Age at AE Onset 4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 166): Alanine Aminotransferase: 19 [12 - 65] U/L; Alkaline Phosphatase: 110 [38 - 126] U/L; Aspartate Aminotransferase: 15 [15 - 37] U/L; Bilirubin: 3.420778 [0 - 20.524668] UMOL/L; Blood Urea Nitrogen: 4.99758 [2.14182 - 8.56728] MMOL/L; Calcium: 2.320443 [2.120835 - 2.569953] MMOL/L; Chloride: 108 [97 - 109] MMOL/L; Creatinine: 76.910836 [44.20163 - 132.60489] UMOL/L; Glucose: 5.661714 [3.607955 - 5.495193] MMOL/L; Hematocrit: 0.374 [0.34 - 0.466] FRACTION OF 1; Hemoglobin: 124 [111 - 159] G/L; Leukocytes: 6.4 [3.4 - 10.8] 10^9/L; NPTST136-CO2: 23 [22 - 32] MEQ/L; NPTST416-PT/INR: 0.9 [0.8 - 1.1] UNIT NOT KNOWN; Platelets: 277 [150 - 379] 10^9/L; Potassium: 3.6 [3.5 - 5.2] MMOL/L; Protein: 72 [63 - 83] G/L; Sodium: 144 [134 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 166): CT CHEST: POSITIVE FOR BILATERAL PULMONARY THROMBOEMBOLI WITH FINDINGS SUGGESTIVE OF RIGHT HEART STRAIN. CONSIDER ECHOCARDIOGRAPHY FOR FURTHER EVALUATION. SLIDING-TYPE HIATAL HERNIA WITH THICKENING OF THE DISTA L INTRATHORACIC ESOPHAGUS THAT MAY BE RELATED TO ESOPHAGITIS OR GERD. ENDOSCOPY OR ESOPHAGOGRAPHY MAY BE HELPFUL IN FURTHER EVALUATION.; [redacted]20[redacted] (RX DAY 170): ECHOCARDIOGRAM: THE LEFT VENTRICULAR SYSTOLIC FUNCTION IS NORMAL (55-65%). GRAD I (MILD) LEFT VENTRICULAR DIASTOLIC DYSFUNCTION PRESENT, CONSISTENT WITH IMPAIRED RELAXATION. THE SINUSES OF VALSALVA ARE MILDLY DILATED . THE RIGHT ATRIUM IS MILDLY DILATED. THE LEFT ATRIUM IS MILDLY DILATED. MILD AORTIC VALVE REGURGITATION.

AE Stopped Initial Rx Day	227
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，敗血症及び RS ウイルス感染の事象を発現した。関連

する病歴は，ベンゾジアゼピン中毒，高血圧，尿路感染症の再発及び潰瘍性大腸炎であった。

Event 1 の臨床経過：

投与28日後＊，被験者は敗血症及び RS ウイルス感染を発現した。投与31日後＊，敗血症及びRS ウイルス感染は消失した。

投与28日後＊，被験者は意識障害を呈し，自分の近況を思い出せない状態で救急治療室を受診した。被験者は胸部 X 線検査及び頭部 CT 検査を受け，入院前に救急科で輸液，ゾシン及び cipro を投与された。腰椎穿刺が試みられたが，被験者の体質のために成功しなかった。被験者は輸液の静脈内投与及び抗生物質の経験的治療を開始し，その後改善した。投与31日後＊，被験者は退院した。被験者は退院にあたり，治験薬の投与を再開した。

投与された薬剤は，塩化ナトリウム 0.9%，アセトアミノフェン，ゾシン，cipro 及びオキシコドンであった。

The patient's past medications include:

CIPRO for UTI ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

FLAGYL for UTI ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Sepsis (10040047) (Sepsis (10040047)) [v.20.0] [10040047]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2) Respiratory syncytial virus infection (10061603) (Respiratory syncytial virus infection (10061603)) [v.20.0] [10061603]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of SEPSIS

- Investigator: N/A

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** Low lung volumes and mild infiltrate in left mid lung and potential very mild medial right basilar infiltrate.

[redacted] **20[redacted] CREATININE:** 2.64 mg/dL (normal 0.5 to 1.5)

[redacted] **20[redacted] HEAD CT:** Mild motion artifact but no acute intracranial abnormali

[redacted] **20[redacted] WBC:** 20.3 K/UL (normal 3.8 to 12.8)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺塞栓症の事象を発現した。関連する病歴は，双極性障害，ベンゾジアゼピン中毒，線維筋痛，高血圧，骨粗鬆症，尿路感染症の再発，潰瘍性大腸炎，元喫煙者（1 日 0.5 箱を 1 年間），不安状態，特定不能の慢性疼痛症候群，電子タバコの喫煙者（1 日 10 回を 1 年間），過性脳虚血発作の家族歴（母親），及び心筋梗塞の家族歴（父親）であった。被験者には高血圧の家族歴もあった。

Event 2 の臨床経過：

投与225日後＊，被験者は肺塞栓症を発現した。投与227日後＊，肺塞栓症は消失した。

投与224日後＊，被験者は息切れ及びめまいを感じて起床した。投与225日後＊，症状が持続したため，被験者は救急科を受診した。被験者は胸部不快感及び胸部痛，頭痛，並びに両腕の脱力も訴えた。被験者は，発熱，悪寒，悪心，嘔吐，下痢，咳嗽及び排尿困難はなかった。投与225日後＊ ，造影剤を用いた胸部 CT 肺血管造影を受け，右心の緊張を示唆する所見を伴う両側の肺血栓塞栓症が認められた。被験者は，下肢の腫脹はなかった。下肢に外傷はなく，深部静脈血栓症や肺塞栓症の病歴もなく，ふくらはぎの圧痛もなかった。同日，被験者は入院した。入院時の身体検査では，急性型の苦痛はなく，A/O は x4 であり，心拍は規則的な数及びリズムであり，心雑音，奔馬音及び擦過音があり，聴診時には両肺の音は明瞭で，笛音，水泡音及びラ音はなく，呼吸努力は通常であった。脈拍は均等で，両側の四肢に浮腫はなかった。

投与226 日後＊，被験者の症状は改善していた。被験者は完全な文章で会話し，飲食し，歩行し，正常血圧で，室内気で呼吸していた。投与227日後＊，被験者は退院し，その後 6 ヵ月間，エリキュースを経口投与された。

治験責任医師によると，被験者は座りがちではなく，現在喫煙しておらず，ホルモン補充も行っていなかった。また，長時間の旅行にも行っていなかった。

投与された薬剤は，エリキュース及び lovenox であった。

The patient's past medications include:

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

SOLUMEDROL for ULCERATIVE COLITIS ([redacted])

CIPRO for ULCERATIVE COLITIS, URINARY TRACT INFECTION and SEPSIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

INFLUENZA VIRUS VACCINE for UNKNOWN INDICATION

MELOXICAM for UNKNOWN INDICATION

PENICILLIN for UNKNOWN INDICATION

SALSALATE for UNKNOWN INDICATION

ZOFRAN for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.20.1] [10037377]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of PULMONARY EMBOLISM

- **Investigator:** Not Applicable

- **AbbVie:** Not Applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BASOPHILS ABS:** 0.1 TH/mm3 (normal <0.1)

[redacted] **20[redacted] BLOOD PRESSURE:** 143/89 mmHg

[redacted] **20[redacted] BODY TEMPERATURE:** 36.6 Degrees C

[redacted] **20[redacted] BUN:** 14 mg/dL (normal 6 to 24)

[redacted] **20[redacted] CALCIUM:** 9.3 mg/dL

[redacted] **20[redacted] CHEST X-RAY:** Norma no acute cardiopulmonary pathology

[redacted] **20[redacted] CHEST X-RAY:** The heart does not appear significantly enlarged. There ware long lung volumes,. There is mild infiltrate in the left mid lung and potential very mild medial right basilar infiltrate.

[redacted] **20[redacted] CHLORIDE:** 108 MMOL/L (normal 97 to 109)

[redacted] **20[redacted] CO2:** 23 MMOL/L

[redacted] **20[redacted] CREATININE:** 0.87 mg/dL

[redacted] **20[redacted] CT PULMONARY ANGIOGRAM OF THE CHEST WITH CONTRAST:** Positive for bilateral pulmonary thromboemboli with findings suggestive of right heart strain. Consider echocardiography for further evaluation. Sliding-type hiatal hernia with thickening of the distal intrathoracic esophagus that may be related to esophagitis or gerd. Endoscopy or esophagography may be helpful in further evaluation.

[redacted] **20[redacted] ECHOCARDIOGRAM:** The left ventricular systolic function is normal (55-65%). Grad I (mild) left ventricular diastolic dysfunction present, consistent with impaired relaxation. The sinuses of valsalva are mildly dilated. The right atrium is mildly dilated. The left atrium is mildly dilated. Mild aortic valve regurgitation

[redacted] **20[redacted] EKG:** Normal sinus rhythm. Essentially normal EKG. No S1Q3T3 pattern that sometimes seen with acute pulmonary embolus. Patient may have a little bit of a nubbin of a Q-wave in 3.

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Normal

[redacted] **20[redacted] EOSINOPHILS ABS:** 0 (normal <0.7)

[redacted] **20[redacted] GLUCOSE:** 102 mg/dL

[redacted] **20[redacted] HEMATOCRIT:** 37.4 % (normal 34.0 to 46.0)

[redacted] **20[redacted] HEMOGLOBIN:** 12.4 G/DL (normal 11.1 to 15.9)

[redacted] **20[redacted] INR:** 0.9 No units (normal 0.8 to 1.1)

[redacted] **20[redacted] PLATELET COUNT:** 241 10^3/uL (normal 150 to 379)

[redacted] **20[redacted] PLATELET COUNT:** 277 10^3/uL (normal 150 to 379)

[redacted] **20[redacted] POTASSIUM:** 3.6 MMOL/L (normal 3.5 to 5.2)

[redacted] **20[redacted] PULSE:** 100 bpm

Unknown date QUANTIFERON-TB: Negative

[redacted] **20[redacted] RED BLOOD CELLS:** 3.9 10^6/uL (normal 3.77 to 5.28)

[redacted] **20[redacted] RESPIRATORY RATE:** 18 /min

[redacted] **20[redacted] SODIUM:** 144 MMOL/L (normal 134 to 145)

[redacted] **20[redacted] SPO2 (Room Air):** 94 %

[redacted] **20[redacted] WBC:** 6.4 10^3/uL (normal 3.4 to 10.8)

[redacted] **20[redacted] WBC:** 8.8 10^3/uL (normal 3.4 to 10.8)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
関節炎	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
OTHER: ENLARGED THYROID GLAND.	20[redacted]
OTHER: REACTIVE ARTHRITIS	20[redacted]
OTHER: REACTIVE ASYMPTOMATIC BACTERIURIA	20[redacted]
SEIZURE DISORDER/CONVULSIONS: THIS WAS DURING CHILDHOOD, NO NEUROLOGICAL EPISODES AFTER PUBERTY.	19[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 224	224

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	25 mg	1 time per week	Y-M: 20[redacted]
MESALAZINE	1.2 mg	QD	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
PARACETAMOL	650.000 mg	PRN	Y-M: 20[redacted] / -324
ADALIMUMAB	40.000 mg/kg	ONCE A WEEK	Y-M: 20[redacted] / -341
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -170
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted] / -46
CEFALEXIN	500 mg	BID	Y-M: 20[redacted] / -67

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1.2 mg	QD	Y-M: 20[redacted]	ONGOING
PREDNISONE	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / -1
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 15
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 30
METHYLPREDNISOLONE	4 mg	OTHER: TID X 3 DAYS,BIDX 3 DAYS,QDX 3 DAYS AND OFF	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 39
OMEPRAZOLE	20 mg	PRN	Y-M: 20[redacted] / 31	ONGOING
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / 43	ONGOING
CAFFEINE;CODEINE;PARACETAMOL;PIPERYLONE	1 PACK mL	TID	Y-M: 20[redacted] / 195	Y-M: 20[redacted] / 203

Event #1: Serious Adverse Event

Event Description	ARTHRITIS OF THE KNEE
Preferred term	関節炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 70

Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 24): ARTHROCENTESIS: FLUID WAS REMOVED FROM THE JOINT TO RELIEVED THE PAIN AND THE INFLAMMATION.	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	WORSENING OF PRE- EXISTING ARTHRITIS.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，膝の関節炎の事象を発現した。関連する病歴は，潰瘍性大腸炎及び反応性関節炎であった。被験者には潰瘍性大腸炎の家族歴もあった。

Event 1 の臨床経過：

投与70日後＊，被験者は膝の関節炎を発現した。

被験者は，潰瘍性大腸炎に反応した関節炎を患っていた。この重篤な有害事象に関連する徴候及び症状は，疼痛，運動制限及び炎症であった。投与80日後＊ ，関節穿刺が 2 度実施された。疼痛及び炎症を和らげるために関節から液体が除去され，被験者はステロイドの投与を再開した。年月不明日に，関節穿刺が再び行われた。

投与された薬剤は，メドロール，omeprazol 及び prednisone であった。

The patient's past medications include:

METHOTREXATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Knee arthritis (10067624) (Arthritis (10003246)) [v.20.1] [10067624]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of ARTHRITIS OF THE KNEE

- Investigator: Worsening of pre-existing arthritis.

- AbbVie: The event is related to a pre-existing condition

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
結腸異形成	X	X		
肺塞栓症	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	5[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: INTERMITTENT FEVER, RELATED TO STUDY CONDITION	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: BIOPSY, COLON	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	More than 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 2	2

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	NOT REPORTED	EVERY OTHER WEEK	Y-M: 20[redacted]
INFLIXIMAB	5.000 mg/kg	EVERY 8 WEEKS	Y-M: 20[redacted]
PREDNISONE	35 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300.000 mg	2 WEEKS	Y-M: 20[redacted]
LOPERAMIDE	UNK mg	PRN	Y-M: 20[redacted] / -271
DICYCLOVERINE	20 mg	BID	Y-M: 20[redacted] / -106
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / -55
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -18
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -26
IRON	300 mg	OTHER: 3 TIMES	Y-M: 20[redacted] / -27
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -33
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / -11
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -4
MESALAZINE	4.8 g	QD	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LOPERAMIDE	UNK mg	PRN	Y-M: 20[redacted] / -271	ONGOING
DICYCLOVERINE	20 mg	BID	Y-M: 20[redacted] / -106	ONGOING
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / -55	Y-M: 20[redacted] / -31
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -18	Y-M: 20[redacted] / -12
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -26	Y-M: 20[redacted] / -19
IRON	300 mg	OTHER: 3 TIMES	Y-M: 20[redacted] / -27	Y-M: 20[redacted] / -13
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -33	Y-M: 20[redacted] / -27
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / -11	Y-M: 20[redacted] / -5
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -4	Y-M: 20[redacted] / 4
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 12
ENOXAPARIN	90 mg	BID	Y-M: 20[redacted] / 35	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	HIGH GRADE DYSPLASIA IN LEFT COLON
Preferred term	結腸異形成
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY -1): NPTST474-SURGICAL PATHOLOGY: FOCAL HIGH GRADE DYS [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY -1): BIOPSY, COLON: LEFT COLON, FOCAL HIGH GRADE DYSPLASIA; [redacted]20[redacted] (RX DAY 36): COLECTOMY: DISCHARGED [redacted]/[redacted]/20[redacted]

AE Stopped Initial Rx Day	93 (34 DAYS AFTER LAST TREATMENT)
Duration of AE	37 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 88 (29 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 29): CT CHEST/ABDOMEN/PELVIS WITH CONTRAST: CT COLONIC FINDINGS CONSISTENT WITH KNOWN ULCERATIVE COLITIS AND WITHOUT EVIDENCE OF MASS, COMPLICATIONS, OR METASTASIS IN ABDOMEN OR PELVIS. INCIDENTAL NEAR COMPLETELY OCCLUSIVE SEGMENTAL ACUTE PU LMONARY EMBOLI BILATERALLY. NO EVIDENCE OF HEART STRAIN OR PULMONARY INFARCT.; [redacted]20[redacted] (RX DAY 35): RETRIEVABLE IVC FILTER PLACED: FILTER PLACED AND PROCEDURE

WELL TOLERATED, CONVENTIONAL CAVAL ANATOMY	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SEVERE UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Generated: [redacted]20[redacted]:16:18
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左結腸の高度異形成の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 4 杯以上）であった。

Event 1 の臨床経過：

投与57日後＊，被験者は左結腸の高度異形成を発現した。投与93日後＊，左結腸の高度異形成は消失した。

本事象発現前に，被験者は潰瘍性大腸炎の症状の悪化を経験していた。投与57日後＊，結腸内視鏡検査における病理組織学的検査で，高度異形成が確認された。治験薬の投与は完全に中止され，結腸切除術が計画された。投与86日後＊ ，結腸切除術前の画像診断で，両側の肺塞栓が確認され，被験者は回収型下大静脈フィルターを留置された。投与92日後＊ ，被験者は高度異形成のための腹腔内結腸切除術を受けるため，入院した。投与93日後＊ ，被験者は腹腔内結腸全摘術を受けた。結腸切除術の病理組織学的検査では，潰瘍性大腸炎に対応する活動期の慢性大腸炎の所見が著しく認められた。組織は，軽度異形成及び局所的には高度異形成を示していた。癌の徴候は認められなかった。組織の断端では，異形成は認められなかった。また，虫垂では線維性の閉塞が認められた。投与98日後＊，被験者は退院した。

診療記録によると，被験者は結腸切除術によく耐え，術後の経過に問題はなかった。痛みは自己調節鎮痛法での麻酔薬でコントロールされ，その後経口鎮痛薬に移行した。また，電解質の状態が注意深く観察され，必要に応じて水分を補給した。腸の機能が回復したため経口食を開始し，摂取できた。ストーマの管理を行う看護師と協力してストーマの管理を行った。退院時，被験者は悪心や嘔吐もなく経口食を摂取し，痛みは経口の鎮痛薬で十分に管理され，予想通りに歩行及び排泄が可能であった。

The patient's past medications include:

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VENOFER for ULCERATIVE COLITIS / IRON DEFICIENCY ANEMIA and ULCERATIVE COLITIS / IRON DEFICIENCY ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

MESALAMINE for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) Colon dysplasia (10071161) (Colon dysplasia (10071161)) [v.21.0] [10071161]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of HIGH GRADE DYSPLASIA IN LEFT COLON

- Investigator: Not applicable

- AbbVie: Weak temporal association with close to 2 months of study drug exposure. Additional risk factors include pre-existing ulcerative colitis and alcohol consumption of more than 4 drinks per day.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BICARB:** 23 no units

[redacted] **20[redacted] BIOPSY, COLON:** Left colon, focal high grade dysplasia

[redacted] **20[redacted] BODY TEMPERATURE:** 98.5 degrees F

[redacted] **20[redacted] BUN:** 12 no units

[redacted] **20[redacted] CALCIUM:** 8.9 no units

[redacted] **20[redacted] CL:** 101 no units

[redacted] **20[redacted] COLONOSCOPY:** High grade dysplasia

[redacted] **20[redacted] CREATININE:** 0.99 no units

[redacted] **20[redacted] CT CHEST/ABDOMEN/PELVIS WITH CONTRAST:** CT colonic findings consistent with known ulcerative colitis and without evidence of mass, complications, or metastasis in abdomen or pelvis. Incidental near completely occlusive segmental acute pulmonary emboli bilaterally. No evidence of heart strain or pulmonary infarct.

