (0.6)	1 (0.2)	1 (0.2)	4 (0.2)
カンジダ感染	0	0	0	1 (0.2)	1 (<0.1)
蜂巣炎	0	0	4 (0.9)	0	5 (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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
クロストリジウム・ディフィシレ感染	3 (2.5)	1 (0.9)	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
毛嚢虫症	0	1 (0.9)	2 (0.3)
皮膚糸状菌症	0	0	1 (0.2)
爪の皮膚糸状菌症	0	0	1 (0.2)
感染性下痢	0	0	0
耳感染	0	0	1 (0.2)
丹毒	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
クロストリジウム・ディフィシレ感染	0	1 (0.3)	1 (0.2)	4 (0.9)	8 (0.4)
結膜炎	0	0	0	2 (0.5)	2 (0.1)
ウイルス性結膜炎	0	1 (0.3)	0	0	1 (<0.1)
膀胱炎	0	1 (0.3)	0	0	1 (<0.1)
毛嚢虫症	0	0	4 (0.9)	4 (0.9)	11 (0.6)
皮膚糸状菌症	0	1 (0.3)	0	0	1 (<0.1)
爪の皮膚糸状菌症	0	0	0	2 (0.5)	3 (0.2)
感染性下痢	0	0	0	1 (0.2)	1 (<0.1)
耳感染	0	0	2 (0.4)	0	3 (0.2)
丹毒	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
眼感染	0	0	0
毛包炎	0	0	2 (0.3)
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 (0.2)
ウイルス性胃腸炎	0	0	1 (0.2)
性器カンジダ症	0	0	1 (0.2)
陰部ヘルペス	0	0	1 (0.2)
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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
眼感染	0	0	1 (0.2)	0	1 (<0.1)
毛包炎	1 (4.2)	3 (0.8)	2 (0.4)	13 (2.9)	20 (1.1)
真菌感染	0	0	0	0	0
皮膚真菌感染	0	1 (0.3)	0	1 (0.2)	2 (0.1)
せつ	0	0	1 (0.2)	1 (0.2)	2 (0.1)
胃腸炎	0	1 (0.3)	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 (0.2)
陰部単純ヘルペス	0	1 (0.3)	1 (0.2)	1 (0.2)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
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
単純ヘルペス	0	5 (4.6)	2 (0.3)
単純ヘルペス性咽頭炎	0	1 (0.9)	0
帯状疱疹	0	4 (3.7)	14 (2.4)
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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
歯肉炎	0	3 (0.8)	0	0	3 (0.2)
肛径部膿瘍	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
ヘモフィルス感染	0	1 (0.3)	0	0	0
単純ヘルペス	0	2 (0.6)	1 (0.2)	1 (0.2)	11 (0.6)
単純ヘルペス性咽頭炎	0	0	0	0	1 (<0.1)
帯状疱疹	6 (24.9)	5 (1.4)	24 (5.1)	15 (3.4)	66 (3.6)
播種性帯状疱疹	0	1 (0.3)	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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
膿痂疹	0	0	1 (0.2)
感染性皮膚嚢腫	0	0	0
伝染性単核症	0	0	1 (0.2)
インフルエンザ	0	0	2 (0.3)
潜伏結核	0	0	2 (0.3)
限局性感染	0	0	1 (0.2)
下気道感染	0	0	0
上咽頭炎	2 (1.7)	2 (1.8)	8 (1.4)
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
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)
伝染性単核症	0	0	0	0	1 (<0.1)
インフルエンザ	0	2 (0.6)	6 (1.3)	6 (1.4)	15 (0.8)
潜伏結核	0	0	1 (0.2)	2 (0.5)	5 (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	13 (3.6)	21 (4.5)	15 (3.4)	53 (2.9)
爪真菌症	0	4 (1.1)	2 (0.4)	1 (0.2)	6 (0.3)
口腔カンジダ症	0	1 (0.3)	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
口腔ヘルペス	1 (0.8)	5 (4.6)	12 (2.0)
真菌性外耳炎	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	1 (0.8)	0	2 (0.3)
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 (1.8)	7 (1.2)

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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
口腔ヘルペス	0	5 (1.4)	2 (0.4)	4 (0.9)	25 (1.4)
真菌性外耳炎	0	1 (0.3)	0	0	1 (<0.1)
急性中耳炎	0	1 (0.3)	0	0	1 (<0.1)
爪囲炎	0	1 (0.3)	0	0	1 (<0.1)
直腸周囲膿瘍	0	1 (0.3)	0	0	1 (<0.1)
咽頭炎	1 (4.2)	1 (0.3)	3 (0.6)	1 (0.2)	8 (0.4)
レンサ球菌性咽頭炎	0	1 (0.3)	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 (0.3)	0	0	0
肺炎	1 (4.2)	3 (0.8)	0	2 (0.5)	13 (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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
クリプトコッカス性肺炎	0	0	0
肺炎球菌性肺炎	0	0	1 (0.2)
処置後感染	1 (0.8)	0	0
歯髄炎	0	0	0
膿疱	0	0	0
腎盂腎炎	0	0	1 (0.2)
膿疱性皮疹	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 (0.2)

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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
クリプトコッカス性肺炎	0	0	0	1 (0.2)	1 (<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)
膿疱	0	0	2 (0.4)	0	2 (0.1)
腎盂腎炎	0	1 (0.3)	1 (0.2)	0	2 (0.1)
膿疱性皮疹	0	1 (0.3)	0	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 (0.2)
ウイルス性気道感染	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
鼻炎	1 (0.8)	0	1 (0.2)
根管感染	0	0	1 (0.2)
敗血症	0	0	1 (0.2)
セラチア感染	0	0	0
副鼻腔炎	1 (0.8)	1 (0.9)	7 (1.2)
皮膚カンジダ	0	0	1 (0.2)
皮膚感染	0	0	0
ブドウ球菌感染	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 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
鼻炎	0	0	0	1 (0.2)	2 (0.1)
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 (0.3)	0	0	0
副鼻腔炎	0	2 (0.6)	5 (1.1)	2 (0.5)	16 (0.9)
皮膚カンジダ	0	0	0	0	1 (<0.1)
皮膚感染	0	0	0	2 (0.5)	2 (0.1)
ブドウ球菌感染	0	1 (0.3)	0	0	0
白癬感染	0	2 (0.6)	0	0	0
足部白癬	0	2 (0.6)	0	2 (0.5)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
癜風	0	0	0
扁桃炎	0	0	1 (0.2)
歯膿瘍	0	0	0
歯感染	0	0	1 (0.2)
結核	0	0	1 (0.2)
上気道感染	3 (2.5)	5 (4.6)	23 (3.9)
尿路感染	2 (1.7)	1 (0.9)	9 (1.5)
尿路性敗血症	0	0	1 (0.2)
腟感染	0	0	1 (0.2)
水痘	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
癜風	0	0	2 (0.4)	0	2 (0.1)
扁桃炎	0	0	2 (0.4)	1 (0.2)	4 (0.2)
歯膿瘍	0	0	2 (0.4)	0	2 (0.1)
歯感染	0	0	0	2 (0.5)	3 (0.2)
結核	0	0	0	0	1 (<0.1)
上気道感染	1 (4.2)	16 (4.5)	11 (2.4)	13 (2.9)	64 (3.5)
尿路感染	0	5 (1.4)	8 (1.7)	1 (0.2)	21 (1.2)
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
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 (0.9)	0
ウイルス性上気道感染	0	1 (0.9)	2 (0.3)
女性外陰部蜂巣炎	0	0	1 (0.2)
外陰部腟カンジダ症	0	0	3 (0.5)
外陰腟真菌感染	0	0	1 (0.2)
創傷感染	1 (0.8)	0	0
傷害、中毒および処置合併症	4 (3.3)	2 (1.8)	10 (1.7)
偶発的過量投与	3 (2.5)	2 (1.8)	5 (0.9)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
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)	1 (0.3)	0	2 (0.5)	4 (0.2)
ウイルス性心膜炎	0	0	0	0	0
ウイルス性上気道感染	0	2 (0.6)	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 (0.3)	2 (0.4)	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 (1.4)	1 (0.2)	2 (0.5)	19 (1.0)
偶発的過量投与	0	0	1 (0.2)	2 (0.5)	10 (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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
挫傷	1 (0.8)	0	0
筋断裂	0	0	2 (0.3)
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 (0.2)
創傷	0	0	0
臨床検査	21 (17.4)	19 (17.6)	77 (13.1)
アラニンアミノトランスフェラーゼ増加	3 (2.5)	2 (1.8)	7 (1.2)
αヒドロキシ酪酸脱水素酵素増加	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
挫傷	0	0	0	0	0
筋断裂	0	0	0	0	2 (0.1)
過量投与	0	0	0	0	2 (0.1)
肋骨骨折	0	1 (0.3)	0	0	0
皮膚裂傷	0	1 (0.3)	0	0	1 (<0.1)
皮下血腫	0	0	0	0	1 (<0.1)
創傷	0	3 (0.8)	0	0	3 (0.2)
臨床検査	17 (70.6)	83 (23.1)	146 (31.3)	150 (33.8)	464 (25.5)
アラニンアミノトランスフェラーゼ増加	0	4 (1.1)	9 (1.9)	10 (2.3)	30 (1.6)
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
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 (2.5)	1 (0.9)	7 (1.2)
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 (0.2)
血中カルシウム増加	0	0	0
血中クロール減少	0	0	0
血中コレステロール減少	0	0	0
血中コレステロール増加	0	1 (0.9)	3 (0.5)
血中クレアチンホスホキナーゼ増加	1 (0.8)	9 (8.3)	19 (3.2)