[redacted] **20[redacted] HCT:** 35 no units

[redacted] **20[redacted] HGB:** 11.3 no units

[redacted] **20[redacted] K:** 3.9 no units

[redacted] **20[redacted] NA:** 140 no units

[redacted] **20[redacted] PLT:** 348 no units

[redacted] **20[redacted] WBC:** 10.8 no units
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺塞栓症の事象を発現した。関連する病歴は，広範囲な潰瘍性大腸炎（全大腸炎型），非喫煙者及び現飲酒者（1 日 4 杯以上）であった。

Event 2 の臨床経過：

投与88日後＊，被験者は肺塞栓症を発現した。

被験者は，投与88日後＊に行われた術前の画像診断で確認された肺塞栓症に対して，投与92日後＊　に回収型下大静脈フィルターを留置された。被験者には本事象に関連する徴候及び症状はなく，本事象は術前の画像診断で発見された。被験者は，投与93日後＊に予定された結腸摘出術を受け，抗凝固療法を開始し，投与98日後＊に退院した。

投与された薬剤は，エノキサパリンであった。

The patient's past medications include:

MESALAMINE for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for WORSENING OF ULCERATIVE COLITIS SYMPTOMS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ACETAMINOPHEN for WORSENIG OF ULCERATIVE COLITIS SYMPTOMS and FEVER ([redacted] 20[redacted] - [redacted] 20[redacted])

VENOFER for ULCERATIVE COLITIS and IRON DEFICIENCY ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1)　Pulmonary embolism (10037377)　(Pulmonary embolism (10037377))　[v.21.0]　[10037377]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of PULMONARY EMBOLISM

- Investigator: Severe UC

- AbbVie: Lack of temporal association. Last dose of study drug was approximately one month prior to onset of event.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT CHEST/ABDOMEN/PELVIS WITH CONTRAST:** CT COLONIC FINDINGS CONSISTENT WITH KNOWN ULCERATIVE COLITIS AND WITHOUT EVIDENCE OF MASS, COMPLICATIONS, OR METASTASIS IN ABDOMEN OR PELVIS. INCIDENTAL NEAR COMPLETELY OCCLUSIVE SEGMENTAL ACUTE PULMONARY EMBOLI BILATERALLY. NO EVIDENCE OF HEART STRAIN OR PULMONARY INFARCT.

[redacted] **20[redacted] TRANSTHORACIC ECHOCARDIOGRAM:** Pericardium and non cardiac findings: There is no pericardial effusion. Left ventricle is normal in size with normal systolic function. Normal diastolic function Right ventricle appears mildly enlarged with normal systolic function. Mild bilateral enlargement No significant valvular disease identified

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
不安	X			
うつ病	X			
精神障害	X			
自殺念慮	X			

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
DIABETES MELLITUS: BORDERLINE	NOT REPORTED
EXTENSIVE UC/PANCOLITIS	20[redacted]
MIGRAINE HEADACHE	20[redacted]
OTHER: BIPOLAR	NOT REPORTED
OTHER: DRUG ALLERGY TO ASOCOL	20[redacted]
OTHER: DRUG ALLERGY TO ASPIRIN	20[redacted]
OTHER: DRUG ALLERGY TO CODINE	20[redacted]
OTHER: DRUG ALLERGY TO REMICADE	20[redacted]
OTHER: DRUG ALLERGY TO TRAMADOL	20[redacted]
OTHER: NEUROPATHY	20[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: HIGH CHOLESTEROL	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: HYSTERECTOMY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	1	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			

PIPES	NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 54	54
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 364	364

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
GABAPENTIN	300 mg	QD	Y-M: 20[redacted] / -175
MESALAZINE	1600 mg	BID	Y-M: 20[redacted] / -91
MESALAZINE	800.000 mg	NOT REPORTED	Y-M: 20[redacted] / -91
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	5.86 g	OTHER: ONCE	Y-M: 20[redacted] / -64
MACROGOL 3350	17 g	PRN	Y-M: 20[redacted] / -74
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	5.86 g	OTHER: ONCE	Y-M: 20[redacted] / -1
NAPROXEN	500 mg	OTHER: BIDPRN	Y-M: 20[redacted] / -2
SIMVASTATIN	20 mg	QD	Y: 20[redacted]
TOPIRAMATE	200 mg	BID	Y: 20[redacted]
TRAZODONE	50 mg	QD	Y: 20[redacted]
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y: 20[redacted]
FLUPHENAZINE	25 mg	OTHER: Q MONTHLY	Y: 20[redacted]
VENLAFAXINE	75 mg	QD	Y: 20[redacted]
BENZATROPINE	1 mg	QD	Y: 20[redacted]
GOLIMUMAB	200.000 mg	QMONTH	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
			RX Day	
GABAPENTIN	300 mg	QD	Y-M: 20[redacted] / -175	ONGOING
PARACETAMOL	1000 mg	OTHER: Q8 HRS PRN	Y-M: 20[redacted] / 59	ONGOING
RIZATRIPTAN	10 mg	PRN	Y-M: 20[redacted] / 79	ONGOING
ZOLPIDEM	5 mg	QD	Y-M: 20[redacted] / 117	ONGOING
SIMVASTATIN	20 mg	QD	Y: 20[redacted]	ONGOING
TOPIRAMATE	200 mg	BID	Y: 20[redacted]	ONGOING
TRAZODONE	50 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 117
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING
FLUPHENAZINE	25 mg	OTHER: Q MONTHLY	Y: 20[redacted]	ONGOING
VENLAFAXINE	75 mg	QD	Y: 20[redacted]	ONGOING
BENZATROPINE	1 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	PSYCHIATRIC PROBLEMS, INCREASE DEPRESSION, INCREASE ANXIETY, SUICIDAL IDEATION
Preferred term	不安，うつ病，精神障害，自殺念慮
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 167
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY -10): Chloride: 104 [102 - 112] MMOL/L; [redacted]20[redacted] (RX DAY 113): Alanine Aminotransferase: 11 [5 - 55] U/L; Albumin: 45 [30 - 45] G/L; Alkaline Phosphatase: 59 [37 - 59] U/L; Aspartate Aminotransferase: 14 [8 - 42] U/L; Bilirubin: 3.420778 [5.131167 - 20.524668] UMOL/L; Blood Urea Nitrogen: 4.64061 [1.78485 - 8.92425] MMOL/L; Calcium: 2.395296 [2.170737 - 2.669757] MMOL/L; Creatinine: 76.910836 [26.520978 - 123.764564] UMOL/L; Glucose: 5.772728 [3.88549 - 6.10577] MMOL/L; NPTST016-ALBUMIN/GLOBULIN RATIO: 1.5 [1 - 20] G/DL; NPTST028-ANION GAP: 10.0 [3 - 11] MMOL/L; NPTST074-BUN/CREA RATIO: 15 [7 - 25] MG/DL; NPTST086-CA CORRECTED: 9.2 [8.7 - 10.7] MG/DL; NPTST190-EGFR AFRICAN AMERICAN: > 60 [60 - 60] UNIT NOT REPORTED; NPTST191-EGFR NON AFRICAN: >60 [60 - 60] UNIT NOT REPORTED; NPTST242-GLOBULIN: 3.1 [2.2 - 4] G/DL; Potassium: 3.5 [3.5 - 5.3] MMOL/L; Protein: 76 [60 - 80] G/L; Sodium: 138 [135 - 143] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 113): OTHER TOXICOLOGY NPTST491-TOXICOLOGY: POSITIVE-MDS MDMA UR QL; URINE NPTST514-URINALYSIS: NEGATIVE-UR WBC AUTO RESULT 28/HPE. UR RBC AUTO RESULT 15/HPE

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day	188
Duration of AE	22 DAYS

Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECT HAS A DIAGNOSIS OF DEPRESSION AND ANXIETY THAT ARE CURRENTLY UNDER CARE OF PSYCHIATRIST. PER SUBJECT MEDICATIONS WILL BE ADJUSTED APPROPRIATLY BASED ON CURRENT SITUATION.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Generated: [redacted]20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，精神医学的問題，うつ病の悪化，不安の増加及び自殺念慮の事象を発現した。関連する病歴は，片頭痛，子宮摘出，コレステロール高値，静脈の末梢血管疾患，潰瘍性大腸炎，元喫煙者（1 日 0.5 箱を 1 年間），ニューロパチー，双極性うつ病，境界型糖尿病及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与167日後＊，被験者は精神医学的問題，うつ病の悪化，不安の増加及び自殺念慮を発現した。投与188日後＊，精神医学的問題，うつ病の悪化，不安の増加及び自殺念慮は消失した。

投与167日後＊，被験者との電話での評価後の精神科医の指示により，被験者は入院した。被験者は，うつ病及び自殺念慮の症状があった。本事象の臨床経過には，薬物療法の継続，並びに個人療法，集団療法，レクリエーション療法及び作業療法が含まれた。投与173日後＊，被験者は退院した。

The patient's past medications include:

PREDNISONE for UC FLARE UP ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Depression aggravated (10012379) (Depression (10012378)) [v.24.0] [10012379]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2) Suicidal ideation (10042458) (Suicidal ideation (10042458)) [v.24.0] [10042458]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

3) Psychiatric disorder NOS (10037174) (Mental disorder (10061284)) [v.24.0] [10037174]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

4) Anxiety aggravated (10048339) (Anxiety (10002855)) [v.24.0] [10048339]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of PSYCHIATRIC PROBLEMS, INCREASE DEPRESSION, INCREASE ANXIETY, SUICIDAL IDEATION- Investigator: Subject has a diagnosis of depression and anxiety that are currently under care of psychiatrist. Per subject, medications will be adjusted appropriately based on current situation.

- AbbVie: Event is more likely related to pre-existing bipolar disorder and urine toxicology screen positive for MDMA.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 4.5 G/DL (normal 3.0 to 4.5)

[redacted] **20[redacted] ALBUMIN GLOBULIN RATIO:** 1.5 G/DL (normal 1.0 to 20)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 59 U/L (normal 37 to 47)

[redacted] **20[redacted] ALT:** 11 U/L (normal 5 to 55)

[redacted] **20[redacted] ANION GAP:** 10 MMOL/L (normal 3.0 to 11.0)

[redacted] **20[redacted] AST:** 14 U/L (normal 8 to 42)

[redacted] **20[redacted] BILIRUBIN:** 0.2 mg/dL (normal 0.3 to 1.2)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 13 mg/dL (normal 5 to 25)

[redacted] **20[redacted] BUN CREATININE RATIO:** 15 mg/dL (normal 7 to 25)

[redacted] **20[redacted] CA CORRECTED:** 9.2 mg/dL (normal 8.7 to 10.7)

[redacted] **20[redacted] CALCIUM:** 9.6 mg/dL (normal 8.7 to 10.7)

[redacted] **20[redacted] CHLORIDE:** 104 MMOL/L (normal 102 to 112)

[redacted] **20[redacted] COLONOSCOPY:** Was a clear demarcation between normal and inflamed colonic mucosa seen? Yes If yes, specify distance of demarcation from the anal verge 20 If no, specify reason Central Reader Endoscopy Subscore 2

[redacted] **20[redacted] CREATININE:** 0.87 mg/dL (normal 0.30 to 1.40)

[redacted] **20[redacted] EGFR (AFRICAN AMERICAN):** > 60

[redacted] **20[redacted] EGFR (NON AFRICAN AMERICAN):** 60

[redacted] **20[redacted] GLOBULIN:** 3.1 G/DL (normal 2.2 to 4.0)

[redacted] **20[redacted] GLUCOSE:** 104 mg/dL (normal 70 to 110)

[redacted] **20[redacted] POTASSIUM:** 3.5 MMOL/L (normal 3.5 to 5.3)

[redacted] **20[redacted] SODIUM:** 138 MMOL/L (normal 135 to 143)

[redacted] **20[redacted] PROTEIN:** 7.6 G/DL (normal 6.0 to 8.0)

[redacted] **20[redacted] TOXICOLOGY:** MDS MDMA UR QL, The patient does not have a history of drug abuse. The patient was having relations with a guard at her complex and he informed her "drink this drink and it will help you relax"

[redacted] **20[redacted] URINALYSIS:** negative, UR WBC auto result 28/HPE. UR RBC auto result 15/HPE

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
気管支炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
ASTHMA	1992
EXTENSIVE UC/PANCOLITIS	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 364	364

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETONOGESTREL	68 mg	OTHER: Q 3 YEARS	Y-M: 20[redacted]
ADALIMUMAB	80.000 mg	EVERY 2 WEEKS	Y-M: 20[redacted] / -252
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -107
MACROGOL 3350	0.5 g	PRN	Y-M: 20[redacted] / -39
BISACODYL	5 mg	OTHER: BID PRN	Y-M: 20[redacted] / -43
SALBUTAMOL	2 OTHER: PUFF	PRN	Y: 19[redacted]
CETIRIZINE	10 mg	QD	Y: 20[redacted] / -204
PREDNISONE	20 mg	QD	Y: 20[redacted] / -204

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ETONOGESTREL	68 mg	OTHER: Q 3 YEARS	Y-M: 20[redacted]	ONGOING
MACROGOL 3350	0.5 g	PRN	Y-M: 20[redacted] / -39	ONGOING
BISACODYL	5 mg	OTHER: BID PRN	Y-M: 20[redacted] / -43	ONGOING
LOPERAMIDE	2 mg	OTHER: QD PRN	Y-M: 20[redacted] / 52	ONGOING
AZITHROMYCIN	250 mg	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 126
FLUTICASONE;SALMETEROL	1 OTHER: PUFF	BID	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 192
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 141
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 135
SALBUTAMOL	2 OTHER: PUFF	PRN	Y: 19[redacted]	ONGOING
CETIRIZINE	10 mg	QD	Y: 20[redacted] / -204	Y-M: 20[redacted] / 131
PREDNISONE	20 mg	QD	Y: 20[redacted] / -204	Y-M: 20[redacted] / 131

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	ACUTE BRONCHITIS
Preferred term	気管支炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 186
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 131): Albumin: 27 [34 - 50] G/L; Alkaline Phosphatase: 79 [45 - 117] U/L; Basophils: 0.04 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.4 [0 - 2] %; Bilirubin: 3.420778 [0 - 17.10389] UMOL/L; Blood Urea Nitrogen: 2.14182 [2.49879 - 6.42546] MMOL/L; Calcium: 2.070933 [2.120835 - 2.520051] MMOL/L; Chloride: 107 [98 - 108] MMOL/L; Creatinine: 78.678901 [48.621793 - 90.171325] UMOL/L; Eosinophils: 0.51 [0 - 0.5] 10^9/L; Eosinophils/Leukocytes: 5.7 [1 - 4] %; Erythrocytes: 4.3 [3.7 - 5.17] 10^12/L; Glucose: 5.217658 [3.88549 - 6.10577] MMOL/L; Hematocrit: 0.337 [0.304 - 0.446] FRACTION OF 1; Hemoglobin: 108 [110 - 151] G/L; Leukocytes: 8.85 [3.7 - 11.5] 10^9/L; Lymphocytes: 1.6 [1.1 - 3.8] 10^9/L; Lymphocytes/Leukocytes: 17.9 [20 - 44] %; Monocytes: 0.95 [0.3 - 0.9] 10^9/L; Monocytes/Leukocytes: 10.6 [2 - 9] %; NPTST018-ALT/SGPT: 15 [13 - 56] U/L; NPTST044-AST/SGOT: 12 [15 - 37] U/L; NPTST136-CO2: 29.0 [21 - 32] MMOL/L; NPTST319-MAGNESIUM: 2.0 [1.6 - 2.6] MG/DL; NPTST320-MCH: 25.1 [24.3 - 33.2] PG; NPTST321-MCHC: 32.0 [31.9 - 35.1] G/DL; NPTST323-MCV: 78.4 [75.6 - 97.8] FL; NPTST341-MPV: 10.9 [7 - 10.7] FL; NPTST425-RDW CV: 15.6 [12.1 - 16.8] %; NPTST518-URINE CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 5.83 [1.7 - 8] 10^9/L; Neutrophils/Leukocytes: 65.2 [50 - 70] %; Platelets: 349 [156 - 380] 10^9/L; Potassium: 3.2 [3.5 - 5.1] MMOL/L; Protein: 75 [64 - 82] G/L; Sodium: 140 [133 - 143] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 131): CHEST CT: NEGATIVE; CHEST X RAY: NEGATIVE