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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
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	6 (1.7)	11 (2.4)	7 (1.6)	30 (1.6)
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	6 (1.3)	2 (0.5)	9 (0.5)
血中カルシウム増加	0	0	1 (0.2)	0	1 (<0.1)
血中クロール減少	0	1 (0.3)	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	0	2 (0.4)	5 (1.1)	11 (0.6)
血中クレアチンホスホキナーゼ増加	5 (20.8)	21 (5.9)	31 (6.7)	41 (9.2)	120 (6.6)

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
血中クレアチニン増加	1 (0.8)	0	1 (0.2)
血中葉酸減少	0	1 (0.9)	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
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 (1.8)	1 (0.2)
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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
血中クレアチニン増加	0	0	1 (0.2)	5 (1.1)	7 (0.4)
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 (0.3)	0	0	1 (<0.1)
血中カリウム減少	0	0	1 (0.2)	0	1 (<0.1)
血圧上昇	0	1 (0.3)	1 (0.2)	0	2 (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 (0.3)
血中尿素増加	0	0	1 (0.2)	0	1 (<0.1)
尿中血陽性	0	0	0	1 (0.2)	1 (<0.1)
クロストリジウム検査陽性	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
凝固時間延長	0	0	1 (0.2)
尿中結晶陽性	1 (0.8)	0	0
心電図再分極異常	0	0	1 (0.2)
γ-グルタミルトランスフェラーゼ増加	2 (1.7)	1 (0.9)	1 (0.2)
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	6 (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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
凝固時間延長	0	0	0	0	1 (<0.1)
尿中結晶陽性	0	0	0	0	0
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	3 (0.8)	2 (0.4)	1 (0.2)	6 (0.3)
糸球体濾過率減少	1 (4.2)	1 (0.3)	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 (0.6)	1 (0.2)	4 (0.9)	8 (0.4)
肝酵素上昇	4 (16.6)	1 (0.3)	1 (0.2)	2 (0.5)	14 (0.8)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
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 (0.2)
肝機能検査異常	0	1 (0.9)	0
肝機能検査値上昇	1 (0.8)	0	1 (0.2)
低比重リポ蛋白減少	0	0	0
低比重リポ蛋白増加	0	1 (0.9)	0
リンパ球数減少	1 (0.8)	0	6 (1.0)
リンパ球数増加	0	0	0
リンパ球百分率減少	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
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 (0.6)	3 (0.7)	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 (0.5)	3 (0.2)
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 (1.1)	7 (0.4)
リンパ球数減少	0	4 (1.1)	14 (3.0)	6 (1.4)	28 (1.5)
リンパ球数増加	0	2 (0.6)	1 (0.2)	4 (0.9)	6 (0.3)
リンパ球百分率減少	0	0	6 (1.3)	1 (0.2)	7 (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)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
平均赤血球容積異常	0	0	0
単球数増加	0	0	0
好中球数減少	0	0	5 (0.9)
好中球数増加	1 (0.8)	0	2 (0.3)
好中球百分率増加	0	0	0
血小板数減少	0	0	1 (0.2)
血小板数増加	0	0	0
総蛋白増加	0	0	0
尿中蛋白陽性	1 (0.8)	0	0
赤血球数減少	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
平均赤血球容積異常	0	0	0	1 (0.2)	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)	16 (4.5)	18 (3.9)	18 (4.1)	58 (3.2)
好中球数増加	0	2 (0.6)	3 (0.6)	3 (0.7)	8 (0.4)
好中球百分率増加	0	0	0	1 (0.2)	1 (<0.1)
血小板数減少	0	1 (0.3)	0	1 (0.2)	2 (0.1)
血小板数増加	0	0	0	3 (0.7)	3 (0.2)
総蛋白増加	0	0	0	1 (0.2)	1 (<0.1)
尿中蛋白陽性	0	1 (0.3)	1 (0.2)	1 (0.2)	2 (0.1)
赤血球数減少	0	0	2 (0.4)	3 (0.7)	5 (0.3)

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

Program Source Code: [redacted]

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
網状赤血球数減少	0	0	0
網状赤血球数増加	0	0	1 (0.2)
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 (0.2)
体重増加	0	0	2 (0.3)
白血球数減少	3 (2.5)	0	5 (0.9)
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 (3.3)	1 (0.9)	8 (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 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
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)
トランスアミナーゼ上昇	0	0	2 (0.4)	0	2 (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 (0.4)	0	3 (0.2)
体重増加	0	1 (0.3)	0	2 (0.5)	4 (0.2)
白血球数減少	2 (8.3)	14 (3.9)	12 (2.6)	10 (2.3)	40 (2.2)
白血球数増加	0	0	1 (0.2)	0	1 (<0.1)
尿中白血球陽性	0	0	0	1 (0.2)	3 (0.2)
代謝および栄養障害	0	9 (2.5)	11 (2.4)	8 (1.8)	36 (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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
食欲減退	0	1 (0.9)	0
脂質異常症	0	0	1 (0.2)
高コレステロール血症	0	0	4 (0.7)
高血糖	3 (2.5)	0	1 (0.2)
高リパーゼ血症	0	0	0
高脂血症	0	0	1 (0.2)
高尿酸血症	0	0	0
低ナトリウム血症	0	0	0
低リン酸血症	1 (0.8)	0	1 (0.2)
低蛋白血症	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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
食欲減退	0	1 (0.3)	0	0	2 (0.1)
脂質異常症	0	1 (0.3)	1 (0.2)	1 (0.2)	4 (0.2)
高コレステロール血症	0	2 (0.6)	4 (0.9)	2 (0.5)	12 (0.7)
高血糖	0	0	2 (0.4)	1 (0.2)	4 (0.2)
高リパーゼ血症	0	1 (0.3)	0	0	0
高脂血症	0	0	3 (0.6)	1 (0.2)	5 (0.3)
高尿酸血症	0	0	0	1 (0.2)	1 (<0.1)
低ナトリウム血症	0	1 (0.3)	0	0	1 (<0.1)
低リン酸血症	0	1 (0.3)	0	2 (0.5)	4 (0.2)
低蛋白血症	0	1 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
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	11 (9.1)	4 (3.7)	19 (3.2)
関節痛	1 (0.8)	1 (0.9)	8 (1.4)
関節炎	0	1 (0.9)	0
関節障害	0	0	2 (0.3)
背部痛	1 (0.8)	1 (0.9)	1 (0.2)
骨痛	0	0	0
指炎	0	0	0
関節弛緩	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
食欲亢進	0	1 (0.3)	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)	26 (7.2)	11 (2.4)	22 (5.0)	71 (3.9)
関節痛	1 (4.2)	5 (1.4)	2 (0.4)	8 (1.8)	22 (1.2)
関節炎	0	0	0	0	0
関節障害	0	3 (0.8)	1 (0.2)	1 (0.2)	5 (0.3)
背部痛	0	3 (0.8)	1 (0.2)	0	4 (0.2)
骨痛	0	0	0	1 (0.2)	1 (<0.1)
指炎	0	1 (0.3)	0	0	1 (<0.1)
関節弛緩	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
関節ロック	0	0	0
筋拘縮	0	0	0
筋痙縮	4 (3.3)	0	1 (0.2)
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 (0.2)
筋肉痛	3 (2.5)	0	4 (0.7)
四肢痛	1 (0.8)	0	1 (0.2)
顎痛	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
関節ロック	0	0	0	2 (0.5)	2 (0.1)
筋拘縮	0	0	1 (0.2)	0	1 (<0.1)
筋痙縮	1 (4.2)	1 (0.3)	1 (0.2)	1 (0.2)	5 (0.3)
筋緊張	1 (4.2)	0	0	0	1 (<0.1)
筋骨格系胸痛	0	4 (1.1)	0	0	2 (0.1)
筋骨格痛	0	2 (0.6)	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 (0.8)	2 (0.4)	3 (0.7)	10 (0.5)
四肢痛	0	1 (0.3)	1 (0.2)	3 (0.7)	6 (0.3)
顎痛	0	0	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
関節周囲炎	0	0	0
横紋筋融解症	0	0	0
関節リウマチ	0	1 (0.9)	0
仙腸骨炎	1 (0.8)	0	0
顎関節症候群	0	0	0
腱炎	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	2 (1.8)	1 (0.2)
基底細胞癌	0	2 (1.8)	0
ボーエン病	0	0	0
線維性組織球腫	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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)					
関節周囲炎	0	2 (0.6)	0	0	2 (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 (0.3)	0	0	1 (<0.1)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)	0	2 (0.6)	1 (0.2)	4 (0.9)	9 (0.5)
基底細胞癌	0	0	0	2 (0.5)	4 (0.2)
ボーエン病	0	0	0	1 (0.2)	1 (<0.1)
線維性組織球腫	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
浸潤性乳癌	0	0	0
皮膚乳頭腫	0	0	1 (0.2)
皮膚有棘細胞癌	0	0	0
神経系障害	10 (8.3)	3 (2.8)	13 (2.2)
灼熱感	0	0	0
脳虚血	0	0	0
浮動性めまい	0	0	1 (0.2)
構語障害	0	0	1 (0.2)
頭痛	8 (6.6)	3 (2.8)	9 (1.5)
知覚過敏	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）(Cont.)					
浸潤性乳癌	0	1 (0.3)	0	0	0
皮膚乳頭腫	0	0	1 (0.2)	0	2 (0.1)
皮膚有棘細胞癌	0	1 (0.3)	0	0	1 (<0.1)
神経系障害	6 (24.9)	8 (2.2)	24 (5.1)	18 (4.1)	63 (3.5)
灼熱感	1 (4.2)	0	1 (0.2)	0	2 (0.1)
脳虚血	0	0	2 (0.4)	0	2 (0.1)
浮動性めまい	0	1 (0.3)	4 (0.9)	6 (1.4)	11 (0.6)
構語障害	0	0	0	0	1 (<0.1)
頭痛	3 (12.5)	7 (2.0)	14 (3.0)	6 (1.4)	34 (1.9)
知覚過敏	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
神経系障害 (Cont.)			
感覚鈍麻	0	0	0
記憶障害	0	0	0
片頭痛	2 (1.7)	0	1 (0.2)
末梢性ニューロパチー	0	0	0
錯感覚	0	0	0
ヘルペス後神経痛	0	0	0
視野欠損	0	0	0
精神障害	3 (2.5)	2 (1.8)	3 (0.5)
不安	0	1 (0.9)	0
抑うつ気分	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)					
感覚鈍麻	0	0	1 (0.2)	1 (0.2)	2 (0.1)
記憶障害	0	0	0	1 (0.2)	1 (<0.1)
片頭痛	0	0	2 (0.4)	1 (0.2)	4 (0.2)
末梢性ニューロパチー	1 (4.2)	0	0	0	1 (<0.1)
錯感覚	0	0	0	1 (0.2)	1 (<0.1)
ヘルペス後神経痛	1 (4.2)	0	0	1 (0.2)	2 (0.1)
視野欠損	0	0	0	1 (0.2)	1 (<0.1)
精神障害	1 (4.2)	4 (1.1)	1 (0.2)	6 (1.4)	14 (0.8)
不安	0	1 (0.3)	1 (0.2)	0	2 (0.1)
抑うつ気分	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
精神障害 (Cont.)			
うつ病	1 (0.8)	0	0
不眠症	1 (0.8)	0	1 (0.2)
易刺激性	0	1 (0.9)	1 (0.2)
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 (1.7)	0	10 (1.7)
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 (0.2)
排尿困難	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害 (Cont.)					
うつ病	0	0	0	2 (0.5)	2 (0.1)
不眠症	1 (4.2)	1 (0.3)	0	4 (0.9)	7 (0.4)
易刺激性	0	0	0	0	1 (<0.1)
リビドー減退	0	1 (0.3)	0	0	1 (<0.1)
睡眠障害	0	1 (0.3)	0	0	0
腎および尿路障害	2 (8.3)	11 (3.1)	5 (1.1)	7 (1.6)	31 (1.7)
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)
排尿困難	0	4 (1.1)	0	2 (0.5)	7 (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)

MedDRA 23.0 System Organ Class Preferred Term	Induction = PBO [A] PBO (N=378) (PYs=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
血尿	0	0	1 (0.2)
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 (0.2)
腎結石症	0	0	1 (0.2)
頻尿	0	0	1 (0.2)
蛋白尿	2 (1.7)	0	2 (0.3)
腎仙痛	0	0	0
腎機能障害	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
血尿	0	0	1 (0.2)	0	2 (0.1)
水腎症	0	1 (0.3)	0	0	0
ケトン尿	0	1 (0.3)	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 (0.3)	0	0	2 (0.1)
蛋白尿	0	4 (1.1)	1 (0.2)	2 (0.5)	7 (0.4)
腎仙痛	0	0	0	1 (0.2)	1 (<0.1)
腎機能障害	0	0	2 (0.4)	0	3 (0.2)

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

Program Source Code: [redacted]

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
腎および尿路障害 (Cont.)			
腎臓痛	0	0	1 (0.2)
生殖系および乳房障害	0	1 (0.9)	4 (0.7)
バルトリン嚢腫	0	0	0
良性前立腺肥大症	0	0	1 (0.2)
勃起不全	0	0	0
性器びらん	0	0	1 (0.2)
不規則月経	0	0	1 (0.2)
月経前頭痛	0	0	0
前立腺炎	0	1 (0.9)	1 (0.2)
精液変色	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
腎および尿路障害 (Cont.)					
腎臓痛	0	0	0	0	1 (<0.1)
生殖系および乳房障害	0	5 (1.4)	2 (0.4)	4 (0.9)	14 (0.8)
バルトリン嚢腫	0	1 (0.3)	0	0	0
良性前立腺肥大症	0	0	0	0	1 (<0.1)
勃起不全	0	0	1 (0.2)	0	1 (<0.1)
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)
前立腺炎	0	1 (0.3)	0	0	3 (0.2)
精液変色	0	1 (0.3)	0	2 (0.5)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)			
腟分泌物	0	0	0
外陰腟そう痒症	0	0	0
呼吸器、胸郭および縦隔障害	4 (3.3)	1 (0.9)	15 (2.6)
気管支拡張症	0	0	0
咳嗽	0	0	4 (0.7)
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)					
腟分泌物	0	0	1 (0.2)	0	1 (<0.1)
外陰腟そう痒症	0	2 (0.6)	0	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	3 (12.5)	12 (3.3)	8 (1.7)	16 (3.6)	48 (2.6)
気管支拡張症	0	1 (0.3)	0	0	0
咳嗽	1 (4.2)	1 (0.3)	1 (0.2)	2 (0.5)	9 (0.5)
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 (0.3)	0	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
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 (0.5)
非感染性気管支炎	0	0	0
口腔咽頭痛	0	1 (0.9)	5 (0.9)
肺臓炎	1 (0.8)	0	0
湿性咳嗽	0	0	0
肺塞栓症	1 (0.8)	0	1 (0.2)
気道うっ血	0	0	0
アレルギー性鼻炎	0	0	1 (0.2)
鼻漏	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
間質性肺疾患	0	1 (0.3)	0	0	0
鼻閉	0	1 (0.3)	0	2 (0.5)	5 (0.3)
非感染性気管支炎	0	0	0	1 (0.2)	1 (<0.1)
口腔咽頭痛	0	4 (1.1)	2 (0.4)	2 (0.5)	11 (0.6)
肺臓炎	0	0	0	0	0
湿性咳嗽	0	0	1 (0.2)	1 (0.2)	2 (0.1)
肺塞栓症	1 (4.2)	0	1 (0.2)	0	3 (0.2)
気道うっ血	0	1 (0.3)	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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)			
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
上気道咳症候群	0	0	1 (0.2)
皮膚および皮下組織障害	11 (9.1)	11 (10.2)	29 (4.9)
ざ瘡	2 (1.7)	1 (0.9)	4 (0.7)
嚢胞性ざ瘡	0	0	0
脱毛症	0	1 (0.9)	6 (1.0)
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)					
副鼻腔うっ血	0	0	2 (0.4)	3 (0.7)	5 (0.3)
副鼻腔障害	0	0	0	1 (0.2)	1 (<0.1)
上気道の炎症	0	1 (0.3)	0	0	0
上気道咳症候群	0	1 (0.3)	0	1 (0.2)	3 (0.2)
皮膚および皮下組織障害	10 (41.5)	54 (15.0)	57 (12.2)	64 (14.4)	191 (10.5)
ざ瘡	3 (12.5)	6 (1.7)	15 (3.2)	18 (4.1)	45 (2.5)
嚢胞性ざ瘡	0	0	1 (0.2)	0	1 (<0.1)
脱毛症	1 (4.2)	2 (0.6)	3 (0.6)	5 (1.1)	18 (1.0)
水疱	0	0	0	1 (0.2)	1 (<0.1)
皮膚炎	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (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	0
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	1 (0.9)	0
異汗性湿疹	0	0	0
斑状出血	0	0	0
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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
ざ瘡様皮膚炎	0	0	0	1 (0.2)	3 (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	1 (0.3)	0	0	0
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 (0.3)	0	0	1 (<0.1)
皮膚乾燥	0	2 (0.6)	1 (0.2)	0	1 (<0.1)
異汗性湿疹	0	1 (0.3)	0	0	0
斑状出血	0	0	0	1 (0.2)	1 (<0.1)
湿疹	1 (4.2)	3 (0.8)	0	1 (0.2)	3 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
紅斑	1 (0.8)	0	1 (0.2)
環状紅斑	0	0	1 (0.2)
結節性紅斑	0	0	0
過角化	0	0	0
多毛症	0	1 (0.9)	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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
紅斑	0	3 (0.8)	2 (0.4)	4 (0.9)	7 (0.4)
環状紅斑	0	0	0	0	1 (<0.1)
結節性紅斑	0	1 (0.3)	0	0	0
過角化	0	1 (0.3)	0	0	1 (<0.1)
多毛症	0	0	0	0	0
神経皮膚炎	0	1 (0.3)	0	0	0
寝汗	0	0	1 (0.2)	0	1 (<0.1)
爪破損	0	1 (0.3)	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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
丘疹	0	0	1 (0.2)
光線性皮膚症	0	0	0
光線過敏性反応	0	0	0
そう痒症	4 (3.3)	2 (1.8)	0
壊疽性膿皮症	0	0	0
発疹	2 (1.7)	2 (1.8)	11 (1.9)
紅斑性皮疹	1 (0.8)	0	0
毛孔性皮疹	0	0	0
斑状皮疹	0	0	0
斑状丘疹状皮疹	0	2 (1.8)	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
丘疹	0	1 (0.3)	2 (0.4)	3 (0.7)	7 (0.4)
光線性皮膚症	0	1 (0.3)	0	0	0
光線過敏性反応	0	0	1 (0.2)	0	1 (<0.1)
そう痒症	0	5 (1.4)	3 (0.6)	3 (0.7)	8 (0.4)
壊疽性膿皮症	1 (4.2)	0	0	0	1 (<0.1)
発疹	2 (8.3)	9 (2.5)	9 (1.9)	14 (3.2)	44 (2.4)
紅斑性皮疹	0	0	2 (0.4)	0	2 (0.1)
毛孔性皮疹	1 (4.2)	0	1 (0.2)	0	2 (0.1)
斑状皮疹	0	0	2 (0.4)	1 (0.2)	3 (0.2)
斑状丘疹状皮疹	0	1 (0.3)	2 (0.4)	4 (0.9)	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 4.3.5