AE Stopped Initial Rx Day	189
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性気管支炎の事象を発現した。関連する病歴は，喘息，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与186日後＊，被験者は急性気管支炎を発現した。投与189日後＊，急性気管支炎は消失した。

投与186日後＊，被験者は咳嗽の症状があり入院し，急性気管支炎及び喘息の急性増悪（非重篤）と診断された。被験者は問題なく呼吸していた。入院中，被験者は静脈内輸液及び抗生物質での治療を受けた。投与189日後＊ ，被験者は抗生物質及びステロイドを投与され，退院した。

投与された薬剤は，フルチカゾン・サルメテロール合剤，prednisone，レボフロキサシン及び cetrizine であった。

The patient's past medications include:

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZITHROMYCIN for BRONCHITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute bronchitis (10000687) (Bronchitis (10006451)) [v.23.1] [10000687]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE BRONCHITIS

- Investigator: Not applicable

- AbbVie: Acute bronchitis is one of the most common conditions encountered in the clinical practice. Incidence is highest in fall and winter and viruses are the most commonly identified pathogens. Additional risk factor includes pre-existing asthma.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 2.7 G/DL (normal 3.4 to 5.0)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 79 U/L (normal 45 to 117)

[redacted] **20[redacted] ALT/SGPT:** 15 U/L (normal 13 to 56)

[redacted] **20[redacted] AST/SGOT:** 12 U/L (normal 15 to 37)

[redacted] **20[redacted] BILIRUBIN:** 0.2 mg/dL (normal 0.0 to 1.0)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 6 mg/dL (normal 7 to 18)

[redacted] **20[redacted] CHEST CT:** Negative

[redacted] **20[redacted] CHEST X-RAY:** Negative

[redacted] **20[redacted] CO2:** 29.0 MMOL/L (normal 21.0 to 32.0)

[redacted] **20[redacted] HEMATOCRIT:** 33.7 % (normal 30.4 to 44.6)

[redacted] **20[redacted] HEMOGLOBIN:** 10.8 G/DL (normal 11.0 to 15.1)

[redacted] **20[redacted] LYMPHOCYTES %:** 17.9 %

[redacted] **20[redacted] NEUTROPHILS %:** 65.2 %

[redacted] **20[redacted] NEUTROPHILS ABS:** 5.83 X10**3/MCL (normal 1.70 to 8.00)

[redacted] **20[redacted] PLATELET COUNT:** 349 X10**3/MCL (normal 156 to 380)

[redacted] **20[redacted] URINE CULTURE:** Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.85 X10**3/MCL (normal 3.70 to 11.50)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
深部静脈血栓症	X			
皮膚潰瘍	X			

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	5[redacted]	MALE	WHITE

Medical History	Onset Year
ASTHMA	1964
HYPERTENSION	20[redacted]
LEFT SIDED UC	19[redacted]
OTHER: BACITRACIN ALLERGY	19[redacted]
OTHER: BILATERAL LEG ULCERS	19[redacted]
OTHER: CHRONIC STOMACH PAIN	19[redacted]
OTHER: CONSTIPATION	19[redacted]
OTHER: DIARRHEA	19[redacted]
OTHER: PENICILLIN ALLERGY	19[redacted]
OTHER: PERIPHERAL VASCULAR DISEASE STENTS LEGS	20[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: DEEP VEIN THROMBOSIS	19[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: LEFT LOWER LEG RECURRENT DVT'S	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: VEIN SURGERY	19[redacted]
SURGERY: VEIN SURGERY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			

PIPES	NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 1	[redacted] / 365	365

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	5 mg	QD	Y-M: 19[redacted]
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted]
ENOXAPARIN	80 mg	BID	Y-M: 20[redacted]
PENTOXIFYLLINE	400 mg	TID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted] / -159
AZATHIOPRINE	50 mg	BID	Y: 19[redacted]
BUDESONIDE;FORMOTEROL	160.45 uL	PRN	Y: 20[redacted]
SALBUTAMOL	1-2 OTHER: PUFFS	PRN	Y: 20[redacted]
PREDNISONE	40 mg	QD	Y: 20[redacted]
APIXABAN	2.5 mg	QD	Y: 20[redacted]
OMEPRAZOLE	40 mg	QD	Y: 20[redacted]
MESALAZINE	.375 mg	QD	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5 mg	QD	Y-M: 19[redacted]	ONGOING
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted]	ONGOING
ENOXAPARIN	80 mg	BID	Y-M: 20[redacted]	ONGOING
PENTOXIFYLLINE	400 mg	TID	Y-M: 20[redacted]	ONGOING
CLINDAMYCIN	300 mg	BID	Y-M: 20[redacted] / 263	Y-M: 20[redacted] / 271
SULFAMETHOXAZOLE;TRIMETHOPRIM	800 mg	QD	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 285

VANCOMYCIN	500 mg	BID	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 285
BUDESONIDE;FORMOTEROL	160.45 uL	PRN	Y: 20[redacted]	ONGOING
SALBUTAMOL	1-2 OTHER: PUFFS	PRN	Y: 20[redacted]	ONGOING
APIXABAN	2.5 mg	QD	Y: 20[redacted]	ONGOING
OMEPRAZOLE	40 mg	QD	Y: 20[redacted]	ONGOING
MESALAZINE	.375 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	RECURRENT BILATERAL LOWER EXTREMITY DVTS
Preferred term	深部静脈血栓症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 275
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 265): DVT DUPLEX: CELLULITIS OF LOWER LEGS	
AE Stopped Initial Rx Day	346
Duration of AE	72 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RECURRENT BILATERAL LOWER EXTREMITY DVTS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	VENOUS STASIS ULCERS ON LEFT LOWER EXTREMITY.
Preferred term	皮膚潰瘍
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 318
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 265): DVT DUPLEX: CELLULITIS OF LOWER LEGS

AE Stopped Initial Rx Day	346
Duration of AE	29 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	VENOUS STASIS ULCER ON LOWER LEFT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:18
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，両下肢の深部静脈血栓症の再発及び左下肢の静脈うっ血性潰瘍の事象を発現した。関連する病歴は，深部静脈血栓症，潰瘍性大腸炎，高血圧，左下肢の深部静脈血栓症の再発，下肢の PVD ステント留置，下肢の S/P ステント留置，非喫煙者及び非飲酒者であった。

Event 1 及び 2 の臨床経過：

投与275日後＊，被験者は両下肢の深部静脈血栓症の再発を発現した。投与318日後＊，被験者は左下肢の静脈うっ血性潰瘍を発現した。投与346日後＊，両下肢の深部静脈血栓症の再発及び左下肢の静脈うっ血性潰瘍は消失した。

本事象発現前の投与から約9ヵ月後＊，被験者は既存の両下肢の静脈うっ血性潰瘍に対して硬化療法を受けた。その後，被験者は再び激しい下肢痛を発症し，投与318日後＊　に入院した。被験者は DVT デュプレックス・スキャン検査を受け，両下肢の慢性深部静脈血栓症と診断された。下肢の潰瘍に対し，被験者は毎日のドライドレッシングを開始した。入院中の経過では，被験者は蜂巣炎（非重篤）を発症し，クリンダマイシンで治療された。投与323日後＊　，被験者は改善を示し，退院した。

治験責任医師は次のように述べた。被験者は既存の両下肢の慢性静脈うっ血性潰瘍を有しており，投与275日後＊に硬化療法を受けた。

投与された薬剤は，バンコマイシン，bactrim 及びクリンダマイシンであった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISON for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

BACITRACIN for UNKNOWN INDICATION

PENICILLIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Deep vein thrombosis recurrent (10066529) (Deep vein thrombosis (10051055)) [v.24.0] [10066529]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

2) Venous stasis ulcer (10047246) (Skin ulcer (10040943)) [v.24.0] [10047246]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of RECURRENT BILATERAL LOWER EXTREMITY DVTS

- Investigator: RECURRENT BILATERAL LOWER EXTREMITY DVTS

- AbbVie: Event is more likely related to pre-existing chronic venous insufficiency and pre-existing left lower leg recurrent DVTs.

Event of VENOUS STASIS ULCERS LEFT LOWER LOWER EXTREMITY

- Investigator: VENOUS STASIS ULCER ON LOWER LEFT

- AbbVie: Event is more likely related to pre-existing bilateral leg ulcers and chronic venous insufficiency associated with left lower leg recurrent DVTs.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] DVT DUPLEX:** cellulitis of lower extremities

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
慢性閉塞性肺疾患	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	7[redacted]	MALE	WHITE

Medical History	Onset Year
A. FIB	20[redacted]
ASTHMA	20[redacted]
ATRIAL FIBRILLATION	20[redacted]
BENIGN COLON POLYPS	20[redacted]
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20[redacted]
CORONARY ARTERY DISEASE	20[redacted]
DEGENERATIVE DISC DISEASE	20[redacted]
DIVERTICULOSIS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HEART FAILURE	20[redacted]
HIGH CHOLESTEROL	20[redacted]
HYPERCHOLESTEROLEMIA	20[redacted]
HYPERTENSION	20[redacted]
OBESITY	19[redacted]
SLEEP APNEA	20[redacted]
TRIPLE BYPASS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: KYPHOPLASTY	19[redacted]
PRIOR PROCEDURES: QUADRICEP TENDON REPAIR	20[redacted]
PRIOR PROCEDURES: TRIPLE BYPASS	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			

CIGARETTES	FORMER	2 PACK	30	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-675 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 113	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 355	355

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -211
METOPROLOL	12.5 mg	QD	Y-M: 20[redacted] / -120
RIVAROXABAN	20 mg	QD	Y-M: 20[redacted] / -107
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -24
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -27
OXYGEN	2 L	PRN	Y-M: 20[redacted] / -34
ACETYLSALICYLIC ACID	81 mg	QD	Y: 20[redacted]
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y: 20[redacted]
ATORVASTATIN	40 mg	QD	Y: 20[redacted]
FUROSEMIDE	40 mg	QD	Y: 20[redacted]
IPRATROPIUM;SALBUTAMOL	0.5/2.5 mg	PRN	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
METOPROLOL	12.5 mg	QD	Y-M: 20[redacted] / -120	Y-M: 20[redacted] / 43
RIVAROXABAN	20 mg	QD	Y-M: 20[redacted] / -107	ONGOING
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -24	Y-M: 20[redacted] / 42

PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -27	ONGOING
OXYGEN	2 L	PRN	Y-M: 20[redacted] / -34	Y-M: 20[redacted] / 41
OXYGEN	2 L	OTHER: CONTINUOUS	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 45
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 45
FAMOTIDINE	40 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 45
FUROSEMIDE	40 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 45
GUAIFENESIN	1200 mg	BID	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 45
LACTOBACILLUS ACIDOPHILUS	1 OTHER: CAP	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 45
LEVOFLOXACIN	750 mg	OTHER: ONCE	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 43
METHYLPREDNISOLONE	40 mg	BID	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 45
METOPROLOL	25 mg	QD	Y-M: 20[redacted] / 43	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 44
PAROXETINE	40 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 45
PIPERACILLIN;TAZOBACTAM	3.375 g	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 43
ACETYLSALICYLIC ACID	81 mg	QD	Y: 20[redacted]	ONGOING
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y: 20[redacted]	ONGOING
ATORVASTATIN	40 mg	QD	Y: 20[redacted]	ONGOING
FUROSEMIDE	40 mg	QD	Y: 20[redacted]	ONGOING
IPRATROPIUM;SALBUTAMOL	0.5/2.5 mg	PRN	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF COPD
Preferred term	慢性閉塞性肺疾患
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 155
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 43): NPTST072-BNP: 150 [0 - 100] PG; NPTST500-TROPONIN I: <0.0010 [0 - 0.033] NG/ML

Microbiology

[redacted]20[redacted] (RX DAY 42): BLOOD NPTST069-BLOOD CULTURE: NEGATIVE-NO GROWTH AFTER 5 DAYS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 42): CXR: NEGATIVE

AE Stopped Initial Rx Day	158
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PT HAS A H/O EX SMOKER 30 PACK YEARS, OBESITY, COPD, OSA, HF, A.FIB, ASTHMA THAT CAN CONTRIBUTE TO WORSENING COPD

Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:18
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，慢性閉塞性肺疾患の悪化の事象を発現した。関連する病歴は，肥満，元喫煙者（1 日 2 箱を 30 年間），喘息，慢性閉塞性肺疾患，睡眠時無呼吸，高コレステロール血症，高血圧，冠動脈疾患，心房細動，心不全，潰瘍性大腸炎，憩室症及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与155日後＊，被験者は慢性閉塞性肺疾患の悪化を発現した。投与158日後＊，慢性閉塞性肺疾患の悪化は消失した。

投与155日後＊，被験者は感冒を発症して息切れが増え，慢性閉塞性肺疾患の症状が悪化し，入院した。同日，被験者はうっ血性心不全とも診断されたが，この事象は治験責任医師が非重篤と判断した。被験者は，ネブライザー，酸素及び安静での治療を受け，回復した。投与158日後＊，被験者は退院した。

投与された薬剤は，ソル・メドロール，酸素，レボフロキサシン及び mucinex であった。

Causality for UPADACITINIB (Blinded)

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1) COPD exacerbation (10010953) (Chronic obstructive pulmonary disease (10009033)) [v.23.1] [10010953]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of EXACERBATION OF COPD

- Investigator: The patient has a H/O ex smoker 30 pack years, obesity, COPD, OSA, HF, A Fib, asthma that can contribute to worsening COPD.

- AbbVie: Event is more likely related to pre-existing history of chronic obstructive pulmonary disease and asthma.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD CULTURE:** Negative (No growth after 5 days)

[redacted] **20[redacted] BNP:** 150 PG (normal 0 to 100)

[redacted] **20[redacted] CHEST X-RAY:** Abnormal: COPD and cardiomegaly NCS

[redacted] **20[redacted] CHEST X-RAY:** Negative

[redacted] **20[redacted] TROPONIN I:** <0.0010 ng/mL (Normal >0.000 to <=0.033 ng/mL)

[redacted] **20[redacted] WEIGHT:** 16[redacted] KG

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
急性腎障害				X
急性呼吸不全	X			
心房細動	X			
うっ血性心不全				X
間質性肺疾患	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	6[redacted]	MALE	WHITE

Medical History	Onset Year
ANXIETY	20[redacted]
ATRIAL FIBRILLATION	20[redacted]
BRADYCARDIA	20[redacted]
CARDIOMYOPATHY	20[redacted]
DIVERTICULOSIS	20[redacted]
ERECTILE DYSFUNCTION	20[redacted]
GASTROESOPHOGEAL REFLUX DISEASE	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
SEASONAL ALLERGIES	20[redacted]
SLEEP APNEA	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	40	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	FORMER	1 SESSIONS	6	20[redacted]
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 57	57
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 1	[redacted] / 16	16

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	20 mg	QD	Y-M: [redacted]
SILDENAFIL	50 mg	PRN	Y-M: [redacted]
MESALAZINE	800 mg	QD	Y-M: [redacted]
PREDNISONE	5 mg	QD	Y-M: [redacted]
ATENOLOL	100 mg	BID	Y-M: [redacted] / -207
LISINOPRIL	20 mg	BID	Y-M: [redacted] / -207
CLONIDINE	5 mg	QD	Y-M: [redacted] / -214
MIRIKIZUMAB	300.000 mg	MONTHLY	Y-M: [redacted] / -167
WARFARIN	2.5 mg	QD	Y-M: [redacted] / -85
ACETYLSALICYLIC ACID	81 mg	QD	Y: [redacted]
AMLODIPINE	10 mg	QD	Y: [redacted]
OMEPRAZOLE	40 mg	QD	Y: [redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SILDENAFIL	50 mg	PRN	Y-M: [redacted]	ONGOING
PREDNISONE	5 mg	QD	Y-M: [redacted]	Y-M: [redacted] / 18
ATENOLOL	100 mg	BID	Y-M: [redacted] / -207	ONGOING
LISINOPRIL	20 mg	BID	Y-M: [redacted] / -207	ONGOING
CLONIDINE	5 mg	QD	Y-M: [redacted] / -214	ONGOING
WARFARIN	2.5 mg	QD	Y-M: [redacted] / -85	Y-M: [redacted] / 14
AZITHROMYCIN	250 mg	OTHER: ONCE	Y-M: [redacted] / 10	Y-M: [redacted] / 10
IPRATROPIUM	0.5 mg	TID	Y-M: [redacted] / 10	Y-M: [redacted] / 34
PANTOPRAZOLE	40 mg	QD	Y-M: [redacted] / 10	Y-M: [redacted] / 14