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
丘疹性皮疹	0	0	1 (0.2)
そう痒性皮疹	0	0	1 (0.2)
酒さ	1 (0.8)	0	0
脂漏性皮膚炎	0	0	0
皮膚びらん	0	0	0
皮膚剥脱	0	0	0
皮膚病変	0	0	1 (0.2)
皮膚線条	0	0	0
皮膚潰瘍	0	0	0
日光皮膚炎	0	1 (0.9)	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
丘疹性皮疹	0	3 (0.8)	1 (0.2)	0	5 (0.3)
そう痒性皮疹	0	0	0	0	1 (<0.1)
酒さ	0	2 (0.6)	3 (0.6)	0	5 (0.3)
脂漏性皮膚炎	0	1 (0.3)	0	2 (0.5)	3 (0.2)
皮膚びらん	0	1 (0.3)	0	0	0
皮膚剥脱	0	2 (0.6)	1 (0.2)	0	2 (0.1)
皮膚病変	0	2 (0.6)	2 (0.4)	0	5 (0.3)
皮膚線条	0	0	1 (0.2)	0	1 (<0.1)
皮膚潰瘍	0	0	0	3 (0.7)	3 (0.2)
日光皮膚炎	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
毛細血管拡張症	0	0	0
蕁麻疹	0	0	0
血管障害	2 (1.7)	1 (0.9)	4 (0.7)
深部静脈血栓症	0	1 (0.9)	1 (0.2)
潮紅	0	0	0
血腫	0	0	1 (0.2)
ほてり	0	0	0
高血圧	1 (0.8)	0	1 (0.2)
高血圧クリーゼ	0	0	1 (0.2)
蒼白	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
毛細血管拡張症	0	0	1 (0.2)	0	1 (<0.1)
蕁麻疹	0	2 (0.6)	0	0	0
血管障害	1 (4.2)	5 (1.4)	8 (1.7)	5 (1.1)	22 (1.2)
深部静脈血栓症	1 (4.2)	0	0	0	3 (0.2)
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 (0.3)	0	0	1 (<0.1)
高血圧	0	2 (0.6)	4 (0.9)	5 (1.1)	11 (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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
血管障害 (Cont.)			
骨盤静脈血栓症	1 (0.8)	0	0
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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
血管障害 (Cont.)					
骨盤静脈血栓症	0	0	0	0	0
レイノー現象	0	0	1 (0.2)	0	1 (<0.1)
血栓性静脈炎	0	1 (0.3)	0	0	1 (<0.1)
静脈血栓症	0	1 (0.3)	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

表 2.7.4.7-33.

[redacted]20[redacted] 11:08 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 1.3.6

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
Any adverse event	28 (7.4) [7.2]	22 (3.1) [3.1]
血液およびリンパ系障害	1 (0.3) [0.3]	3 (0.4) [0.4]
貧血	1 (0.3) [0.3]	0
リンパ球減少症	0	3 (0.4) [0.4]
胃腸障害	21 (5.6) [5.5]	8 (1.1) [1.2]
腹痛	0	1 (0.1) [0.1]
肛門潰瘍	0	1 (0.1) [0.2]
大腸炎	3 (0.8) [0.7]	0
潰瘍性大腸炎	15 (4.0) [4.0]	6 (0.8) [0.9]
下痢	0	1 (0.1) [0.1]
血性下痢	0	1 (0.1) [0.1]
排便困難	1 (0.3) [0.2]	0
鼓腸	1 (0.3) [0.3]	0
大腸穿孔	1 (0.3) [0.3]	0
感染症および寄生虫症	3 (0.8) [0.7]	4 (0.6) [0.6]
虫垂炎	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.6

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
感染症および寄生虫症 (Cont.)		
蜂巣炎	2 (0.5) [0.5]	0
COVID-19肺炎	0	1 (0.1) [0.1]
ノロウイルス性胃腸炎	0	1 (0.1) [0.1]
RSウイルス感染	0	1 (0.1) [0.2]
敗血症	0	1 (0.1) [0.2]
副鼻腔炎	1 (0.3) [0.2]	0
臨床検査	2 (0.5) [0.6]	7 (1.0) [1.0]
アミラーゼ増加	0	1 (0.1) [0.1]
血中クレアチンホスホキナーゼ増加	1 (0.3) [0.3]	2 (0.3) [0.3]
血中リン減少	0	1 (0.1) [0.1]
ヘモグロビン減少	1 (0.3) [0.3]	1 (0.1) [0.1]
好中球数減少	0	2 (0.3) [0.3]
白血球数増加	0	1 (0.1) [0.1]
代謝および栄養障害	2 (0.5) [0.5]	1 (0.1) [0.1]
低アルブミン血症	1 (0.3) [0.3]	0
低リン酸血症	1 (0.3) [0.2]	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 2.4 1.3.6

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(Placebo-Controlled Induction Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=378) n (%) [SSA%]	UPA 45 mg QD (N=719) n (%) [SSA%]
神経系障害	1 (0.3) [0.3]	0
頭痛	1 (0.3) [0.3]	0
呼吸器、胸郭および縦隔障害	0	1 (0.1) [0.2]
肺塞栓症	0	1 (0.1) [0.2]
皮膚および皮下組織障害	0	1 (0.1) [0.1]
多形紅斑	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug and up to 30 days past the last dose of study drug in the 8-week induction period or until one day prior to the first dose of study drug in the Part 2 induction period or any subsequent maintenance or long-term extension period.
SSA = Study-size adjusted.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表 2.7.4.7-34.

[redacted]20[redacted] 11:19 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - 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]	19 (7.6) [7.6]	23 (8.1) [8.1]	29 (10.0) [10.0]
血液およびリンパ系障害	2 (0.8) [0.8]	0	1 (0.4) [0.4]	0	2 (0.7) [0.7]
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]
心臓障害	1 (0.4) [0.4]	0	2 (0.8) [0.8]	0	2 (0.7) [0.7]
急性心筋梗塞	1 (0.4) [0.4]	0	0	0	0
慢性左室不全	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%]
心臓障害 (Cont.)					
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
胃腸障害	11 (4.5) [4.5]	1 (0.4) [0.4]	2 (0.8) [0.8]	3 (1.1) [1.1]	2 (0.7) [0.7]
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]	1 (0.3) [0.3]
大腸穿孔	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%]
胃腸障害 (Cont.)					
膵炎	1 (0.4) [0.4]	0	0	0	0
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]	6 (2.4) [2.4]	10 (3.5) [3.5]	10 (3.4) [3.4]
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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
肛門膿瘍	0	1 (0.4) [0.4]	0	1 (0.4) [0.3]	0
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	1 (0.4) [0.3]	1 (0.3) [0.3]
COVID-19肺炎	0	0	2 (0.8) [0.8]	0	3 (1.0) [1.0]
単純ヘルペス	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.)					
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]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
クリプトコッカス性肺炎	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
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
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]

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

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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）	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
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]	2 (0.7) [0.7]
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]

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were remained re-randomized to 15 mg or 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.)					
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
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]	2 (0.8) [0.8]	1 (0.4) [0.3]	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	1 (0.4) [0.3]	0
肺腫瘤	0	0	1 (0.4) [0.4]	0	1 (0.3) [0.3]
皮膚および皮下組織障害	1 (0.4) [0.4]	0	0	0	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 3.3.8

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%]
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]	0
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 2.7.4.7-35.