PIPERACILLIN;TAZOBACTAM	3.375 g	BID	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 14
SODIUM CHLORIDE	2000 mg	BID	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 11
SULFAMETHOXAZOLE;TRIMETHOPRIM	2 OTHER: CAPS	BID	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 16
TEMAZEPAM	15 mg	PRN	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 29
DILTIAZEM	30 mg	TID	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 13
NYSTATIN	500000 OTHER: UNITS	BID	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 19
DILTIAZEM	120 mg	QD	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 14
DILTIAZEM	180 mg	QD	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 14
PHYTOMENADIONE	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 14
DILTIAZEM	300 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 22
HEPARIN	25000 OTHER: UNITS	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 21
SODIUM CHLORIDE	3 g	BID	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 23
AMPHOTERICIN B	300 mg	BID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 20
LIDOCAINE	200 mg	OTHER: ONCE	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
MIDAZOLAM	0.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 17
PREDNISONE	40 mg	BID	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 23
WARFARIN	5 mg	QD	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 17
MAGNESIUM SULFATE	1 g	PRN	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 19
OXYGEN	40 L	PRN	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 33
FUROSEMIDE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
ITRACONAZOLE	200 mg	QD	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 31
OXYGEN	35 L	OTHER: CONTINUOUS	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 30
WARFARIN	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 23
AMIODARONE	150 mg	OTHER: ONCE	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 24
AMIODARONE	450 mg	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 25
BENZONATATE	100 mg	PRN	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 30
DIGOXIN	0.5 mg	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 25
DILTIAZEM	125 mg	OTHER: ONCE	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 24
IPRATROPIUM;SALBUTAMOL	0.5-2.5 mg	PRN	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 24
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 37
METHYLPREDNISOLONE	40 mg	BID	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 29
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 25
DIGOXIN	0.25 mg	QD	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 34
DILTIAZEM	90 mg	TID	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 34

ITRACONAZOLE	200 mg	BID	Y-M: 20[redacted] / 26	Y-M: 20[redacted] / 29
VITAMIN K NOS	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 4	Y-M: 20[redacted] / 10
CEFTRIAXONE	1 g	OTHER: ONCE	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 9
FUROSEMIDE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 9
IPRATROPIUM;SALBUTAMOL	0.5/2.5 mg	OTHER: STAT	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 9
OXYGEN	2 L	OTHER: CONTINUOUS	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 21
DEXTROMETHORPHAN;GUAIFENESIN	10-100 mg	PRN	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 30
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 33
ENOXAPARIN	100 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 33
OXYGEN	5 L	PRN	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 36
POTASSIUM	100 mL	OTHER: ONCE	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 31
WARFARIN	5 mg	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 47
ACETYLSALICYLIC ACID	81 mg	QD	Y: 20[redacted]	ONGOING
AMLODIPINE	10 mg	QD	Y: 20[redacted]	ONGOING
OMEPRAZOLE	40 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Event of Interest - Adjudicated Cardiovascular events

Event Description	ACUTE CONGESTIVE HEART FAILURE
Preferred term	うっ血性心不全
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 66
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day	86 (13 DAYS AFTER LAST TREATMENT)
Duration of AE	21 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	UNSPECIFIED INTERSTITIAL PNEUMONITIS
Preferred term	間質性肺疾患
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 66
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 9): Bicarbonate: 22 [21 - 28] MMOL/L; Leukocytes: 8.2 [4.5 - 11] 10^9/L; NPTST072-BNP: 400 [0 - 100] PG; NPTST296-INR: 3.7 [0.8 - 1.2] RATIO; NPTST411-PROTIME: 36.1 [9 - 11.8] SEC; Sodium: 125 [136 - 145] MMOL/L; pH: 7.489 [7.35 - 7.45] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 10): Platelets: 105 [150 - 500] 10^9/L; [redacted]20[redacted] (RX DAY 16): NPTST274-HISTOPLASMA ANTIBODY TEST: POSITIVE AB [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 9): BLOOD NPTST069-BLOOD CULTURE: NEGATIVE-NO GROWTH AFTER 5 DAYS; [redacted]20[redacted] (RX DAY 16): OTHER LUNG TISSUE NPTST026-ANAEROBIC CULTURE: NEGATIVE-NO ANAEROBIC ORGANISMS ISOLATED; OTHER LUNG TISSUE NPTST165-CULTURE AFB W SMEAR: NEGATIVE-NO GROWTH, NO FUNGAL ELEMENTS; OTHER BODY FLUID OF LUNGS NPTST166-CULTURE LOWER RESPIRATORY: NEGATIVE-BILATERAL WASHING LUNGS- NORMAL FLORA; [redacted]20[redacted] (RX DAY 28): SPUTUM NPTST457-SMEAR GRAM STAIN: NEGATIVE-< 10 EPITHELIAL CELLS BARTLETT SCORE= 1-2

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 9): 12 LEAD EKG: ABNORMAL- FINDINGS OF A. FIB; CHEST X-RAY: ACUTE CONGESTIVE HEART FAILURE; [redacted]20[redacted] (RX DAY 10): CT CHEST ANGIOGRAPHY: APICAL PULMONARY FIBRTIC CHANGES SEEN WITH GROUNDGLASS OPACITIES SEEN IN RLL WITH MILD DEPENDENT ATELECTASIS. MASS LIKE OPACITY MEASSURING 5.0X 2.4 CM IN RLL. FINDINGS MAY REPRESENT SEQUELA OF AN IN FECTIONS INFILTRATE VS MALIGNANCY. FINDINGS MAY ALSO REPRESENT CHRONIC HYPERSENSITIVITY PNEUMONITIS OR POSSIBLE IDIOPATHIC INTERSTITIAL FIBROSIS.; [redacted]20[redacted] (RX DAY 12): RIGHT UPPER QUADRANT ABDOMINAL ULTRASOUND: NEGATIVE FINDINGS; [redacted]20[redacted] (RX DAY 16): BRONCHOSCOPY: NEGATIVE FOR MALIGNANCY & HISTOPLASMOSIS; CHEST X-RAY: S/P RLL LUNG BX. NO PNEUMOTHRORAX.; CT GUIDED RIGHT LOWER LOBE LUNG BIOPSY: UNSPECIFIED INTERSTITIAL PNEUMONITIS; CT OF THE CHEST: 5 X 2.4 MASS LIKE OPACITY IN RLL-NEGATIVE FOR MALIGNANCY AND INFECTION- NO FUNGAL, VIRAL OR BACTERIA NOTED IN CULTURES.; [redacted]20[redacted] (RX DAY 24): CHEST X-RAY: WORSENING INTERSTITIAL OPACITIES & CONSOLIDATED CHANGES IN THE RLL, POSSIBLE PULMONARY EDEMA; [redacted]20[redacted] (RX DAY 30): PACE MAKER: TO CONTROL A. FIB; [redacted]20[redacted] (RX DAY 34): AV NODE ABLATION: COMPLETE HEART BLOCK ACHIEVED AND PACING THE RIGHT VENTRICLE.; [redacted]20[redacted] (RX DAY 36): CT OF CHEST WITHOUT CONTRAST: SIGNIFICANT IMPROVEMENT OF BILATERAL INFILTRATES, BILATERAL PLUERAL EFFUSIONS AND COMPRESSIVE ATELECTASIS SEEN GREATER IN THE LEFT .

AE Stopped Initial Rx Day	94 (21 DAYS AFTER LAST TREATMENT)
Duration of AE	29 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED

Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	UNCONTROLLED ATRIAL FIBRILLATION WITH RAPID VENTRICULAR HEART RATE
Preferred term	心房細動
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 74 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 17): NPTST151-CORTISOL: 5.78 [4.3 - 22.4] UG/DL; [redacted]20[redacted] (RX DAY 25): NPTST072-BNP: 1324 [0 - 100] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 11): TRANSTHORACIC ECHOCARDIOGRAPHY: LEFT VENTRICLE 50-55% EF WITH LEFT ATRIUM ENLARGEMENT; [redacted]20[redacted] (RX DAY 29): PACEMAKER IMPLANTATION: SUCCESSFUL SINGLE CHAMBER PERMANENT PACEMAKER IMPLANTATION- ONGOING TACHYCARDIA. SCHEDULED FOR AV NODE ABLATION.; [redacted]20[redacted] (RX DAY 34): AV NODE ABLATION: TOTAL RF TIME 529 SECONDS TOTAL NUMBER OF RF APPLICATIONS 10. SET LOWER RATE TO 80BPM

AE Stopped Initial Rx Day	91 (18 DAYS AFTER LAST TREATMENT)
Duration of AE	18 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	A. FIB, PULMONARY HEMORRHAGE, HTN, ACUTE CHF
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #4: Event of Interest - Renal Dysfunction

Event Description	ACUTE KIDNEY INJURY
Preferred term	急性腎障害
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 78 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day	80 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #5: Serious Adverse Event

Event Description	ACUTE HYPERCAPNIA HYPOXEMIC RESPIRATORY FAILURE
Preferred term	急性呼吸不全
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 79 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 15): NPTST039-APTT: 44 [23 - 31] SEC; [redacted]20[redacted] (RX DAY 16): NPTST296-INR: 1.2 [0.8 - 1.2] RATIO; NPTST413-PT: 11.9 [9 - 11.8] SEC; [redacted]20[redacted] (RX DAY 17): NPTST039-APTT: 137 [23 - 31] SEC; [redacted]20[redacted] (RX DAY 20): NPTST039-APTT: 29 [23 - 31] SEC; [redacted]20[redacted] (RX DAY 22): NPTST296-INR: 3.4 [0.8 - 1.2] RATIO; NPTST413-PT: 33.8 [9 - 11.8] SEC; [redacted]20[redacted] (RX DAY 36): NPTST296-INR: 1.3 [2.5 - 3.5] RATIO; NPTST411-PROTIME: 13.5 [11 - 13.5] SEC

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day	90 (17 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNCONTROLED A. FITH RAPID VENTRICULAR RATE, ACUTE CHF, OSA, RESPIRATORY ALKALOSIS, INTERSTITIAL PNEUMONITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:16:18
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，特定不能の間質性肺臓炎，心室性の心拍数の増加を伴う制御不能の心房細動，及び急性高炭酸ガス血症の低酸素血症性呼吸不全の事象を発現した。関連する病歴は，睡眠時無呼吸，高血圧，徐脈，心筋症，潰瘍性大腸炎，心房細動，電子タバコの元喫煙者（1 日 1 回を 6 年間），元喫煙者（1 日 1 箱を 40 年間）及び現飲酒者（1 日 2 杯未満）であった。

この被験者は，以前に M14-675 試験に登録されており，20[redacted] 年[redacted] 月[redacted] 日から 20[redacted] 年[redacted] 月[redacted] 日まで盲検化された治験薬を投与された。20[redacted] 年[redacted] 月[redacted] 日，被験者は M14-234 試験に参加した。

Event 2，3 及び 5 の臨床経過：

投与66日後＊，被験者は特定不能の間質性肺臓炎を発現した。投与74日後＊，被験者は心室性の心拍数の増加を伴う制御不能の心房細動を発現した。投与79日後＊，被験者は急性高炭酸ガス血症の低酸素血症性呼吸不全を発現した。投与90日後＊　，急性高炭酸ガス血症の低酸素血症性呼吸不全は消失した。投与91日後＊　，心室性の心拍数の増加を伴う制御不能の心房細動は消失した。投与94日後＊，特定不能の間質性肺臓炎は消失した。

投与61日後＊，被験者は非重篤なインフルエンザ様症状を呈し始め，華氏102.0°F の発熱，悪寒及び疲労感の悪化があった。被験者が治験実施施設に連絡したところ，緊急治療室に行くように指示された。被験者は緊急治療室で評価を受け，未詳のウイルス感染症と診断され，タイレノールを処方され，帰宅した。被験者は，安静にして，症状が悪化したり，改善しない場合には数日後に再受診するように指示された。

投与66日後＊ ，被験者は息切れが悪化し，発熱が続いて華氏 101°F であり，喀血があるため，治験実施施設に連絡した。被験者は診断のために治験実施施設を訪問するように指示された。聴診では右下葉に水泡音が確認され，パルスオキシメーターの測定値は，安静時には室内気で86%であり，歩行時には 81%に低下した。被験者は評価を受けるために救急治療室に行くように指示された。

投与73日後＊，被験者は追加の精密検査のために入院した。入院中，被験者は低ナトリウム血症及び急性腎不全であることが判明した。被験者は腎臓内科で経過観察され，厳格な摂取量と排出量の管理が実施され，必要に応じて塩分タブレットが投与された。急性腎不全は，腎機能の改善（結果は報告されていない）により消失した。胸部 CT 検査で，肺の右下に 5 × 2.4 cm の腫瘤を認めた。腫瘤の CT ガイド下での生検が完了した。病理組織学的検査では，悪性腫瘍や真菌由来である根拠は認められなかった。喀痰培養は陰性であった。最終的な肺生検では，特定不能の間質性肺臓炎で，薬剤性の可能性があると診断された。投与73 日後＊，粘液の抗ヒストプラスマ抗体検査が陽性となった。また，被験者は，鳥やコウモリの糞で汚染された土壌に曝露した可能性があった。特定不能の真菌に対する治療が開始されたが，急性腎不全のために中止された。同日，気管支鏡検査が行われ，ヒストプラスマ症は除外された。

気管支鏡検査の後，投与74日後＊に胸部 CT 検査を行い，肺出血を指摘された。

同日，被験者は集中治療室に入った。被験者は，酸素飽和度を維持するための BPAP 装置，及び高流量の鼻カニューレを必要とした。被験者は息切れ，不安及び頻脈を呈していた。被験者は心室性の心拍数の増加を伴う制御不能の心房細動を発症した。喀血のためにワルファリンの投与は中止された。複数の薬剤を静脈内投与したが，心室性の心拍数の増加を伴う心房細動は改善しなかった。心臓除細動を試みたが，心房細動及び心室性の心拍数の増加は消失しなかった。投与86日後＊ ，被験者は，永久的シングルチャンバーペースメーカーの植え込みに成功した。被験者は継続的な頻拍を呈しており，房室結節アブレーションが予定された。投与91日後＊，被験者は転院し，房室結節アブレーションを受けた。アブレーションは成功し，被験者の状態は安定していた。同日，被験者の症状は消失し，肺の管理のために最初の病院に戻された。急性うっ血性心不全は消失した。被験者は室内気で呼吸し，心拍数はコントロールされていた。喀血が消失したためワルファリンを再開し，INR は2.0 であった。

投与92日後＊ ，被験者の状態は安定しており，循環器科及び呼吸器科は，退院して外来で診察を受けることを許可した。投与94日後＊，被験者は退院した。

投与された薬剤は，アジスロマイシン，ゾシン，bactrim ds，ジルチアゼム，coumadin，硫酸マグネシウム，アミオダロン，ジゴキシン，デキストロメトルファンデキストロメトルファン臭化水素酸塩水和物・グアイフェネシン合剤，塩化カリウム，ヘパリン，ベンゾナテート，イプラトロピウム，duoneb，セフトリアキソン，prednisone，酸素及び zofran であった。

The patient's past medications include:

MESALAMINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MIRIKISUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Interstitial pneumonitis (10022618) (Interstitial lung disease (10022611)) [v.22.0] [10022618]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Atrial fibrillation with rapid ventricular response (10058331) (Atrial fibrillation (10003658)) [v.22.0] [10058331]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

3) Acute respiratory failure (10001053) (Acute respiratory failure (10001053)) [v.22.0] [10001053]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Causality for ABT-494 (Blinded)

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1) Interstitial pneumonitis (10022618) (Interstitial lung disease (10022611)) [v.22.0] [10022618]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

2) Atrial fibrillation with rapid ventricular response (10058331) (Atrial fibrillation (10003658)) [v.22.0] [10058331]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

3) Acute respiratory failure (10001053) (Acute respiratory failure (10001053)) [v.22.0] [10001053]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of UNSPECIFIED INTERSTITIAL PNEUMONITIS

- Investigator: Not applicable

- AbbVie: Risk factors include extensive recent smoking history.

Event of UNCONTROLLED ATRIAL FIBRILLATION WITH RAPID VENTRICULAR HEART RATE

- Investigator: A. fib, pulmonary hemorrhage, HTN, acute CHF.

- AbbVie: Event more likely related to pre-existing history of atrial fibrillation.

Event of ACUTE HYPERCAPNIA HYPOXEMIC RESPIRATORY FAILURE

- Investigator: Uncontrolled A. Fib rapid ventricular rate, acute CHF, OSA, respiratory alkalosis, interstitial pneumonitis.

- AbbVie: Event is more likely related to interstitial pneumonitis.

Alternative Etiology for ABT-494 (Blinded)

Event of UNSPECIFIED INTERSTITIAL PNEUMONITIS

- Investigator: Not applicable

- AbbVie: Risk factors include extensive recent smoking history.

Event of UNCONTROLLED ATRIAL FIBRILLATION WITH RAPID VENTRICULAR HEART RATE

- Investigator: A. fib, pulmonary hemorrhage, HTN, acute CHF.

- AbbVie: Event more likely related to pre-existing history of atrial fibrillation.

Event of ACUTE HYPERCAPNIA HYPOXEMIC RESPIRATORY FAILURE

- Investigator: Uncontrolled A. Fib rapid ventricular rate, acute CHF, OSA, respiratory alkalosis, interstitial pneumonitis.

- AbbVie: event is more likely related to interstitial pneumonitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] 12 LEAD EKG:** Abnormal - findings of A. fib

[redacted] **20[redacted] ANAEROBIC CULTURE:** Negative, no anaerobic organisms isolated.

[redacted] **20[redacted] AV NODE ABLASION:** TOTAL rf TIME 529 seconds total number of RF applications 10. set lower rate to 80bpm

[redacted] **20[redacted] BLOOD BICARB:** 22 MMOL/L (normal 21 to 28)

[redacted] **20[redacted] BLOOD CULTURE:** Negative, no growth after 5 days.

[redacted] **20[redacted] BNP:** 400 PG (normal 0 to 100)[redacted] 20[redacted] BNP: 1324 pg/ml (normal 0 to 100)

[redacted] **20[redacted] BODY TEMPERATURE:** 102 degrees F

[redacted] **20[redacted] BODY TEMPERATURE:** 101 degrees F

[redacted] **20[redacted] BRONCHOSCOPY:** Negative for malignancy and histoplasmosis

[redacted] **20[redacted] CHEST X-RAY:** Acute congestive heart failure.