[redacted]20[redacted] 10:46 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
Any adverse event	51 (42.3)	5 (4.6)	66 (11.3)
血液およびリンパ系障害	1 (0.8)	0	1 (0.2)
貧血	1 (0.8)	0	1 (0.2)
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
慢性左室不全	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 4.3.4

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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
Any adverse event	20 (83.1)	55 (15.3)	45 (9.7)	50 (11.3)	209 (11.5)
血液およびリンパ系障害	1 (4.2)	5 (1.4)	0	3 (0.7)	8 (0.4)
貧血	1 (4.2)	0	0	0	2 (0.1)
鉄欠乏性貧血	0	1 (0.3)	0	0	0
リンパ球減少症	0	2 (0.6)	0	2 (0.5)	4 (0.2)
好中球減少症	0	2 (0.6)	0	1 (0.2)	2 (0.1)
心臓障害	0	2 (0.6)	0	2 (0.5)	3 (0.2)
急性心筋梗塞	0	1 (0.3)	0	0	0
心房細動	0	1 (0.3)	0	0	1 (<0.1)
慢性左室不全	0	0	0	1 (0.2)	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.4

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
心臓障害 (Cont.)			
上室性頻脈	0	0	0
耳および迷路障害	0	0	1 (0.2)
突発性難聴	0	0	1 (0.2)
眼障害	0	0	0
白内障	0	0	0
胃腸障害	39 (32.4)	3 (2.8)	19 (3.2)
腹部腫瘤	0	0	0
腹痛	0	0	1 (0.2)
裂肛	0	0	1 (0.2)
痔瘻	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
心臓障害 (Cont.)					
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)
胃腸障害	13 (54.0)	19 (5.3)	7 (1.5)	6 (1.4)	53 (2.9)
腹部腫瘤	0	1 (0.3)	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	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 4.3.4

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
肛門潰瘍	0	0	0
大腸炎	6 (5.0)	0	0
潰瘍性大腸炎	26 (21.6)	2 (1.8)	12 (2.0)
結腸異形成	0	0	1 (0.2)
下痢	0	0	0
血性下痢	0	0	0
排便困難	1 (0.8)	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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
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)	16 (4.5)	6 (1.3)	3 (0.7)	39 (2.1)
結腸異形成	0	0	0	0	1 (<0.1)
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
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
胃腸障害 (Cont.)			
イレウス	0	0	1 (0.2)
腸閉塞	1 (0.8)	0	0
大腸穿孔	1 (0.8)	0	1 (0.2)
大腸ポリープ	0	0	1 (0.2)
口腔内潰瘍形成	0	1 (0.9)	0
悪心	1 (0.8)	0	0
膵炎	0	0	0
直腸出血	0	0	1 (0.2)
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 (0.9)

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 4.3.4

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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
胃腸障害 (Cont.)					
イレウス	0	0	0	0	1 (<0.1)
腸閉塞	0	0	0	0	0
大腸穿孔	0	1 (0.3)	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 (0.3)	0	1 (0.2)	1 (<0.1)
直腸出血	0	0	0	0	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 (0.3)	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)			
悪寒	0	0	1 (0.2)
疲労	0	0	1 (0.2)
疼痛	0	0	1 (0.2)
発熱	0	0	2 (0.3)
肝胆道系障害	0	0	0
肝障害	0	0	0
感染症および寄生虫症	5 (4.2)	1 (0.9)	16 (2.7)
腹部膿瘍	0	0	0
急性心内膜炎	0	0	0
肛門膿瘍	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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)					
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 (0.3)	1 (0.2)	0	3 (0.2)
肝胆道系障害	0	0	0	1 (0.2)	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 (1.7)	15 (3.2)	15 (3.4)	50 (2.7)
腹部膿瘍	0	1 (0.3)	0	0	0
急性心内膜炎	0	1 (0.3)	0	0	0
肛門膿瘍	0	0	1 (0.2)	0	1 (<0.1)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.4

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
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 (2.5)	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	0	0	2 (0.3)
医療機器関連敗血症	0	0	0
大腸菌感染	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.4

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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
虫垂炎	0	0	1 (0.2)	0	1 (<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	1 (0.2)	1 (0.2)	2 (0.1)
COVID-19肺炎	0	1 (0.3)	0	6 (1.4)	9 (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)
クロストリジウム・ディフィシレ感染	0	0	1 (0.2)	0	3 (0.2)
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
大腸菌性敗血症	0	0	1 (0.2)
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 (0.9)	0
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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
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 (0.3)	2 (0.4)	1 (0.2)	5 (0.3)
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
毛巣嚢胞	0	0	2 (0.3)
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 (0.2)
クリプトコッカス性肺炎	0	0	0
肺炎球菌性肺炎	0	0	1 (0.2)
ウイルス性肺炎	0	0	1 (0.2)
処置後感染	1 (0.8)	0	0
RSウイルス感染	0	0	0
敗血症	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.4

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
毛巣嚢胞	0	0	0	0	2 (0.1)
ニューモシスチス・イロベチイ肺炎	0	1 (0.3)	0	0	0
肺炎	0	1 (0.3)	0	1 (0.2)	3 (0.2)
細菌性肺炎	0	0	0	0	1 (<0.1)
クリプトコッカス性肺炎	0	0	0	1 (0.2)	1 (<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
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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
副鼻腔炎	1 (0.8)	0	0
上気道感染	0	0	1 (0.2)
尿路性敗血症	0	0	1 (0.2)
傷害、中毒および処置合併症	1 (0.8)	0	4 (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
処置による腸管穿孔	0	0	1 (0.2)
肺挫傷	0	0	0
肋骨骨折	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.4

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)					
副鼻腔炎	0	0	0	0	0
上気道感染	0	0	0	0	1 (<0.1)
尿路性敗血症	0	0	0	0	1 (<0.1)
傷害、中毒および処置合併症	0	3 (0.8)	2 (0.4)	0	9 (0.5)
腓骨骨折	0	1 (0.3)	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 (0.3)	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)
肋骨骨折	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
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	0
子宮穿孔	0	0	1 (0.2)
創傷	0	0	1 (0.2)
臨床検査	2 (1.7)	1 (0.9)	6 (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 (0.9)	1 (0.2)
血中リン減少	0	0	0
血中トリグリセリド増加	0	0	1 (0.2)

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

Program Source Code: [redacted]

TABLE 2.4 4.3.4

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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)					
胸椎骨折	0	0	1 (0.2)	0	1 (<0.1)
脛骨骨折	0	1 (0.3)	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 (1.4)	6 (1.3)	5 (1.1)	24 (1.3)
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 (0.5)	5 (0.3)
血中リン減少	0	1 (0.3)	0	0	1 (<0.1)
血中トリグリセリド増加	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
臨床検査 (Cont.)			
ヘモグロビン減少	1 (0.8)	0	2 (0.3)
肝酵素上昇	0	0	1 (0.2)
肝機能検査値上昇	0	0	0
リンパ球数減少	0	0	1 (0.2)
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
代謝および栄養障害	2 (1.7)	0	1 (0.2)
高血糖	0	0	1 (0.2)
低アルブミン血症	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 4.3.4

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
臨床検査 (Cont.)					
ヘモグロビン減少	0	0	1 (0.2)	0	3 (0.2)
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 (1.1)	2 (0.4)	1 (0.2)	6 (0.3)
白血球数増加	1 (4.2)	0	0	0	1 (<0.1)
代謝および栄養障害	0	0	1 (0.2)	3 (0.7)	5 (0.3)
高血糖	0	0	0	0	1 (<0.1)
低アルブミン血症	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 4.3.4

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
代謝および栄養障害 (Cont.)			
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	4 (0.7)
関節痛	0	0	1 (0.2)
関節炎	0	0	0
背部痛	0	0	1 (0.2)
滑液包炎	0	0	0
四肢痛	0	0	1 (0.2)
肩回旋筋腱板症候群	0	0	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	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 4.3.4

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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
代謝および栄養障害 (Cont.)					
低リン酸血症	0	0	0	3 (0.7)	3 (0.2)
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	0	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)
背部痛	0	0	0	0	1 (<0.1)
滑液包炎	0	0	0	1 (0.2)	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	1 (0.3)	2 (0.4)	4 (0.9)	8 (0.4)

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

Program Source Code: [redacted]

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
結腸腺癌	0	0	0
膵腺癌	0	0	1 (0.2)
浸潤性乳癌	0	0	0
悪性黒色腫	0	0	1 (0.2)
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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)					
結腸腺癌	0	0	0	1 (0.2)	1 (<0.1)
膵腺癌	0	0	0	0	1 (<0.1)
浸潤性乳癌	0	1 (0.3)	1 (0.2)	0	1 (<0.1)
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	3 (0.8)	2 (0.4)	4 (0.9)	7 (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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
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
精神障害	0	0	1 (0.2)
不安	0	0	0
うつ病	0	0	0
精神障害	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 4.3.4

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=358.9) Events (E/100 PYs)	 UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	 UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	 Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
神経系障害 (Cont.)					
脳血管発作	0	0	0	1 (0.2)	1 (<0.1)
頭痛	0	2 (0.6)	0	0	1 (<0.1)
片頭痛	0	1 (0.3)	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	1 (0.2)	1 (<0.1)
くも膜下出血	0	0	0	1 (0.2)	1 (<0.1)
精神障害	0	7 (2.0)	1 (0.2)	2 (0.5)	7 (0.4)
不安	0	2 (0.6)	0	1 (0.2)	2 (0.1)
うつ病	0	2 (0.6)	1 (0.2)	1 (0.2)	3 (0.2)
精神障害	0	1 (0.3)	0	0	0

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

Program Source Code: [redacted]

TABLE 2.4 4.3.4

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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
精神障害 (Cont.)			
自殺念慮	0	0	0
自殺企図	0	0	1 (0.2)
腎および尿路障害	0	0	2 (0.3)
出血性膀胱炎	0	0	1 (0.2)
排尿困難	0	0	0
腎結石症	0	0	0
尿管結石症	0	0	1 (0.2)
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

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
精神障害 (Cont.)					
自殺念慮	0	2 (0.6)	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 (0.6)	0	0	4 (0.2)
出血性膀胱炎	0	0	0	0	1 (<0.1)
排尿困難	0	1 (0.3)	0	0	1 (<0.1)
腎結石症	0	1 (0.3)	0	0	1 (<0.1)
尿管結石症	0	0	0	0	1 (<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)

NM = Subject did not receive any dose of study drug during maintenance or long-term extension; PBO = Placebo; UPA = Upadacitinib.
Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100 PYs = Events per 100 patient-years.
Treatment-emergent adverse events are adverse events that occur within the SAP defined cohort treatment period or 30 days past the last dose of study drug for subjects who withdraw from study drug treatment.
[A] Includes all subjects who received PBO as initial study drug induction. Note that some subjects in this cohort also appear in one of the other cohorts, if they took any dose of UPA. However, only events that occurred and associated exposure time while patient was receiving PBO are counted in this column.
[B] Includes all subjects who received UPA 15 or 30 mg and re-randomized to PBO or took UPA 30 mg or less during induction, or took only PBO during induction and received at least one dose of UPA 15-30 mg during LTE. Subjects are further categorized by primary dose received during maintenance (or LTE).
[C] Includes all subjects who received at least one dose of UPA 45 mg during any 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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
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 (0.2)
慢性閉塞性肺疾患	0	0	0
肺塞栓症	0	0	1 (0.2)
肺腫瘤	0	0	0
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 (0.2)
ざ瘡	0	0	1 (0.2)
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 4.3.4

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=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害	1 (4.2)	0	2 (0.4)	3 (0.7)	8 (0.4)
急性呼吸不全	0	0	0	1 (0.2)	1 (<0.1)
喘息	0	0	0	0	1 (<0.1)
慢性閉塞性肺疾患	0	0	1 (0.2)	0	1 (<0.1)
肺塞栓症	1 (4.2)	0	1 (0.2)	0	3 (0.2)
肺腫瘤	0	0	0	1 (0.2)	1 (<0.1)
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 (0.3)	1 (0.2)	0	3 (0.2)
ざ瘡	0	0	0	0	1 (<0.1)
湿疹	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=120.5) Events (E/100 PYs)	------ Induction Dose < 45 mg QD [B] ------- UPA 15-30 mg/ PBO (N=36) (PYs=108.2) Events (E/100 PYs)	 UPA < 45 mg/ <= 30 mg (N=281) (PYs=586.0) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)			
多形紅斑	0	0	0
結節性紅斑	0	0	0
外科および内科処置	0	0	0
人工流産	0	0	0
血管障害	0	0	1 (0.2)
深部静脈血栓症	0	0	1 (0.2)
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)

	Induction Dose = 45 mg QD [C]				
MedDRA 23.0 System Organ Class Preferred Term	UPA 45 mg/ NM (N=129) (PYs=24.1) Events (E/100 PYs)	UPA 45 mg/ PBO (N=245) (PYs=358.9) Events (E/100 PYs)	UPA 45 mg/ 15 mg (N=306) (PYs=466.1) Events (E/100 PYs)	UPA 45 mg/ 30 mg (N=307) (PYs=443.4) Events (E/100 PYs)	Any UPA (N=1304) (PYs=1821.1) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)					
多形紅斑	1 (4.2)	0	0	0	1 (<0.1)
結節性紅斑	0	1 (0.3)	0	0	0
外科および内科処置	0	0	1 (0.2)	0	1 (<0.1)
人工流産	0	0	1 (0.2)	0	1 (<0.1)
血管障害	0	0	1 (0.2)	0	2 (0.1)
深部静脈血栓症	0	0	0	0	1 (<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 2.7.4.7-36.

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UPADACITINIB (ULCERATIVE COLITIS)
INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 6.1.1 J

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=53.5)	(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)	381 (712.5) [642.8, 787.8]	270 (456.6) [403.7, 514.4]	317 (522.4) [466.4, 583.2]	318 (450.7) [402.5, 503.1]	361 (515.2) [463.4, 571.2]
COVID-19 infection related AE	4 (7.5) [2.0, 19.2]	3 (5.1) [1.0, 14.8]	0	4 (5.7) [1.5, 14.5]	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) [12.9, 41.6]	0	4 (6.6) [1.8, 16.9]	0	6 (8.6) [3.1, 18.6]
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 (211.3) [174.2, 254.1]	83 (140.4) [111.8, 174.0]	118 (194.4) [161.0, 232.9]	93 (131.8) [106.4, 161.5]	135 (192.7) [161.5, 228.0]
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 J

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#	0/53.5	0/59.1	0/60.7	0/70.6	0/70.1
Deaths occurring <= 30 days after last dose of study drug	0/53.5	0/59.1	0/60.7	0/70.6	0/70.1
Deaths occurring > 30 days after last dose of study drug	0/53.5	0/59.1	0/60.7	0/70.6	0/70.1
COVID-19 infection related deaths	0/53.5	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 J

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=34.8)	(PYs=51.7)	(PYs=55.1)	(PYs=65.2)	(PYs=63.1)
	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)	116 (333.3) [275.4, 399.8]	130 (251.4) [210.0, 298.5]	137 (248.6) [208.7, 293.9]	174 (266.7) [228.5, 309.4]	165 (261.7) [223.3, 304.8]
COVID-19 infection related AE	3 (8.6) [1.8, 25.2]	0	4 (7.3) [2.0, 18.6]	0	5 (7.9) [2.6, 18.5]
Any serious AE	9 (25.9) [11.8, 49.1]	9 (17.4) [8.0, 33.0]	7 (12.7) [5.1, 26.2]	11 (16.9) [8.4, 30.2]	9 (14.3) [6.5, 27.1]
Any AE leading to discontinuation of study drug	7 (20.1) [8.1, 41.4]	4 (7.7) [2.1, 19.8]	3 (5.4) [1.1, 15.9]	6 (9.2) [3.4, 20.0]	3 (4.8) [1.0, 13.9]
Any severe AE	7 (20.1) [8.1, 41.4]	5 (9.7) [3.1, 22.6]	7 (12.7) [5.1, 26.2]	9 (13.8) [6.3, 26.2]	7 (11.1) [4.5, 22.9]
Any AE with reasonable possibility of being related to study drug$	34 (97.7) [67.7, 136.5]	41 (79.3) [56.9, 107.6]	48 (87.1) [64.2, 115.5]	56 (85.8) [64.8, 111.5]	55 (87.2) [65.7, 113.5]
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 J

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#	0/34.8	0/51.7	0/55.1	0/65.2	0/63.1
Deaths occurring <= 30 days after last dose of study drug	0/34.8	0/51.7	0/55.1	0/65.2	0/63.1
Deaths occurring > 30 days after last dose of study drug	0/34.8	0/51.7	0/55.1	0/65.2	0/63.1
COVID-19 infection related deaths	0/34.8	0/51.7	0/55.1	0/65.2	0/63.1

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 J

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=116)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=208)	UPA 15 mg QD (N=242)	UPA 30 mg QD (N=237)
Subgroup: >= 6 - < 9 Month					
Exposure-adjusted event rate:	(PYs=23.7)	(PYs=41.1)	(PYs=46.5)	(PYs=53.0)	(PYs=53.1)
	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)	99 (417.6) [339.4, 508.4]	142 (345.6) [291.1, 407.4]	115 (247.5) [204.3, 297.1]	174 (328.5) [281.5, 381.2]	136 (256.2) [214.9, 303.0]
COVID-19 infection related AE	2 (8.4) [1.0, 30.5]	0	4 (8.6) [2.3, 22.0]	3 (5.7) [1.2, 16.6]	5 (9.4) [3.1, 22.0]
Any serious AE	4 (16.9) [4.6, 43.2]	5 (12.2) [4.0, 28.4]	7 (15.1) [6.1, 31.0]	7 (13.2) [5.3, 27.2]	8 (15.1) [6.5, 29.7]
Any AE leading to discontinuation of study drug	5 (21.1) [6.8, 49.2]	1 (2.4) [0.1, 13.6]	3 (6.5) [1.3, 18.9]	2 (3.8) [0.5, 13.6]	3 (5.7) [1.2, 16.5]
Any severe AE	7 (29.5) [11.9, 60.8]	6 (14.6) [5.4, 31.8]	5 (10.8) [3.5, 25.1]	6 (11.3) [4.2, 24.7]	5 (9.4) [3.1, 22.0]
Any AE with reasonable possibility of being related to study drug$	30 (126.5) [85.4, 180.7]	31 (75.5) [51.3, 107.1]	33 (71.0) [48.9, 99.7]	44 (83.1) [60.4, 111.5]	36 (67.8) [47.5, 93.9]
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 J

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=116)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=208)	UPA 15 mg QD (N=242)	UPA 30 mg QD (N=237)
Subgroup: >= 6 - < 9 Month (Cont.)					
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#	0/23.7	0/41.1	0/46.5	0/53.0	0/53.1
Deaths occurring <= 30 days after last dose of study drug	0/23.7	0/41.1	0/46.5	0/53.0	0/53.1
Deaths occurring > 30 days after last dose of study drug	0/23.7	0/41.1	0/46.5	0/53.0	0/53.1
COVID-19 infection related deaths	0/23.7	0/41.1	0/46.5	0/53.0	0/53.1