[redacted] **20[redacted] CHEST X-RAY:** S/P RLL LUNG Bx. No Pneumothorax.

[redacted] **20[redacted] CHEST X-RAY:** WORSENING INTERSTITIAL OPACITIES & CONSOLIDATED CHANGES IN THE RLL, POSSIBLE PULMONARY EDEMA

[redacted] **20[redacted] CORTISOL:** 5.78 ug/dl (normal 4.3 to 22.40)

[redacted] **20[redacted] CT:** ground glass opacities seen bilaterally to upper lobes - possible ARDS, sarcoidosis

[redacted] **20[redacted] CT CHEST ANGIOGRAPHY:** APICAL PULMONARY FIBRTIC CHANGES SEEN WITH GROUNDGLASS OPACITIES SEEN IN RLL WITH MILD DEPENDENT ATELECTASIS. MASS LIKE OPACITY MEASSURING 5.0X 2.4 CM IN RLL. FINDINGS MAY REPRESENT SEQUELA OF AN INFECTIONS INFILTRATE VS MALIGNANCY. FINDINGS MAY ALSO REPRESENT CHRONIC HYPERSENSITIVITY PNEUMONITIS OR POSSIBLE IDIOPATHIC INTERSTITIAL FIBROSIS.

[redacted] **20[redacted] CT GUIDED RIGHT LOWER LOBE LUNG BIOPSY:** Unspecified interstitial pneumonitis.

[redacted] **20[redacted] CT OF CHEST WITHOUT CONTRAST:** SIGNIFICANT IMPROVEMENT OF BILATERAL INFILTRATES, BILATERAL PLUERAL EFFUSIONS AND COMPRESSIVE ATELECTASIS SEEN GREATER IN THE LEFT .

[redacted] **20[redacted] CT OF THE CHEST:** 5 x 2.4 mass like opacity in RLL- negative for malignancy and infection-no fungal, viral or bacteria noted in cultures.

[redacted] **20[redacted] CULTURE AFB W SMEAR:** Negative, no growth, no fungal elements.

[redacted] **20[redacted] CULTURE LOWER RESPIRATORY:** Negative, bilateral washing lungs-normal flora.

[redacted] **20[redacted] EKG:** Abnomal- findings of A. fib

[redacted] **20[redacted] HISTOPLASMA ANTIBODY TEST (MUCUS):** positive AB (lower range of normal: negative, upper range of normal: positive)

[redacted] **20[redacted] INR:** 3.7 ratio (normal 0.8 to 1.2)

[redacted] **20[redacted] INR:** 2.0 ratio (normal 0.8 to 1.2)

[redacted] **20[redacted] INR:** 1.3 ratio (normal 2.5 to 3.5)

[redacted] **20[redacted] PH:** 7.489 no unit (normal 7.35 to 7.45)

[redacted] **20[redacted] PLATELET COUNT:** 105 X10**3/MCL (normal 150 to 500)

[redacted] **20[redacted] PROTIME:** 36.1 SEC (normal 9.0 to 11.8)

[redacted] **20[redacted] PROTIME:** 13.5 sec (normal 11.0 to 13.5)

[redacted] **20[redacted] RIGHT UPPER QUADRANTABDOMINAL ULTRASOUND:** Negative findings.

[redacted] **20[redacted] SODIUM:** 125 MMOL/L (normal 136 to 145)

[redacted] **20[redacted] SPO2:** 86% on Room air at rest

[redacted] **20[redacted] SPO2:** 86% on Room air with ambulation

[redacted] **20[redacted] SPUTUM SMEAR GRAM STAIN:** Negative < 10 epithelial cell, Bartlett score = 1-2.

[redacted] **20[redacted] TRANSTHORACIC ECHOCARDIOGRAM:** left ventricle 50-55% EF with left atrium enlargement

[redacted] **20[redacted] WBC:** 8.2 X10**3/MCL (normal 4.5 to 11.0)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Cardiac failure congestive: Cardiac biomarkers measurements taken.
Acute kidney injury: Symptoms of fluid retention and weight gain. Prior history or risk factors of recent infection, exposure to IV Contrast agents, and use of new prescription or over the counter medication.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
感染性滑液包炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
ATTENTION DEFICIT HYPERACTIVITY DISORDER	19[redacted]
BOATING ACCIDENT	19[redacted]
BRONCHITIS	20[redacted]
CHRONIC ABDOMINAL PAIN	19[redacted]
CHRONIC DIARRHEA	19[redacted]
CHRONIC INTERMITTENT CONSTIPATION	20[redacted]
FATIGUE	20[redacted]
HEAD ACHE	20[redacted]
HEARING LOSS	20[redacted]
HEMATOCHEZIA	19[redacted]
HEMORRHOIDS	19[redacted]
INTERMITTENT ANEMIA	20[redacted]
JAW FRACTURE	19[redacted]
LEFT EYE INJURY	19[redacted]
LEFT SIDED UC	19[redacted]
OSTEOARTHRITIS	20[redacted]
PERIPHERAL ARTHRLAGIA	20[redacted]
PERIPHERAL ARTHROPATHY	20[redacted]
RECTAL BLEEDING	19[redacted]
SCIATIC NERVE PAIN	20[redacted]
SEASONAL ALLERGIES	19[redacted]
ULCERATIVE PROCTITIS	19[redacted]
WEIGHT LOSS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: COLONOSCOPY WITH ASPIRATE AND BIOPSIES	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	19[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH HOT BIOPSY OF POLYP	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 355	355

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	800 mg	TID	Y-M: 20[redacted]-[redacted]
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted]-[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	1.2 g	QD	Y-M: 20[redacted]-[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]-[redacted]
METHYLPREDNISOLONE	8 mg	TID	Y-M: 20[redacted]-[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -121
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]-[redacted] / -121

DEXAMFETAMINE	10 mg	TID	Y: 19[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted]	ONGOING
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -121	Y-M: 20[redacted] / 28
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / -121	ONGOING
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 36
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 50
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 57
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TAB	BID	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 62
PREDNISONE	5.0 mg	QD	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 65
CEFALEXIN	500 mg	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 72
CALCIUM ALGINATE	1 OTHER: APPLICATION	OTHER: WEEKLY	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 153
IODOFORM	1 OTHER: APPLICATTION	OTHER: WEEKLY	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 139
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 73
DEXAMFETAMINE	10 mg	TID	Y: 19[redacted]	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description RIGHT SEPTIC OLECRANON BURITIS

Preferred term 感染性滑液包炎

AE Onset Date / Initial Rx Day [redacted]20[redacted] / 108

Age at AE Onset 6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 55): WOUND NPTST011-AEROBIC AND ANAEROBIC GRAM STAI: POSITIVE-RARE STAPH

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 55): ASPIRATION OF FLUID: POSITIVE WOUND CULTURE

AE Stopped Initial Rx Day 142

Duration of AE 35 DAYS

Severity SEVERE

Relation to Study Drug by Investigator REASONABLE POSSIBILITY

Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右肘頭の敗血症性滑液包炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，変形性関節症，関節周囲炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与108日後＊，被験者は右肘頭の敗血症性滑液包炎を発現した。投与142日後＊，右肘頭の敗血症性滑液包炎は消失した。

投与100日後＊ ，被験者は外傷後の滑液包炎を経験した。投与111日後＊，被験者は体液の吸引を受け，創傷の組織培養では，稀なブドウ球菌に陽性であった。その後，被験者は抗生物質の投与を開始した。被験者は家の改修を行っていて，作業中に肘を物にぶつけてしまった。被験者はデブリードマンによる創傷の治療を受け，包帯が巻かれた。

投与された薬剤は，calcium alginate，セファレキシン及び bactrim ds であった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CANASA SUPPOSITORY for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MEDROL DOSE PAK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Septic bursitis (10040065) (Bursitis infective (10061022)) [v.23.1] [10040065]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of RIGHT SEPTIC OLECRANON BURITIS

- Investigator: Not applicable

- AbbVie: More likely related to previous trauma. Additional risk factor is chronic steroid use.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] WOUND CULTURE:** Positive: Rare staph

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
蜂巣炎	X			X
腸閉塞	X			
処置後感染	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	7[redacted]	MALE	WHITE

Medical History	Onset Year
ADRENAL INSUFFICIENCY	20[redacted]
ASBESTOSIS	20[redacted]
AZATHIOPINE INTOLERANCE	20[redacted]
BENIGN PROSTATIC HYPERTROPHY	20[redacted]
BILATERAL INGUINAL HERNIA	19[redacted]
BILATERAL PEDAL EDEMA	20[redacted]
BLURRED VISION	20[redacted]
CELLULITIS OF TOE	20[redacted]
CHRONIC ABDOMINAL PAIN	19[redacted]
CHRONIC ARTHRALGIA	20[redacted]
CHRONIC BACK PAIN	20[redacted]
CHRONIC DIARRHEA	19[redacted]
CHRONIC ECCHYMOSIS	20[redacted]
CHRONIC FATIGUE	20[redacted]
CHRONIC HAIR LOSS	20[redacted]
CHRONIC INDIGESTION	20[redacted]
CHRONIC INTERMITTENT ANEMIA	20[redacted]
CHRONIC INTERMITTENT APHTHOUS ULCERS	19[redacted]
CHRONIC INTERMITTENT CONSTIPATION	19[redacted]
CHRONIC NAUSEA	19[redacted]
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20[redacted]
CHRONIC RIGHT LOWER EXTREMITY ERYTHEMA	20[redacted]
CHRONIC TACHYCARDIA	20[redacted]

COMMUNITY ACQUIRED PNEUMONIA	20[redacted]
CORONARY ARTERY DISEASE	20[redacted]
DEEP VEIN THROMBOSIS	20[redacted]
DEGENERATIVE DISC DISEASE	20[redacted]
DEPRESSION	20[redacted]
DIABETES MELLITUS, TYPE 2	20[redacted]
DIABETIC PERIPHERAL NEUROPATHY	20[redacted]
DYSPHAGIA	20[redacted]
DYSPNEA ON EXERTION	20[redacted]
FEVER BLISTER	20[redacted]
FREQUENT PREMATURE VENTRICULAR CONTRACTIONS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HIATAL HERNIA	20[redacted]
HISTORY OF SEPSIS	20[redacted]
HYPERLIPIDEMIA	19[redacted]
HYPERTENSION	19[redacted]
HYPOKALEMIA	20[redacted]
HYPOKALEMIA	20[redacted]
HYPOMAGNESEMIA	20[redacted]
HYPOTENSION	20[redacted]
INTERMITTENT CONSTIPATION	19[redacted]
INTERMITTENT DIZZINESS	20[redacted]
INTERMITTENT GASTRITIS	20[redacted]
IRRITABLE BOWEL SYNDROME	19[redacted]
LEFT SIDED UC	19[redacted]
LOWER ESOPHAGEAL RING	20[redacted]
NEPHROLITHIASIS	20[redacted]
NON ST ELEVATION MYOCARDIAL INFARCTION	20[redacted]
NONPRODUCTIVE COUGH	20[redacted]
NONSPECIFIC INTRAVENTRICULAR BLOCK	20[redacted]
OBESITY	20[redacted]
OBSTRUCTIVE SLEEP APNEA	20[redacted]
ORAL APHTHOUS ULCERS	20[redacted]
OSTEOARTHRITIS	20[redacted]
PULMONARY EMOBOLISM	20[redacted]
PULMONARY FIBROSIS	20[redacted]
RECTAL BLEEDING	20[redacted]

REMICADE INTOLERANCE	20[redacted]
RENAL INSUFFICIENCY	20[redacted]
SCLERAL REDNESS	20[redacted]
SORE THROAT	20[redacted]
STABLE PULMONARY NODULES	20[redacted]
STEROID INDUCED INSOMNIA	20[redacted]
THROMBOPHLEBITIS	20[redacted]
VITAMIN INSUFFIENCY	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: BILATERAL INGUINAL HERNIA REPAIR	1977
PRIOR PROCEDURES: BILATERAL LOWER EXTREMITY VENOUS DOPPLERS	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH ASPIRATE AND BIOPSIES	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSY	20[redacted]
PRIOR PROCEDURES: CT ANGIOGRAM OF THE CHEST	20[redacted]
PRIOR PROCEDURES: CT SCAN OF THORAX	20[redacted]
PRIOR PROCEDURES: CYSTOSCOPY	20[redacted]
PRIOR PROCEDURES: CYSTOSCOPY WITH STENT PLACEMENT	20[redacted]
PRIOR PROCEDURES: ESOPHAGEAL DILATATION	20[redacted]
PRIOR PROCEDURES: ESOPHAGEAL DILATATION	20[redacted]
PRIOR PROCEDURES: ESOPHAGODUODENOSCOPY WITH BIOPSY	20[redacted]
PRIOR PROCEDURES: ESOPHAGODUODENOSCOPY WITH BIOPSY	20[redacted]
PRIOR PROCEDURES: FINGER BIOPSY	20[redacted]
PRIOR PROCEDURES: PERCUTANEOUS CORONARY INTERVENTION	20[redacted]
PRIOR PROCEDURES: RIGHT KNEE ARTHROSCOPY	20[redacted]
PRIOR PROCEDURES: RIGHT LOWER EXTREMITY VENOUS DOPPLER	20[redacted]
PRIOR PROCEDURES: RIGHT TOTAL KNEE ARTHROPLASTY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	26	19[redacted]

CIGARS	NEVER
E-CIGARETTES	NEVER
PIPES	NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted] / 1	[redacted] / 57	57
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 1	[redacted] / 371	371

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	40 mg	BID	Y-M: 19[redacted]
MESALAZINE	800 mg	QID	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
MESALAZINE	2.4 g	QD	Y-M: 20[redacted]
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
MESALAZINE	800 mg	TID	Y-M: 20[redacted]
MESALAZINE	2.4 g	QD	Y-M: 20[redacted]
FENOFIBRATE	48 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
MAGNESIUM OXIDE	400 mg	QD	Y-M: 20[redacted]
METFORMIN	850 mg	TID	Y-M: 20[redacted]
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	1.25 mg	QD	Y-M: 20[redacted]
PRAVASTATIN	80 mg	QD	Y-M: 20[redacted]
FLUTICASONE;SALMETEROL	1 OTHER: PUFF	BID	Y-M: 20[redacted]

INFLIXIMAB	500.000 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
DIGOXIN	0.125 mg	QD	Y-M: 20[redacted]
GABAPENTIN	600 mg	BID	Y-M: 20[redacted]
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted]
NIFEDIPINE	30 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
PIOGLITAZONE	15 mg	QD	Y-M: 20[redacted]
LOSARTAN	100 mg	QD	Y-M: 20[redacted] / -243
SULFASALAZINE	1000 mg	BID	Y: 19[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	30 %	OTHER: NIGHTLY	Y: 20[redacted]
METOPROLOL	100 mg	QD	Y: 20[redacted]
UMECLIDINIUM;VILANTEROL	1 OTHER: PUFF	QD	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 237
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]	ONGOING
FENOFIBRATE	48 mg	QD	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	ONGOING
MAGNESIUM OXIDE	400 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 34
METFORMIN	850 mg	TID	Y-M: 20[redacted]	ONGOING
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	1.25 mg	QD	Y-M: 20[redacted]	ONGOING
PRAVASTATIN	80 mg	QD	Y-M: 20[redacted]	ONGOING
FLUTICASONE;SALMETEROL	1 OTHER: PUFF	BID	Y-M: 20[redacted]	ONGOING
DIGOXIN	0.125 mg	QD	Y-M: 20[redacted]	ONGOING
GABAPENTIN	600 mg	BID	Y-M: 20[redacted]	ONGOING
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted]	ONGOING
NIFEDIPINE	30 mg	QD	Y-M: 20[redacted]	ONGOING
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 95
PIOGLITAZONE	15 mg	QD	Y-M: 20[redacted]	ONGOING
LOSARTAN	100 mg	QD	Y-M: 20[redacted] / -243	ONGOING
WARFARIN	5 mg	QD	Y-M: 20[redacted] / 1	ONGOING
CEFTRIAXONE	1000 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35
ENOXAPARIN	110 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 41
HYDROCODONE;PARACETAMOL	2 OTHER: TABS	PRN	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 95

INSULIN ASPART	2 OTHER: UNITS	PRN	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 41
PARACETAMOL	975 mg	PRN	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 41
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35
VANCOMYCIN	2000 mg	OTHER: ONCE	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 37
PIPERACILLIN;TAZOBACTAM	3.375 g	TID	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 37
CEFAZOLIN	2000 mg	OTHER: ONCE	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 37
HYDROMORPHONE	0.5 mg	PRN	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 41
CEFEPIME	2000 mg	TID	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 41
MORPHINE	4 mg	PRN	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 41
CEFEPIME	2000 mg	BID	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 78
POTASSIUM	20 mEq	OTHER: Q 4HRS	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 47
POTASSIUM	40 mEq	PRN	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 46
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 45
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 48
POTASSIUM;SODIUM CHLORIDE	50 OTHER: ML/HR	OTHER: CONTINUOUS	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 49
POTASSIUM	20 mEq	BID	Y-M: 20[redacted] / 47	ONGOING
MAGNESIUM OXIDE	400 mg	BID	Y-M: 20[redacted] / 48	ONGOING
ALL OTHER NON-THERAPEUTIC PRODUCTS	30 %	OTHER: NIGHTLY	Y: 20[redacted]	ONGOING
METOPROLOL	100 mg	QD	Y: 20[redacted]	ONGOING
UMECLIDINIUM;VILANTEROL	1 OTHER: PUFF	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	RIGHT LOWER EXTREMITY CELLULITIS
Preferred term	蜂巣炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 91
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 35): Leukocytes: 10.9 [4 - 11] 10^9/L; NPTST077-C REACTIVE PROTEIN: 23.30 [0 - 0.9] MG/DL; [redacted]20[redacted] (RX DAY 41): NPTST259-HEMOGLOBIN A1C: 6.5 [0 - 6.5] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 36): OTHER JOINT FLUID NPTST246-GRAM STAIN AND CULTURE: POSITIVE-GRAM NEGATIVE RODS WITH 15-20 WBCS PER LPF; [redacted]20[redacted] (RX DAY 38): WOUND NPTST475-SURGICAL WOUND CULTURE W/ANAERO: POSITIVE-FEW SERRATIA MARCESCENS ISOLATED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 35): NON-INVASIVE BILATERAL LOWER EXTREMITY VENOUS DUPLEX: NO EVIDENCE OF DEEP OR SUPERFICIAL THROMBOSIS INVOLVING THE RLE AND LLE. MIXED ECHOGENIC STRUCTURES NOTED IN THE RIGHT GROIN. HYPOECHOIC AREA MEASURING APPROX. 2.5CM X 2.4CM IN

THE RIGHT POPLITEAL FOS SA. CLINICAL CORRELATION RECOMMENDED; RIGHT KNEE NEEDLE ASPIRATION: 100CC OF CLOUDY YELLOW FLUID; X-RAY COMPLETE RIGHT KNEE: KNEE PROSTHESIS IS PRESENT. JOINT NORMAL. THERE IS MILD FULLNESS OF THE SUPRAPATELLAR BURSA, SOFT TISSUE IS NORMAL; [redacted]20[redacted] (RX DAY 38): I&D OF RIGHT TOTAL KNEE ARTHROPLASTY WITH POLYETHYLENE CHANGE: GROSS PURULENCE WAS FOUND IN THE KNEE. SUB-PERIOSTEAL MEDIAL RELEASE WAS PERFORMED. A TOTAL SYNOVECTOMY WAS PERFORMED AND THE ORIGINAL POLY WAS REMOVED. KNEE WAS COPIOUSLY IRRIGATED WITH BACITRACIN, N ORMAL SALINE, AND IRRISEPT. FLUID DECOMPRESSION WAS PERFORMED TO THE POPLITEAL FOSSA THEN A NEW POLYETHYLENE WAS PLACED AND A DEEP MEDIUM HEMOVAC WAS LEFT; [redacted]20[redacted] (RX DAY 39): PICC LINE INSERTION TO LEFT UPPER ARM: PICC LINE INSERTED FOR LING TERM IV ANTIBIOTIC THERAPY SCHEDULED

AE Stopped Initial Rx Day	136
Duration of AE	46 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	INFECTED RIGHT TOTAL KNEE ARTHROPLASTY. POST PROCEDURAL INFECTION
Preferred term	処置後感染
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 91
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 35): Leukocytes: 10.9 [4 - 11] 10^9/L; NPTST077-C REACTIVE PROTEIN: 23.30 [0 - 0.9] MG/DL; [redacted]20[redacted] (RX DAY 41): NPTST259-HEMOGLOBIN A1C: 6.5 [0 - 6.5] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 36): OTHER JOINT FLUID NPTST246-GRAM STAIN AND CULTURE: POSITIVE-GRAM NEGATIVE RODS WITH 15-20 WBCS PER LPF; [redacted]20[redacted] (RX DAY 38): WOUND NPTST475-SURGICAL WOUND CULTURE W/ANAERO: POSITIVE-FEW SERRATIA MARCESCENS ISOLATED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 35): NON-INVASIVE BILATERAL LOWER EXTREMITY VENOUS DUPLEX: NO EVIDENCE OF DEEP OR SUPERFICIAL THROMBOSIS INVOLVING THE RLE AND LLE. MIXED ECHOGENIC STRUCTURES NOTED IN THE RIGHT GROIN. HYPOECHOIC AREA MEASURING APPROX. 2.5CM X 2.4CM IN THE RIGHT POPLITEAL FOS SA. CLINICAL CORRELATION RECOMMENDED; RIGHT KNEE NEEDLE ASPIRATION: 100CC OF CLOUDY YELLOW FLUID; X-RAY COMPLETE RIGHT KNEE: KNEE PROSTHESIS IS PRESENT. JOINT NORMAL. THERE IS MILD FULLNESS OF THE SUPRAPATELLAR BURSA, SOFT TISSUE IS NORMAL; [redacted]20[redacted] (RX DAY 38): I&D OF RIGHT TOTAL KNEE ARTHROPLASTY WITH POLYETHYLENE CHANGE: GROSS PURULENCE WAS FOUND IN THE KNEE. SUB-PERIOSTEAL MEDIAL RELEASE WAS PERFORMED. A TOTAL SYNOVECTOMY WAS PERFORMED AND THE ORIGINAL POLY WAS REMOVED.

KNEE WAS COPIOUSLY IRRIGATED WITH BACITRACIN, N ORMAL SALINE, AND IRRISEPT. FLUID DECOMPRESSION WAS PERFORMED TO THE POPLITEAL FOSSA THEN A NEW POLYETHYLENE WAS PLACED AND A DEEP MEDIUM HEMOVAC WAS LEFT; [redacted]20[redacted] (RX DAY 39): PICC LINE INSERTION TO LEFT UPPER ARM: PICC LINE INSERTED FOR LING TERM IV ANTIBIOTIC THERAPY SCHEDULED

AE Stopped Initial Rx Day	136
Duration of AE	46 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #3: Serious Adverse Event

Event Description	BOWEL OBSTRUCTION
Preferred term	腸閉塞
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 98
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 45): Hematocrit: 0.36 [0.397 - 0.489] FRACTION OF 1; Hemoglobin: 116 [134 - 170] G/L; Leukocytes: 10.8 [3.8 - 9.9] 10^9/L; NPTST119-CLOSTRIDIUM DIFFICILE ASSAY: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST239-GIARDIA BY EIA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST359-OCCULT BLOOD: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST363-OVA, CYSTS AND PARASITES: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 3.1 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 46): Hematocrit: 0.299 [0.397 - 0.489] FRACTION OF 1; Hemoglobin: 99 [134 - 170] G/L; Leukocytes: 7.8 [3.8 - 9.9] 10^9/L; NPTST319-MAGNESIUM: 1.8 [1.6 - 2.3] MG/DL; Potassium: 2.5 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 47): Potassium: 2.8 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 48): Potassium: 3.3 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 49): NPTST319-MAGNESIUM: 1.2 [1.6 - 2.3] MG/DL; Potassium: 3.5 [3.5 - 5.1] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 45): STOOL NPTST470-STOOL CULTURE: POSITIVE-FECAL LEUKOCYTES PRESENT IN SMALL NUMBERS. NO ENTERIC PATHOGENS, RARE NORMAL FLORA

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 45): CT ABDOMEN AND PELVIS WITH CONTRAST: THE LUNG BASES ARE CLEAR. CORONARY ARTERY CALCIFICATION. 11CM HIATAL HERNIA. THE GALLBLADDER IS NORMAL. THE LIVER, PANCREAS, AND SPLEEN ARE NORMAL. THE VASCULATURE, ADRENAL GLANDS, AND KIDNEYS ARE NOR MAL. THERE IS A 5CM IMPACTION. THERE IS MODERATE DISTENTION IN THE SIGMOID COLON. THERE IS DISTENTION OF THE REST OF THE COLON WITH AIR ND STOOL. THE CECUM MEASURES 11CM. THE PELVIS IS OTHERWISE NORMA L AND THERE ARE NO BONE LESIONS; [redacted]20[redacted] (RX DAY 48): ABDOMEN XRAY: CONTINUED DISTAL COLONIC OBSTRUCTION. IMPACTION RESOLVED; [redacted]20[redacted] (RX DAY 49): ABDOMEN XRAY: THRE IS EXTENSIVE DISTENTION OF BOWEL LOOPS WITH THE MID ABDOMEN. THIS IS SUGGESTIVE OF AN ILEUS VERSUS OBSTRUCTION.

AE Stopped Initial Rx Day	106
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC FLARE DUE TO WITHDRAWAL OF INVESTIGATIONAL PRODUCT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:18
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右下肢の蜂巣炎及び右膝の全人工膝関節置換術による感染（術後の感染）の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 2 箱を 26 年間），高脂血症，高血圧，冠動脈疾患，2 型糖尿病，肥満，腎機能不全，右膝の関節鏡検査，深部静脈血栓症，糖尿病性末梢性ニューロパチー，足指の蜂巣炎，両足部浮腫，右下肢の慢性紅斑，血栓性静脈炎，元飲酒者（1 日 2 杯以下）及び両下肢の腫脹であった。

Event 1 及び 2 の臨床経過：

投与91日後＊，被験者は右下肢の蜂巣炎及び右膝の全人工膝関節置換術による感染（術後の感染）を発現した。投与135日後＊，右下肢の蜂巣炎及び右膝の全人工膝関節置換術による感染（術後の感染）は消失した。

治験参加前の投与160日前＊，被験者は右膝の全人工膝関節置換術を受けた。

投与92日後＊，被験者は自宅での華氏 103°F の高熱を伴う右膝痛，紅斑及び腫脹のために救急治療室を受診した。診察の結果，被験者は右膝の腫脹，並びに右足首及び踵周囲の腫脹及び紅斑が認められた。同日，被験者は入院し，整形外科医の診察を受けた。被験者は右膝の針穿刺吸引を受け，100 cc の濁った黄色の液体が認められた。被験者は引き続き痛みを感じていた。治験責任医師によると，整形外科医の診察では，右膝の全人工膝関節置換術後の敗血症であると考えられた。下肢の血管機能の非侵襲的（NIV）検査では，新たな深部静脈血栓症は認められなかった。被験者は入院時から抗生物質の静脈内投与を受けていた。投与95日後＊　，被験者

は手術を受け，視診では膝に肉眼的に化膿が確認された。被験者は滑膜全切除術を受け，新しいポリエチレンが装着され，古いポリエチレンは除去された。膝にはバシトラシン，生理食塩水及びirrisept が大量に投与された。被験者は検体検査及び診断検査を受け，残りの入院期間中は抗生物質の静脈内投与で治療された。投与98日後＊　，被験者は PICC ラインを挿入し，退院した。

投与された薬剤は，ロセフィン，アセトアミノフェン，norco，ゾシン，セファゾリン，バンコマイシン，セフェピム，dilaudid，モルヒネ，バシトラシン，生理食塩水及び irrisept であった。

The patient's past medications include:

SULFASALAZINE for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted])

ASACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

COLAZAL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CANASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　Cellulitis of leg (10007912)　(Cellulitis (10007882))　[v.22.1]　[10007912]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2)　Post procedural infection (10067268)　(Post procedural infection (10067268))　[v.22.1]　[10067268]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of RIGHT LOWER EXTREMITY CELLULITIS

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing and ongoing lower limb edema, obesity and diabetes mellitus.

Event of INFECTED RIGHT TOTAL KNEE ARTHROPLASTY. POST PROCEDURAL INFECTION

- Investigator: Not applicable

- AbbVie: Event is more likely related to subject's concurrent cellulitis, obesity and pre-existing diabetes mellitus.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY TEMPERATURE:** 103 Degrees F

[redacted] **20[redacted] CRP:** 23.30 mg/dL (normal 0 to 0.90)

[redacted] **20[redacted] GRAM STAIN AND CULTURE:** JOINT FLUID: Positive-GRAM NEGATIVE RODS WITH 15-20 WBCS PER LPF

[redacted] **20[redacted] HBA1C:** 6.5 % (normal 0 to 6.5)

[redacted] **20[redacted] NON-INVASIVE BILATERAL LOWER EXTREMITY VENOUS DUPLEX:** NO EVIDENCE OF DEEP OR SUPERFICIAL THROMBOSIS INVOLVING THE RLE AND LLE. MIXED ECHOGENIC STRUCTURES NOTED IN THE RIGHT GROIN. HYPOECHOIC AREA MEASURING APPROX. 2.5CM X 2.4CM IN THE RIGHT POPLITEAL FOSSA. CLINICAL CORRELATION RECOMMENDED

[redacted] 20[redacted] **WBC:** 10.9 X10**3/MCL (normal 4 to 11)

[redacted] 20[redacted] **WOUND CULTURE:** Positive-FEW SERRATIA MARCESCENS ISOLATED

[redacted] 20[redacted] **X-RAY COMPLETE RIGHT KNEE:** KNEE PROSTHESIS IS PRESENT. JOINT NORMAL. THERE IS MILD FULLNESS OF THE SUPRAPATELLAR BURSA, SOFT TISSUE IS NORMAL
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，腸閉塞の事象を発現した。関連する病歴は，慢性腹痛，慢性下痢，慢性間欠性アフタ性潰瘍，慢性間欠性便秘，慢性悪心，過敏性腸症候群，潰瘍性大腸炎，元喫煙者（1 日 2 箱を 26 年間），2 型糖尿病，肥満，慢性間欠性貧血，慢性頻脈，うつ病，低マグネシウム血症，直腸出血，慢性消化障害，胃食道逆流性疾患，嚥下障害，間欠性胃炎，口腔内アフタ性潰瘍及び元飲酒者（1 日 2 杯以下）であった。

Event 3 の臨床経過：

投与102日後＊，被験者は腸閉塞を発現した。投与106日後＊，腸閉塞は消失した。

本事象発現前の投与92日後＊から投与98日後＊ まで，被験者は右下肢の蜂巣炎及び感染した右膝の全人工膝関節置換術のために入院していた。投与96日後＊，抗生物質の長期使用のためにPICC ラインを挿入した。

投与102日後＊，被験者は入院 4 日前から始まった下痢のために入院した。被験者は，腹痛及び腹部膨満感があった。カリウム値及びマグネシウム値が低下しており，下痢が原因と考えられた。カリウムの経口投与及び静脈内投与を行い，マグネシウムの経口投与も行った。また，手動での摘便を行った。投与106日後＊ ，被験者は退院し，感染症の経過観察，並びに整形外科及び消化器科での経過観察を受けるように指示された。

投与された薬剤は，生理食塩水，塩化カリウム，酸化マグネシウム，塩化カリウム，パントプラゾール及びカリウムであった。

The patient's past medications include:

SULFASALAZINE for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 19[redacted] - [redacted] 20[redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted])

COLAZAL for ULCERATIVE COLITIS ([redacted])

CANASA for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

LIALDA for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ACETAMINOPHEN for RLE CELLULITIS ([redacted])

INSULIN ASPART for DIABETES MELLITUS, TYPE 2 ([redacted])

LOVENOX for DVT PROPHYLAXIS ([redacted])

NORMAL SALINE for RLE CELLULITIS ([redacted])

ROCEPHIN for RLE CELLULITIS ([redacted])

VANCOMYCIN for RLE CELLULITIS ([redacted])

ZOSYN for RLE CELLULITIS ([redacted])

CEFAZOLIN for INFECTED RIGHT TOTAL ARTHROPLASTY ([redacted])

DILAUDID for INFECTED TOTAL RIGHT KNEE ARTHROPLASTY ([redacted])

MORPHINE for INFECTED RIGHT TOTAL KNEE ARTHROPLASTY ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Bowel obstruction (10006055) (Intestinal obstruction (10022687)) [v.22.1] [10006055]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of BOWEL OBSTRUCTION

- Investigator: UC flare due to withdrawal of investigational product.

- AbbVie: More likely related to pre-existing ulcerativecolitis

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMEN XRAY:** Continued distal colonic obstruction. Impaction resolved.

[redacted] **20[redacted] ABDOMEN XRAY:** There is extensive distention of bowel loops with the mid abdomen. This is suggestive of an ileus versus obstruction.

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE ASSAY:** Negative.

[redacted] **20[redacted] CT ABDOMEN AND PELVIS WITH CONTRAST:** The lung bases are clear. Coronary artery calcification. 11cm hiatal hernia. The gallbladder is normal. The liver, pancreas, and spleen are normal. The vasculature, adrenal glands, and kidneys are normal. There is a 5cm impaction. There is moderate distention in the sigmoid colon. There is distention of the rest of the colon with air and stool. The cecum measures 11cm. The pelvis is otherwise normal and there are no bone lesions.

[redacted] **20[redacted] GIARDIA BY EIA:** Negative.

[redacted] **20[redacted] HEMATOCRIT:** 36.0 % (normal 39.7 to 48.9)

[redacted] **20[redacted] HEMATOCRIT:** 29.9 % (normal 39.7 to 48.9)

[redacted] **20[redacted] HEMOGLOBIN:** 11.6 G/DL (normal 13.4 to 17.0)

[redacted] **20[redacted] HEMOGLOBIN:** 9.9 G/DL (normal 13.4 to 17.0)

[redacted] **20[redacted] MAGNESIUM:** 1.8 mg/dL (normal 1.6 to 2.3)

[redacted] **20[redacted] MAGNESIUM:** 1.2 mg/dL (normal 1.6 to 2.3)

[redacted] **20[redacted] OCCULT BLOOD:** Negative.

[redacted] **20[redacted] OVA, CYSTS AND PARASITES:** Negative.