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 J

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=75)	UPA 15 mg QD (N=143)	UPA 30 mg QD (N=166)	UPA 15 mg QD (N=188)	UPA 30 mg QD (N=189)
Subgroup: >= 9 - < 12 Month					
Exposure-adjusted event rate:	(PYs=15.7)	(PYs=29.9)	(PYs=35.4)	(PYs=41.7)	(PYs=40.5)
	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)	54 (344.1) [258.5, 449.0]	57 (190.6) [144.4, 247.0]	60 (169.3) [129.2, 218.0]	83 (199.2) [158.6, 246.9]	85 (210.1) [167.8, 259.8]
COVID-19 infection related AE	1 (6.4) [0.2, 35.5]	1 (3.3) [0.1, 18.6]	2 (5.6) [0.7, 20.4]	2 (4.8) [0.6, 17.3]	2 (4.9) [0.6, 17.9]
Any serious AE	4 (25.5) [6.9, 65.3]	0	2 (5.6) [0.7, 20.4]	0	3 (7.4) [1.5, 21.7]
Any AE leading to discontinuation of study drug	1 (6.4) [0.2, 35.5]	1 (3.3) [0.1, 18.6]	2 (5.6) [0.7, 20.4]	2 (4.8) [0.6, 17.3]	2 (4.9) [0.6, 17.9]
Any severe AE	4 (25.5) [6.9, 65.3]	0	3 (8.5) [1.7, 24.7]	0	3 (7.4) [1.5, 21.7]
Any AE with reasonable possibility of being related to study drug$	13 (82.8) [44.1, 141.7]	15 (50.2) [28.1, 82.7]	20 (56.4) [34.5, 87.2]	28 (67.2) [44.7, 97.1]	28 (69.2) [46.0, 100.0]
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 J

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=75)	UPA 15 mg QD (N=143)	UPA 30 mg QD (N=166)	UPA 15 mg QD (N=188)	UPA 30 mg QD (N=189)
Subgroup: >= 9 - < 12 Month (Cont.)					
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#	0/15.7	0/29.9	0/35.4	0/41.7	0/40.5
Deaths occurring <= 30 days after last dose of study drug	0/15.7	0/29.9	0/35.4	0/41.7	0/40.5
Deaths occurring > 30 days after last dose of study drug	0/15.7	0/29.9	0/35.4	0/41.7	0/40.5
COVID-19 infection related deaths	0/15.7	0/29.9	0/35.4	0/41.7	0/40.5

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. 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 J

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=21)	UPA 15 mg QD (N=45)	UPA 30 mg QD (N=51)	UPA 15 mg QD (N=122)	UPA 30 mg QD (N=137)
Subgroup: >= 12 - < 15 Month					
Exposure-adjusted event rate:	(PYs=0.4)	(PYs=0.6)	(PYs=1.0)	(PYs=24.1)	(PYs=29.7)
	Events (E/100PYs) [95% CI]	Events (E/100PYs) [95% CI]	Events (E/100PYs) [95% CI]	Events (E/100PYs) [95% CI]	Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any adverse event (AE)	2 (487.0) [59.0, 1759.2]	0	7 (680.0) [273.4, 1401.0]	53 (220.0) [164.8, 287.7]	97 (327.0) [265.2, 399.0]
COVID-19 infection related AE	0	0	0	0	1 (3.4) [0.1, 18.8]
Any serious AE	0	0	0	1 (4.2) [0.1, 23.1]	0
Any AE leading to discontinuation of study drug	0	0	0	3 (12.5) [2.6, 36.4]	0
Any severe AE	0	0	0	1 (4.2) [0.1, 23.1]	3 (10.1) [2.1, 29.6]
Any AE with reasonable possibility of being related to study drug$	0	0	0	14 (58.1) [31.8, 97.5]	40 (134.9) [96.4, 183.6]
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 J

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=21)	UPA 15 mg QD (N=45)	UPA 30 mg QD (N=51)	UPA 15 mg QD (N=122)	UPA 30 mg QD (N=137)
Subgroup: >= 12 - < 15 Month (Cont.)					
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#	0/0.4	0/0.6	0/1.0	0/24.1	0/29.7
Deaths occurring <= 30 days after last dose of study drug	0/0.4	0/0.6	0/1.0	0/24.1	0/29.7
Deaths occurring > 30 days after last dose of study drug	0/0.4	0/0.6	0/1.0	0/24.1	0/29.7
COVID-19 infection related deaths	0/0.4	0/0.6	0/1.0	0/24.1	0/29.7

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. 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 J

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=80)	UPA 30 mg QD (N=103)
Subgroup: >= 15 - < 18 Month					
Exposure-adjusted event rate:	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=17.3) Events (E/100PYs) [95% CI]	(PYs=21.4) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any adverse event (AE)	0	0	0	28 (162.2) [107.8, 234.5]	38 (177.4) [125.5, 243.5]
COVID-19 infection related AE	0	0	0	1 (5.8) [0.1, 32.3]	3 (14.0) [2.9, 40.9]
Any serious AE	0	0	0	1 (5.8) [0.1, 32.3]	3 (14.0) [2.9, 40.9]
Any AE leading to discontinuation of study drug	0	0	0	0	2 (9.3) [1.1, 33.7]
Any severe AE	0	0	0	1 (5.8) [0.1, 32.3]	3 (14.0) [2.9, 40.9]
Any AE with reasonable possibility of being related to study drug$	0	0	0	9 (52.1) [23.8, 99.0]	8 (37.3) [16.1, 73.6]
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 J

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=80)	UPA 30 mg QD (N=103)
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	0/17.3	0/21.4
Deaths occurring <= 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/17.3	0/21.4
Deaths occurring > 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/17.3	0/21.4
COVID-19 infection related deaths	0/0.0	0/0.0	0/0.0	0/17.3	0/21.4

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 J

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=58)	UPA 30 mg QD (N=70)
Subgroup: >= 18 - < 21 Month					
Exposure-adjusted event rate:	(PYs=0.0)	(PYs=0.0)	(PYs=0.0)	(PYs=12.6)	(PYs=13.6)
	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	17 (135.1) [78.7, 216.3]	18 (131.9) [78.2, 208.4]
COVID-19 infection related AE	0	0	0	1 (7.9) [0.2, 44.3]	4 (29.3) [8.0, 75.0]
Any serious AE	0	0	0	1 (7.9) [0.2, 44.3]	2 (14.7) [1.8, 52.9]
Any AE leading to discontinuation of study drug	0	0	0	0	0
Any severe AE	0	0	0	1 (7.9) [0.2, 44.3]	1 (7.3) [0.2, 40.8]
Any AE with reasonable possibility of being related to study drug$	0	0	0	4 (31.8) [8.7, 81.4]	4 (29.3) [8.0, 75.0]
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 J

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=58)	UPA 30 mg QD (N=70)
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	0/12.6	0/13.6
Deaths occurring <= 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/12.6	0/13.6
Deaths occurring > 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/12.6	0/13.6
COVID-19 infection related deaths	0/0.0	0/0.0	0/0.0	0/12.6	0/13.6

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

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=41)	UPA 30 mg QD (N=40)
Subgroup: >= 21 - < 24 Month					
Exposure-adjusted event rate:	(PYs=0.0)	(PYs=0.0)	(PYs=0.0)	(PYs=7.8)	(PYs=6.8)
	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)	0	0	0	14 (180.6) [98.7, 303.0]	7 (102.9) [41.4, 212.0]
COVID-19 infection related AE	0	0	0	1 (12.9) [0.3, 71.9]	1 (14.7) [0.4, 81.9]
Any serious AE	0	0	0	1 (12.9) [0.3, 71.9]	1 (14.7) [0.4, 81.9]
Any AE leading to discontinuation of study drug	0	0	0	0	0
Any severe AE	0	0	0	1 (12.9) [0.3, 71.9]	1 (14.7) [0.4, 81.9]
Any AE with reasonable possibility of being related to study drug$	0	0	0	6 (77.4) [28.4, 168.4]	1 (14.7) [0.4, 81.9]
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 J

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=41)	UPA 30 mg QD (N=40)
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	0/7.8	0/6.8
Deaths occurring <= 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/7.8	0/6.8
Deaths occurring > 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/7.8	0/6.8
COVID-19 infection related deaths	0/0.0	0/0.0	0/0.0	0/7.8	0/6.8

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

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=24)	UPA 30 mg QD (N=16)
Subgroup: >= 24 Month Exposure-adjusted event rate:	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=0.0) Events (E/100PYs) [95% CI]	(PYs=24.8) Events (E/100PYs) [95% CI]	(PYs=5.7) Events (E/100PYs) [95% CI]
Subjects with any treatment-emergent					
Any adverse event (AE)	0	0	0	51 (205.9) [153.3, 270.8]	12 (208.7) [107.8, 364.6]
COVID-19 infection related AE	0	0	0	1 (4.0) [0.1, 22.5]	0
Any serious AE	0	0	0	2 (8.1) [1.0, 29.2]	0
Any AE leading to discontinuation of study drug	0	0	0	1 (4.0) [0.1, 22.5]	0
Any severe AE	0	0	0	2 (8.1) [1.0, 29.2]	0
Any AE with reasonable possibility of being related to study drug$	0	0	0	17 (68.6) [40.0, 109.9]	2 (34.8) [4.2, 125.7]
Any AE leading to death	0	0	0	1 (4.0) [0.1, 22.5]	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. 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 J

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=24)	UPA 30 mg QD (N=16)
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	1/24.8 (4.0) [0.1, 22.5]	0/5.7
Deaths occurring <= 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	1/24.8 (4.0) [0.1, 22.5]	0/5.7
Deaths occurring > 30 days after last dose of study drug	0/0.0	0/0.0	0/0.0	0/24.8	0/5.7
COVID-19 infection related deaths	0/0.0	0/0.0	0/0.0	0/24.8	0/5.7

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. 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.

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表 2.7.4.7-37.

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INTEGRATED SUMMARY OF SAFETY
R&D/20/1310 - CLINICAL/STATISTICAL

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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	381 (712.5)	270 (456.6)	317 (522.4)	318 (450.7)	361 (515.2)
血液およびリンパ系障害	18 (33.7)	19 (32.1)	12 (19.8)	22 (31.2)	15 (21.4)
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)	4 (6.8)	4 (6.6)	4 (5.7)	5 (7.1)
血小板減少症	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 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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.