[redacted] **20[redacted] POTASSIUM:** 3.1 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] POTASSIUM:** 2.5 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] POTASSIUM:** 2.8 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] POTASSIUM:** 3.3 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] POTASSIUM:** 3.5 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] STOOL CULTURE:** Positive; Fecal leukocytes present in small numbers. No enteric pathogens, rare normal flora.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 10.8 10^3/uL (normal 3.8 to 9.9)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.8 10^3/uL (normal 3.8 to 9.9)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19 肺炎	X			X
深部静脈血栓症				X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
ABDOMINAL HERNIA	19[redacted]
EROSIVE ESOPHAGITIS	20[redacted]
GERD	20[redacted]
KIDNEY STONES	20[redacted]
LEFT SIDED UC	20[redacted]
LIPOMA OF UPPER EXTREMITIES	20[redacted]
TINNITUS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: ABDOMINAL HERNIA REPAIR	19[redacted]
PRIOR PROCEDURES: LIPOMA EXCISION	20[redacted]
PRIOR PROCEDURES: VASECTOMY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 150	150

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]-[redacted] / -256
MESALAZINE	1.2 g	QD	Y-M: 20[redacted]-[redacted] / -167

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1.2 g	QD	Y-M: 20[redacted]-[redacted] / -167	ONGOING
AZITHROMYCIN	1 OTHER: DOSE	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 139	Y-M: 20[redacted]-[redacted] / 169
CEFDINIR	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / 148	Y-M: 20[redacted]-[redacted] / 153
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted]-[redacted] / 151	Y-M: 20[redacted]-[redacted] / 155
BUMETANIDE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / 155	ONGOING
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted]-[redacted] / 155	ONGOING
CHLORHEXIDINE	15 mL	BID	Y-M: 20[redacted]-[redacted] / 155	ONGOING
CISATRACURIUM	0.5-10 OTHER: MCG/KG/MIN	OTHER: CONTINUOUS	Y-M: 20[redacted]-[redacted] / 155	ONGOING
DOCUSATE;SENNA ALEXANDRINA	1 OTHER: TABLET	BID	Y-M: 20[redacted]-[redacted] / 155	ONGOING
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted]-[redacted] / 155	ONGOING
HYDROXYCHLOROQUINE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / 155	ONGOING
NOREPINEPHRINE	2-35 OTHER: MCG/MIN	OTHER: CONTINUOUS	Y-M: 20[redacted]-[redacted] / 155	ONGOING
PARAFFIN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]-[redacted] / 155	ONGOING
PROPOFOL	5-100 OTHER: MCG/KG/MIN	OTHER: CONTINUOUS	Y-M: 20[redacted]-[redacted] / 155	ONGOING

SODIUM CHLORIDE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 155	ONGOING
APIXABAN	5 mg	BID	Y-M: 20[redacted] / 185	ONGOING
LEVOSALBUTAMOL	90 ug	OTHER: Q4H PRN	Y-M: 20[redacted] / 186	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	COVID-19 PNEUMONIA INFECTION
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 211 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 151): NPTST153-COVID-19: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 155): Calcium: 1.99608 [2.2 - 2.55] MMOL/L; Chloride: 97 [98 - 107] MMOL/L; Creatinine: 88.40326 [71 - 115] UMOL/L; Eosinophils/Leukocytes: 0 [1 - 4] %; Glucose: 7.21591 [4.6 - 6.4] MMOL/L; Hematocrit: 0.353 [0.39 - 0.5] FRACTION OF 1; Hemoglobin: 122 [131 - 172] G/L; Leukocytes: 7.9 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 6.2 [20 - 44] %; Monocytes/Leukocytes: 2.4 [2 - 9] %; Neutrophils/Leukocytes: 90.4 [50 - 70] %; Platelets: 351 [150 - 400] 10^9/L; Potassium: 3.6 [3.5 - 4.5] MMOL/L; Sodium: 133 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 156): Alanine Aminotransferase: 50 [NOT REPORTED - NOT REPORTED] U/L; Alkaline Phosphatase: 99 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 89 [NOT REPORTED - NOT REPORTED] U/L; Bilirubin: 11.972723 [3 - 19] UMOL/L; Calcium: 2.170737 [2.2 - 2.55] MMOL/L; Chloride: 98 [98 - 107] MMOL/L; Creatinine: 79.562934 [71 - 115] UMOL/L; Eosinophils/Leukocytes: 0.6 [1 - 4] %; Glucose: 6.938375 [4.6 - 6.4] MMOL/L; Hematocrit: 0.366 [0.39 - 0.5] FRACTION OF 1; Hemoglobin: 120 [131 - 172] G/L; Leukocytes: 8.8 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 5.4 [20 - 44] %; Monocytes/Leukocytes: 2.3 [2 - 9] %; NPTST059-BASE EXC ART: 3.0 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST253-HCO3 ART: 28.0 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST319-MAGNESIUM: 2.5 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST357-O2 SAT ART: >99.0 [NOT REPORTED - NOT REPORTED] %; NPTST378-PCO2: 43 [NOT REPORTED - NOT REPORTED] mmHg; NPTST386-PH ART: 7.42 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST393-PHOSPHORUS: 3.9 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST396-PO2 ART: 180 [NOT REPORTED - NOT REPORTED] mmHg; Neutrophils/Leukocytes: 90.3 [50 - 70] %; Platelets: 384 [150 - 400] 10^9/L; Potassium: 4 [3.5 - 4.5] MMOL/L; Sodium: 138 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 185): Chloride: 103 [98 - 107] MMOL/L; Creatinine: 70.722608 [71 - 115] UMOL/L; NPTST138-CO2 TOTAL: 28 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST511-UREA NITROGEN: 12 [NOT REPORTED - NOT REPORTED] mg/dL; Potassium: 3.7 [3.5 - 4.5] MMOL/L; Sodium: 134 [136 - 145] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 151): BLOOD NPTST070-BLOOD CULTURES, 2 SETS: NEGATIVE-NO GROWTH TO DATE; [redacted]20[redacted] (RX DAY 156): SPUTUM NPTST461-SPUTUM GS: NEGATIVE-MODERATE WBC, NO ORGANISMS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 155): X-RAY PORTABLE CHEST SINGLE FRONTAL VIEW: THE CARDIOMEDIASTINAL SILHOUETTE IS NORMAL IN SIZE AND CONTOUR. PATCHY BILATERAL PULMONARY CONSOLIDATION. FINDINGS ARE MOST SEVERE WITHIN THE RIGHT UPPER LOBE AND LATERAL RIGHT LUNG BASE. LEFT-SIDED I NFILTRATES PREDOMINANT WITHIN THE APEX AND MEDIAL LEFT LUNG BASE. THE VISUALIZED BONES ARE UNCHANGED. PATCHY BILATERAL PULMONARY INFILTRATES. MULTIFOCAL PNEUMONIA VERSUS ASYMMETRIC EDEMA.; [redacted]20[redacted] (RX DAY 156): VASCULAR ULTRASOUND VENOUS DUPLEX

LOWER EXTREMITY COMPLETE BILATERAL: VEINS: NO INTRALUMINAL THROMBUS. NORMAL VENOUS COMPRESSION AND NORMAL AUGMENTATION RESPONSE. TINY PERIPHERAL CALF VEIN THROMBI MAY NOT BE DETECTABLE. NEGATIVE FOR DEEP VEIN THROMBOSIS IN BOTH LOWER EX TREMITIES.; X-RAY ABDOMEN: TIP OF ENTERIC TUBE PROJECTS OVER DISTAL STOMACH/PROXIMAL DUODENUM. EXTENSIVE RETICULONODULAR INFILTRATES THROUGHOUT BOTH LUNGS CONSISTENT WITH INTERSTITIAL PNEUMONIA.; X-RAY CHEST SINGLE FRONTAL VIEW: NO DEFINITE CHANGE COMPARED TO THE CHEST X-RAY [redacted]/20[redacted] 3:37PM. EXTENSIVE CONSOLIDATION RIGHT UPPER LOBE, RIGHT MIDDLE LOBE PERIHILAR, WITH PATCHY AREAS OF INFILTRATES SEEN THROUGHOUT THE LEFT LUNG. THERE IS NO SIGNIFICANT PLEURAL EFFUSION.; X-RAY CHEST SINGLE FRONTAL VIEW: THE HEART AND MEDIASTINUM ARE UNCHANGED. DIFFUSE BILATERAL INFILTRATES WITH INTERVAL INCREASE. INCREASED RIGHT UPPER LOBE CONSOLIDATION. INTERVAL PLACEMENT OF ENDOTRACHEAL AND NASOGASTRIC TUBES. PROBA BLE SMALL BILATERAL PLEURAL EFFUSIONS. NO PNEUMOTHORAX.; [redacted]20[redacted] (RX DAY 158): X-RAY CHEST SINGLE FRONTAL VIEW STAT: THE ENDOTRACHEAL TUBE AND GASTRIC TUBE REMAIN IN PLACE. PATCHY BILATERAL PULMONARY INFILTRATES PERSIST AND ARE STABLE. STABLE CARDIAC SIZE.; [redacted]20[redacted] (RX DAY 159): X-RAY CHEST SINGLE FRONTAL VIEW: RIGHT GREATER THAN LEFT MULTIFOCAL PNEUMONIA WITH A PREDOMINANTLY PERIPHERAL DISTRIBUTION OF CONSOLIDATION. INFILTRATES IN THE LEFT LOWER LOBE HAVE MILDLY PROGRESSED. ET TUBE HAS BEEN ADVANCED AND IS NOW WELL POSITIONED IN THE MID TRACHEA APPROXIMATELY 6CM ABOVE THE CARINA. NG TUBE REMAINS POSITIONED IN THE STOMACH. NO PNEUMOTHORAX OR PLEURAL EFFUSION. THE MEDIASTINAL CONTOURS ARE WITHIN NORMAL LI MITS.; X-RAY CHEST SINGLE FRONTAL VIEW: THERE IS REDEMONSTRATION OF ENDOTRACHEAL TUBE WHICH APPEARS SOMEWHAT HIGH IN POSITION WITH TIP PROJECTING 7.6CM ABOVE THE CARINA. THERE IS REDEMONSTRATION OF ENTERIC TUBE AND THE TIP IS NOT VISUALIZED BELOW THE DIAPHRAGM AND THE PROXIMAL SIDEHOLE IS BELOW THE DIAPHRAGM IN THE PROXIMAL STOMACH REGION. THERE HAS BEEN INTERVAL DISTRIBUTION OF A RIGHT-SIDED PICC LINE AND THE TIP IS AT THE SUPERIOR VEN A CAVA RIGHT ATRIAL JUNCTION. THERE IS SIMILAR DISTRIBUTION OF SEVERE PATCHY BILATERAL PULMONARY INFILTRATES WHICH ARE OVERALL WORSE ON THE RIGHT THAN THE LEFT. NO SUBSTANTIAL PLEURAL EFFUSIONS; [redacted]20[redacted] (RX DAY 161): X-RAY CHEST SINGLE FRONTAL VIEW: THE HEART AND MEDIASTINUM ARE UNCHANGED. DIFFUSE BILATERAL INFILTRATES, GREATEST AT THE LUNG BASES, PERIPHERY AND RIGHT UPPER LOBE. DECREASED RIGHT UPPER LOBE CONSOLIDATION. REMAINDER OF THE EXAM NOT SIGNIFICANTLY CHANGED. THE LEFT COSTOPHRENIC ANGLE IS NOT ENTIRELY INCLUDED ON THE FILM. NO PNEUMOTHORAX. TUBES AND LINES IN SATISFACTORY POSITION.; X-RAY CHEST SINGLE FRONTAL VIEW: THE HEART AND MEDIASTINUM ARE UNCHANGED. BILATERAL INFILTRATES WITH GREATEST CONSOLIDATION IN THE RIGHT UPPER LOBE. BIBASILAR INFILTRATES. OVERALL NO SIGNIFICANT INTERVAL CHANGE. INCREASED INTERSTITIA L MARKINGS BILATERALLY. PROBABLE SMALL BILATERAL PLEURAL EFFUSIONS. ENDOTRACHEAL AND NASOGASTRIC TUBES IN PLACE.; [redacted]20[redacted] (RX DAY 162): X-RAY CHEST SINGLE FRONTAL VIEW: THE HEART AND MEDIASTINUM ARE UNCHANGED. SUPPORT TUBES ARE IN EXPECTED AND UNCHANGED POSITIONS. UNCHANGED MULTIFOCAL INTERSTITIAL AND AIRSPACE OPACITIES BILATERALLY. NO PLEURAL EFFUSION OR PNEUMOTHORA X. IMAGED SKELETAL STRUCTURES ARE UNCHANGED.; [redacted]20[redacted] (RX DAY 163): X-RAY CHEST SINGLE FRONTAL VIEW: ONGOING PERIPHERAL INFILTRATES THROUGHOUT BOTH LUNGS WITH SLIGHTLY INCREASED DENSITY IN THE LUNG BASES WHICH MAY REFLECT INCREASED BASILAR INFILTRATES. TUBES AND CATHETERS UNCHANGED. HEART SIZE AND VA SULARITY STABLE. ONGOING DIFFUSE BILATERAL PULMONARY INFILTRATES SLIGHTLY INCREASED FROM THE PRIOR EXAM AS DESCRIBED.; [redacted]20[redacted] (RX DAY 164): X-RAY CHEST SINGLE FRONTAL VIEW: NO SIGNIFICANT CHANGE. STABLE LINES AND TUBES. NO PNEUMOTHORAX. STABLE BILATERAL PULMONARY CONSOLIDATION WORST IN THE PERIPHERAL AND BASILAR PORTIONS OF BOTH LUNGS.; [redacted]20[redacted] (RX DAY 165): X-RAY CHEST SINGLE FRONTAL VIEW: THE HEART AND MEDIASTINUM ARE UNCHANGED. DIFFUSE BILATERAL INFILTRATES WITH MILD INTERVAL IMPROVEMENT. SMALL BILATERAL PLEURAL EFFUSIONS. NO PNEUMOTHORAX. INTERVAL REMOVAL

OF THE ENDOTRACHEAL TUBE. NA SOGASTRIC TUBE IN PLACE. RIGHT PICC TIP IN THE SUPERIOR VENA CAVA.; [redacted]20[redacted] (RX DAY 167): X-RAY CHEST SINGLE FRONTAL VIEW: LUNG AERATION IS STABLE. PATCHY AIRSPACE CONSOLIDATION IS REDEMONSTRATED, BILATERALLY, SLIGHTLY MORE CONFLUENT IN THE LEFT LOWER LUNG FIELD. THERE I

AE Stopped Initial Rx Day	241 (35 DAYS AFTER LAST TREATMENT)
Duration of AE	31 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	VIRAL INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Event #2: Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	DVT OF RIGHT AXILLARY VEIN
Preferred term	深部静脈血栓症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 233 (27 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，COVID-19 ウイルス性肺炎の感染症の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与211日後＊，被験者は COVID-19 ウイルス性肺炎の感染症を発現した。投与241日後＊，COVID-19 ウイルス性肺炎の感染症は消失した。

投与201日後＊，被験者は 5 日前からインフルエンザ様症状があり，体温が華氏 101–102°F であり，救急外来を受診した。インフルエンザの検査は陰性で，症状を管理するように指示された。投与204日後＊，被験者は症状が改善しないため，救急治療室を受診した。胸部X 線検査が行われ，間質性混濁及び気管支炎が確認された。被験者はドキシサイクリンで治療を受け，退院した。

投与211日後＊，被験者は再来院し，発熱，悪寒，寝汗，咳嗽，疲労，及び労作時の息切れがあり，入院した。被験者は呼吸不全が悪化し，挿管された。被験者は COVID-19 の検査で陽性であった。入院中，被験者は，低酸素症を伴う急性呼吸不全，拡張性及びうっ血性の慢性心不全，急性深部静脈血栓症，低ナトリウム血症，発疹，及び入院時から 20°kg の体重減少を経験した。被験者は約 2 週間にわたり人工呼吸器を装着した後，抜管された。投与241日後＊，被験者は退院した。

治験責任医師によると，被験者には糖尿病前症及び高脂血症の病歴があった。

投与された薬剤は，セフジニル，ドキシサイクリン，アジスロマイシン，塩タブレット，クロルヘキシジン，ファモチジン，プラケニル，エリキュース，levalbuterol，bumex 及びセフトリアキソンであった。

The patient's past medications include:

CANASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.23.1] [10084380]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 VIRAL PNEUMONIA INFECTION

- Investigator: Viral infection.

- AbbVie: Event is more likely related to the COVID-19 pandemic outbreak.

Relevant Laboratory & Other Diagnostic Tests

[redacted]**20**[redacted] **ALANINE AMINO TRANSFERASE:** 50 U/L

[redacted] **20**[redacted] **ALKALINE PHOSPHATASE:** 99 U/L

[redacted] **20**[redacted] **ARTERIAL BASE EXCESS:** 3 MMOL/L

[redacted] **20**[redacted] **ARTERIAL O2 SATURATION:** 99 %

[redacted] **20**[redacted] **ARTERIAL PH:** 7.42 no units

[redacted] **20**[redacted] **ASPARTATE AMINO TRANSFERASE:** 89 U/L

[redacted] **20**[redacted] **BILIRUBIN:** 0.7 U/L

[redacted] **20**[redacted] **BLOOD CULTURES:** No growth to date

[redacted] **20**[redacted] **BMI:** 27.52096 kg/m2

[redacted] **20**[redacted] **BMI:** 23.9 kg/m2

[redacted] **20**[redacted] **BODY TEMPERATURE:** 101-102 F

[redacted] **20[redacted] CHEST XRAY:** Interstitial opacities and bronchitis.