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TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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.

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TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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	68 (127.2)	37 (62.6)	42 (69.2)	49 (69.4)	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)
便意切迫	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.

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TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)
口唇腫脹	0	0	1 (1.6)	0	1 (1.4)
口腔嚢胞	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 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)
直腸しぶり	1 (1.9)	0	0	0	0
口内炎	3 (5.6)	0	3 (4.9)	0	3 (4.3)
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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	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)
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)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
感染症および寄生虫症	72 (134.6)	66 (111.6)	69 (113.7)	75 (106.3)	77 (109.9)
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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)	3 (5.1)	0	3 (4.3)	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)
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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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 (22.4)	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)
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)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)
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)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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)
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)

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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	38 (71.1)	15 (25.4)	20 (33.0)	21 (29.8)	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)
肋軟骨炎	1 (1.9)	0	0	0	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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)
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)

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
腎および尿路障害 (Cont.)					
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)
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)

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)
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)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)	35 (49.9)
ざ瘡	6 (11.2)	4 (6.8)	6 (9.9)	4 (5.7)	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)
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)

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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)	7 (10.0)
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)	0	1 (1.6)	0	1 (1.4)
皮膚灼熱感	1 (1.9)	0	0	0	0
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)

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

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

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=245) (PYs=53.5) 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.)					
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
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 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month					
Any adverse event	116 (333.3)	130 (251.4)	137 (248.6)	174 (266.7)	165 (261.7)
血液およびリンパ系障害	2 (5.7)	4 (7.7)	2 (3.6)	5 (7.7)	2 (3.2)
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 (3.1)	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	0	1 (1.8)	0	2 (3.2)
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)
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
内分泌障害	0	0	0	1 (1.5)	1 (1.6)
副腎機能不全	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 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
内分泌障害 (Cont.)					
甲状腺腫	0	0	0	1 (1.5)	0
眼障害	1 (2.9)	3 (5.8)	2 (3.6)	3 (4.6)	2 (3.2)
白内障	0	1 (1.9)	0	1 (1.5)	0
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 (103.4)	21 (40.6)	15 (27.2)	30 (46.0)	16 (25.4)
腹部膨満	1 (2.9)	0	1 (1.8)	0	1 (1.6)
腹痛	1 (2.9)	2 (3.9)	1 (1.8)	2 (3.1)	1 (1.6)
下腹部痛	2 (5.7)	0	0	0	0
上腹部痛	0	2 (3.9)	0	2 (3.1)	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 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
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 (71.8)	8 (15.5)	5 (9.1)	13 (19.9)	5 (7.9)
便秘	1 (2.9)	0	2 (3.6)	1 (1.5)	2 (3.2)
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 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
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 (4.6)	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 (11.6)	4 (7.3)	9 (13.8)	8 (12.7)
胸痛	0	1 (1.9)	1 (1.8)	1 (1.5)	2 (3.2)
疲労	0	0	0	1 (1.5)	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 (3.2)

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 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
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 (5.8)	1 (1.8)	4 (6.1)	2 (3.2)
肝胆道系障害	0	1 (1.9)	0	2 (3.1)	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 (74.7)	33 (63.8)	46 (83.5)	40 (61.3)	55 (87.2)
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 J

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

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
気管支炎	0	3 (5.8)	0	4 (6.1)	0
COVID-19	2 (5.7)	0	2 (3.6)	0	2 (3.2)
COVID-19肺炎	1 (2.9)	0	2 (3.6)	0	2 (3.2)
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 (3.2)
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 (3.2)
歯肉膿瘍	0	0	1 (1.8)	0	1 (1.6)

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

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
帯状疱疹	0	4 (7.7)	2 (3.6)	5 (7.7)	3 (4.8)
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 (4.8)
喉頭炎	1 (2.9)	0	0	0	1 (1.6)
上咽頭炎	5 (14.4)	5 (9.7)	9 (16.3)	5 (7.7)	9 (14.3)
口腔ヘルペス	1 (2.9)	3 (5.8)	1 (1.8)	3 (4.6)	2 (3.2)
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 (3.2)
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
肺炎	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 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
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 (3.9)	0	2 (3.1)	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 (3.2)
歯膿瘍	0	1 (1.9)	0	2 (3.1)	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 (4.8)
尿路感染	1 (2.9)	2 (3.9)	1 (1.8)	4 (6.1)	1 (1.6)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
感染症および寄生虫症 (Cont.)					
水痘帯状疱疹ウイルス感染	0	1 (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 (3.2)
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 (5.8)	2 (3.6)	3 (4.6)	2 (3.2)
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 (3.9)	0	2 (3.1)	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	1 (1.8)	0	1 (1.6)
臨床検査	5 (14.4)	18 (34.8)	16 (29.0)	22 (33.7)	18 (28.5)
アラニンアミノトランスフェラーゼ増加	0	2 (3.9)	1 (1.8)	2 (3.1)	1 (1.6)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
臨床検査 (Cont.)					
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 (3.9)	1 (1.8)	2 (3.1)	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 (3.2)
血中クレアチンホスホキナーゼ増加	1 (2.9)	1 (1.9)	7 (12.7)	1 (1.5)	7 (11.1)
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
握力低下	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 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
臨床検査 (Cont.)					
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 (3.2)
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 (3.9)	1 (1.8)	3 (4.6)	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 (3.1)	0
尿中白血球陽性	0	1 (1.9)	0	1 (1.5)	0
代謝および栄養障害	1 (2.9)	6 (11.6)	4 (7.3)	7 (10.7)	4 (6.3)
食欲減退	0	0	0	1 (1.5)	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
代謝および栄養障害 (Cont.)					
脂質異常症	0	3 (5.8)	0	3 (4.6)	0
痛風	0	1 (1.9)	0	1 (1.5)	0
高コレステロール血症	0	2 (3.9)	1 (1.8)	2 (3.1)	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 (3.2)
筋骨格系および結合組織障害	18 (51.7)	5 (9.7)	5 (9.1)	10 (15.3)	7 (11.1)
強直性脊椎炎	1 (2.9)	0	0	0	0
関節痛	4 (11.5)	2 (3.9)	1 (1.8)	3 (4.6)	2 (3.2)
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
軟骨軟化症	0	0	1 (1.8)	0	1 (1.6)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.
[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).
[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
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
腱痛	1 (2.9)	0	0	0	0

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

Program Source Code: [redacted]

TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
筋骨格系および結合組織障害 (Cont.)					
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 (3.9)	2 (3.6)	2 (3.1)	4 (6.3)
基底細胞癌	0	0	2 (3.6)	0	3 (4.8)
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)
神経系障害	2 (5.7)	7 (13.5)	6 (10.9)	8 (12.3)	7 (11.1)
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 (4.8)
頭痛	1 (2.9)	3 (5.8)	1 (1.8)	4 (6.1)	1 (1.6)
感覚鈍麻	0	1 (1.9)	0	1 (1.5)	0
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)

Note: Treatment-emergent adverse events are adverse events with an onset date on or after the first dose of study drug in the maintenance period and up to 30 days past the last dose of study drug in the maintenance period or until one day prior to the first dose of study drug in the LTE period (for Cohort 1) and up to 30 days after the last dose of study drug in the maintenance or LTE period or until one day prior to the first dose of study drug in which the subject's dose was changed during the LTE period.
E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

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TABLE 2.4 6.1.3 J

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years by Primary MedDRA System Organ Class and Preferred Term by Onset of Adverse Events in 3-Month Interval
(Responders Maintenance Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	M14-234 Substudy 3 (Cohort 1) [A] Placebo QD (N=168) (PYs=34.8) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 15 mg QD (N=221) (PYs=51.7) Events (E/100PYs)	M14-234 Substudy 3 (Cohort 1) [A] UPA 30 mg QD (N=232) (PYs=55.1) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 15 mg QD (N=279) (PYs=65.2) Events (E/100PYs)	M14-234 Substudy 3 (Cohorts 1 and 3) [B] UPA 30 mg QD (N=267) (PYs=63.1) Events (E/100PYs)
Subgroup:>= 3 - < 6 Month (Cont.)					
神経系障害 (Cont.)					
錯感覚	0	0	1 (1.8)	0	1 (1.6)
精神障害	6 (17.2)	1 (1.9)	2 (3.6)	4 (6.1)	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 (3.1)	0
不眠症	1 (2.9)	0	1 (1.8)	1 (1.5)	2 (3.2)
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 (3.1)	3 (4.8)
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
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)

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E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 mg QD during induction and were re-randomized to PBO, 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 1).

[B] Includes 15 mg and 30 mg subjects from Cohort 1 plus M14-234 substudy 2 (Part 2) and M14-675 (Part 2) 45/45 mg responders who were re-randomized to 15 mg or 30 mg and entered into M14-234 substudy 3 (Cohort 3) and additional time from M14-533 while subject remained on same double-blind dose.

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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
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Subgroup:>= 3 - < 6 Month (Cont.)					
腎および尿路障害 (Cont.)					
尿閉	0	1 (1.9)	0	1 (1.5)	0
生殖系および乳房障害	0	3 (5.8)	2 (3.6)	3 (4.6)	2 (3.2)
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
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 (11.5)	3 (5.8)	5 (9.1)	6 (9.2)	7 (11.1)
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)
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 (4.6)	2 (3.2)

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E/100PYs = Number of events per 100 patient-years.

[A] Includes all subjects who responded to UPA 45 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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