[redacted] **20[redacted] CHEST XRAY:** THE CARDIOMEDIASTINAL SILHOUETTE IS NORMAL IN SIZE AND CONTOUR. PATCHY BILATERAL PULMONARY CONSOLIDATION. FINDINGS ARE MOST SEVERE WITHIN THE RIGHT UPPER LOBE AND LATERAL RIGHT LUNG BASE. LEFT-SIDED INFILTRATES PREDOMINANT WITHIN THE APEX AND MEDIAL LEFT LUNG BASE. THE VISUALIZED BONES ARE UNCHANGED. PATCHY BILATERAL PULMONARY INFILTRATES. MULTIFOCAL PNEUMONIA VERSUS ASYMMETRIC EDEMA.

[redacted] **20[redacted] CHLORIDE:** 103 no units

[redacted] **20[redacted] CO2:** 28 no units

[redacted] **20[redacted] COVID 19 TEST:** tested positive

[redacted] **20[redacted] CREATININE:** 1 mg/dL

[redacted] **20[redacted] CREATININE:** 0.8 no units

[redacted] **20[redacted] CT ANGIO CHEST:** No evidence for pulmonary embolism. Mild paraseptal emphysematous changes are present with interstitial thickening in a peripheral distribution and scattered groundglass opacities also predominantly in a posterior and peripheral distribution, most pronounced in the bases. Findings are consistent with patient’s known diagnosis of covid-19 pneumonia

[redacted] **20[redacted] ECHO 2D:** Abnormal echocardiogram study.

[redacted] **20[redacted] GLUCOSE:** 125 mg/dL

[redacted] **20[redacted] HCO3:** 28 MMOL/L

[redacted] **20[redacted] HEMATOCRIT:** 36.6 %

[redacted] **20[redacted] HEMOGLOBIN:** 12.0 G/DL

[redacted] **20[redacted] INFLUENZA TEST:** Negative

[redacted] **20[redacted] LYMPHOCYTES %:** 6.2 %

[redacted] **20[redacted] NASAL SWAB:** Positive

[redacted] **20[redacted] NEUTROPHILS %:** 90.4 %

[redacted] **20[redacted] PCO2:** 43 mmHg

[redacted] **20[redacted] PLATELET COUNT:** 351 X10**3/MCL

[redacted] **20[redacted] PO2:** 180 mmHg

[redacted] **20[redacted] POTASSIUM:** 3.6 MMOL/L

[redacted] **20[redacted] POTASSIUM:** 3.7 no units[redacted] 20[redacted] SODIUM: 133 MMOL/L

[redacted] **20[redacted] SODIUM:** 134 no units

[redacted] **20[redacted] SPUTUM GS:** Moderate WBC, no organisms

[redacted] **20[redacted] UREA NITROGEN:** 12 no units

[redacted] **20[redacted] VASCUALAR ULTRASOUND VENOUS DUPLEX LOWER EXTREMITY COMPLETE BILATERAL:** Veins: small areas of occlusive thrombus involving bilateral gastrocnemius veins. All other vessels in the bilateral lower extremities appear fully compliant and compressible. Thrombus in bilateral gastrocnemius veins, all other vessels appear fully compliant and compressible.

[redacted] **20[redacted] VASCULAR ULTRASOUND VENOUS DUPLEX LOWER EXTREMITY COMPLETE BILATERAL:** Veins: no intraluminal thrombus. Normal venous compression and normal augmentation response. Tiny peripheral calf vein thrombi may not be detectable. Negative for deep vein thrombosis in both lower extremities.

[redacted] **20[redacted] WEIGHT (WEEK 12):** 18[redacted] Pounds

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.9 X10**3/MCL

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.8 X10**3/MCL

[redacted] **20[redacted] X-RAY CHEST SINGLE FRONTAL VIEW:** The heart and mediastinum are unchanged. Bilateral infiltrates with greatest consolidation in the right upper lobe. Bibasilar infiltrates. Overall no significant interval change. Increased interstitial markings bilaterally. Probable small bilateral pleural effusions. Endotracheal and nasogastric tubes in place.

[redacted] **20[redacted] X-RAY CHEST SINGLE FRONTAL VIEW:** Lung aeration is stable. Patchy airspace consolidation is redemonstrated, bilaterally, slightly more confluent in the left lower lung field. There is no pneumothorax. Vasculature stable. Cardiac stable. Mediastinum: mild prominence. Pleura: probable left-sided pleural effusion. Bones: stable. Other: endotracheal tube terminates approximately 4.3cm proximal to the carina. Nasogastric tube terminates beyond the scope of the film. Right -sided picc line terminates at the atriocaval junction. Increasing confluence of patchy bilateral airspace consolidation, particularly within the left lower lung

[redacted] **20[redacted] X-RAY CHEST SINGLE FRONTAL VIEW:** Considerably improved interstitial pneumonitis throughout the right lung and minimal improvement of interstitial pneumonitis throughout the left lung. No pneumothorax. No other interval change.

[redacted] **20[redacted] X-RAY CHEST SINGLE FRONTAL VIEW:** Cardiac silhouette is enlarged. Hazy ground glass densities are noted bilaterally worse in the right lung than the left. Compared to the prior chest radiograph, there is no significant change. Stable right worse than left lung ground glass infiltrates.

[redacted] **20[redacted] XRAY ABDOMEN:** Tip of enteric tube projects over distal stomach/proximal duodenum. Extensive reticulonodular infiltrates throughout both lungs consistent with interstitial pneumonia.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
クロストリジウム・ディフィシレ感染	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	5[redacted]	MALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
DEPRESSION	20[redacted]
DVT	20[redacted]
ELEVATED C- REACTIVE PROTEIN	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HISTORY OF DRUG ABUSE (COCAINE)	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
REVISE MEDIAN N/CARPAL TUNNEL	20[redacted]
RIGHT HIP PAIN	20[redacted]
SUICIDE ATTEMPT	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	20[redacted]
PRIOR PROCEDURES: BUNIONECTOMY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: INCISION OF WRIST CAPSULE	20[redacted]
PRIOR PROCEDURES: TONSILLECTOMY	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	20	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	FORMER	12 SESSIONS	1	20[redacted]

PIPES NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	More than 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 61	61
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 1	[redacted] / 369	369

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	500 mg	PRN	Y-M: [redacted]
MESALAZINE	1.2 g	QD	Y-M: [redacted]
PREDNISONE	60 mg	QD	Y-M: [redacted]
PREDNISONE	60 mg	QD	Y-M: [redacted]
MESALAZINE	4.8 g	QD	Y-M: [redacted]
VITAMINS NOS	1 OTHER: TAB	QD	Y: [redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	500 mg	PRN	Y-M: [redacted]	ONGOING
MESALAZINE	4.8 g	QD	Y-M: [redacted]	ONGOING
METHYLPREDNISOLONE	60 mg	QD	Y-M: [redacted] / 268	Y-M: [redacted] / 270
PREDNISONE	40 mg	QD	Y-M: [redacted] / 268	Y-M: [redacted] / 274
VANCOMYCIN	125 mg	QID	Y-M: [redacted] / 268	Y-M: [redacted] / 278
PREDNISONE	30 mg	QD	Y-M: [redacted] / 275	Y-M: [redacted] / 281
PREDNISONE	20 mg	QD	Y-M: [redacted] / 282	Y-M: [redacted] / 288
PREDNISONE	10 mg	QD	Y-M: [redacted] / 289	Y-M: [redacted] / 295
VITAMINS NOS	1 OTHER: TAB	QD	Y: [redacted]	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	CLOSTRIDIUM DIFFICILE INFECTION
Preferred term	クロストリジウム・ディフィシレ感染
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 329
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
[redacted]20[redacted] (RX DAY 268): STOOL NPTST492-TOXIGENIC C. DIFFICILE: POSITIVE-C. DIFF DETECTED IN THE FECAL TESTING	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day	356
Duration of AE	28 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	C-DIFF EXPOSURE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:18
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，クロストリジウム・ディフィシレ感染の事象を発現した。関連する病歴は，うつ病，高血圧，胃食道逆流性疾患，電子タバコの元喫煙者（1 日 1 箱を 20 年間）及び元飲酒者（1 日 4 杯以上）であった。

Event 1 の臨床経過：

投与329日後＊，被験者はクロストリジウム・ディフィシレ感染を発現した。投与356日後＊，クロストリジウム・ディフィシレ感染は消失した。

投与329日後＊ ，被験者は腹部不快感，悪心，及び 2 日間の血便（1 日約 20 回）のために入院した。入院時，被験者は熱がなく，血圧は 142/78 mmHg であった。被験者は薬物治療を開始し，投与331日後＊に退院した。

治験責任医師によると，被験者は潰瘍性大腸炎でこれらの症状を常に経験しているとのことであった。

投与された薬剤は，prednisone，バンコマイシン及びソル・メドロールであった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Clostridium difficile infection (10054236) (Clostridium difficile infection (10054236)) [v.23.1] [10054236]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of CLOSTRIDIUM DIFFICILE INFECTION

- Investigator: C-DIFF EXPOSURE

- AbbVie: The event is more likely related to pre-existing Ulcerative colitis. Patients with inflammatory bowel disease, including ulcerative colitis, are at an increased risk of developing Clostridium difficile infection, with higher rates of asymptomatic carriage of C. difficile (9.4% in patients with ulcerative

colitis, versus 1% in healthy volunteers).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** 142/78 mmHg

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE TEST:** Positive, C. DIFF DETECTED IN THE FECAL TESTING

[redacted] **20[redacted] CREATININE:** 0.98 No Unit

[redacted] **20[redacted] CRP:** 63 No Unit

[redacted] **20[redacted] HEART RATE:** 76 /min

[redacted] **20[redacted] NASOPHARYNGEAL SWAB:** COVID-19: Negative

[redacted] **20[redacted] POTASSIUM:** 3.9 No Unit

[redacted] **20[redacted] SODIUM:** 137 No Unit

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
基底細胞癌				X
脱水	X			
下痢	X			
悪心	X			
嘔吐	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
ABDOMINAL PAIN	20[redacted]
ACID REFLUX	20[redacted]
ANEMIA	20[redacted]
ARTHRITIS	20[redacted]
DEPRESSION	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GALLSTONES	20[redacted]
RASHES ON PALMS AND SOLES OF FEET	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: CHOLECYSTECTOMY	20[redacted]
PRIOR PROCEDURES: LIGATION OF FALLOPIAN TUBE	20[redacted]
PRIOR PROCEDURES: TOTAL HYSTERECTOMY	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: CHEST X RAY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	UNKNOWN			
CIGARETTES	CURRENT	0.5 PACK	20	
CIGARS	UNKNOWN			
E-CIGARETTES	UNKNOWN			

PIPES UNKNOWN

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 1		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
MESALAZINE	1.2 g	BID	Y-M: 20[redacted]
VEDOLIZUMAB	300.000 mg	EVERY OTHER WEEK	Y-M: 20[redacted] / -202
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -73
GLUCOSE	25 mL	PRN	Y-M: 20[redacted] / -78
SODIUM CHLORIDE	1000 mL	PRN	Y-M: 20[redacted] / -78
URSODEOXYCHOLIC ACID	300 mg	BID	Y-M: 20[redacted] / -57
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -33
CLONAZEPAM	5 mg	QD	Y: 20[redacted]
NORTRIPTYLINE	25 mg	QD	Y: 20[redacted]
ADALIMUMAB	160.000 mg	Q2WK	Y: 20[redacted]
CHLORZOXAZONE	500 mg	TID	Y: 20[redacted]
DOXEPIN	25 mg	QD	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1.2 g	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / -86
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -73	Not reported
GLUCOSE	25 mL	PRN	Y-M: 20[redacted] / -78	Y-M: 20[redacted] / -70
SODIUM CHLORIDE	1000 mL	PRN	Y-M: 20[redacted] / -78	Y-M: 20[redacted] / -70
URSODEOXYCHOLIC ACID	300 mg	BID	Y-M: 20[redacted] / -57	Y-M: 20[redacted] / 29

OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -33	Not reported
CLONAZEPAM	5 mg	QD	Y: 20[redacted]	Not reported
NORTRIPTYLINE	25 mg	QD	Y: 20[redacted]	Not reported
CHLORZOXAZONE	500 mg	TID	Y: 20[redacted]	Not reported
DOXEPIN	25 mg	QD	Y: 20[redacted]	Not reported

Event #1: Serious Adverse Event

Event Description	NAUSEA, DIARRHEA, DEHYDRATION, VOMITTING
Preferred term	脱水，下痢，悪心，嘔吐
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / -20 DAYS BEFORE TREATMENT
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY -77): CHEST X RAY: HEART SIZE NORMAL, NO PLEURAL EFFUSION OR PNEUMOTHORAX

AE Stopped Initial Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SEVERE UC FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Possible Malignancies, Event of Interest - Malignancy, Event of Interest - Non-melanoma Skin Cancer (NMSC)

Event Description	BASAL CELL CARCINOMA LEFT UPPER CHEST
Preferred term	基底細胞癌
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 178
Age at AE Onset	4[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day	188
Duration of AE	11 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:16:18
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で，ウパダシチニブの投与前に悪心，下痢，脱水及び嘔吐の事象を発現した。関連する病歴は，貧血，潰瘍性大腸炎，非飲酒者及び現喫煙者（1 日 0.5 箱）であった。

Event 1 の臨床経過：

投与19日前＊，被験者は悪心，下痢，脱水及び嘔吐を発現した。

投与19日前＊，被験者は入院した。被験者は，悪心，嘔吐及び脱水症状に対して未詳の薬物治療を受けた。投与11日前＊，被験者は退院し，血性及び水様性の下痢は残っていたが，経口摂取が開始できた。

投与された薬剤は，prilosec，prednisone，塩化ナトリウム及び dextrose であった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Lead-In)

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1) Nausea (10028813) (Nausea (10028813)) [v.23.1] [10028813]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

2) Diarrhea (10012727) (Diarrhoea (10012735)) [v.23.1] [10012727]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

3) Vomiting (10047700) (Vomiting (10047700)) [v.23.1] [10047700]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

4) Dehydration (10012174) (Dehydration (10012174)) [v.23.1] [10012174]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Lead-In)

Event of NAUSEA, DIARRHEA, DEHYDRATION, VOMITING

- Investigator: Severe UC flare

- AbbVie: Lack of temporal association. Event occurred during the screening period.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** Heart size normal, no pleural effusion or pneumothorax.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
急性呼吸不全	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
ABDOMINAL PAIN	20[redacted]
BPH	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
VENTRICULAR TACHYCARDIA	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	19[redacted]
PRIOR PROCEDURES: CHOLECYSTECTOMY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: RIGHT HERNIORRHAPHY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	3.75	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 58	58
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted] / 1	[redacted] / 448	448

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ATORVASTATIN	20 mg	QD	Y-M: [redacted]
METOPROLOL	25 mg	QD	Y-M: [redacted]
VERAPAMIL	80 mg	TID	Y-M: [redacted]
AZATHIOPRINE	50 mg	QD	Y-M: [redacted] / -210
FINASTERIDE	0.75 mg	QD	Y-M: [redacted] / -214
PREDNISONE	20 mg	QD	Y-M: [redacted] / -183
INFLIXIMAB	5.000 mg/kg	EVERY 8 WEEKS	Y: [redacted]
ADALIMUMAB	40.000 mg	NOT REPORTED	Y: [redacted]
TAMSULOSIN	0.4 mg	OTHER: EVERY OTHER DAY	Y: [redacted]
VEDOLIZUMAB	300.000 mg	EVERY 4 WEEKS	Y: [redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ATORVASTATIN	20 mg	QD	Y-M: [redacted]	ONGOING
METOPROLOL	25 mg	QD	Y-M: [redacted]	ONGOING
VERAPAMIL	80 mg	TID	Y-M: [redacted]	ONGOING
FINASTERIDE	0.75 mg	QD	Y-M: [redacted] / -214	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: [redacted] / 31	Y-M: [redacted] / 336
ESOMEPRAZOLE	40 mg	QD	Y-M: [redacted] / 250	ONGOING
DEXAMETHASONE	10 mg	QD	Y-M: [redacted] / 317	Y-M: [redacted] / 317
PARACETAMOL	650 mg	PRN	Y-M: [redacted] / 317	ONGOING
REMDESIVIR	200 mg	QD	Y-M: [redacted] / 317	Y-M: [redacted] / 317
ENOXAPARIN	90 mg	OTHER: Q12H	Y-M: [redacted] / 318	ONGOING
REMDESIVIR	100 mg	OTHER: EVERY 24 HOUR	Y-M: [redacted] / 318	Y-M: [redacted] / 321
ALPRAZOLAM	0.25 mg	QD	Y-M: [redacted] / 319	Y-M: [redacted] / 319

LISINOPRIL	5.0 mg	QD	Y-M: 20[redacted] / 331	Y-M: 20[redacted] / 351
TAMSULOSIN	0.4 mg	OTHER: EVERY OTHER DAY	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	ACUTE RESPIRATORY FAILURE
Preferred term	急性呼吸不全
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 375
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 317): Alanine Aminotransferase: 41 [16 - 61] U/L; Albumin: 22 [34 - 50] G/L; Aspartate Aminotransferase: 40 [15 - 37] U/L; Blood Urea Nitrogen: 10.35213 [2.49879 - 6.42546] MMOL/L; Calcium: 2.070933 [2.120835 - 2.520051] MMOL/L; Creatinine: 99.895684 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 4.38 [4.5 - 6] 10^12/L; Hemoglobin: 131 [135 - 180] G/L; Leukocytes: 14.9 [4.5 - 11] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 317): OTHER NASOPHARYNX NPTST153-COVID-19: POSITIVE-COVID-19 VIRUS DETECTED AND SUBJECT PRESENTED WITH ACUTE HYPOXEMIC RESPIRATORY FAILURE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 317): CHEST X-RAY: MULTIFOCAL INTERSTITIAL INFILTRATES IDENTIFIED BILATERALLY, SUSPICIOUS FOR MULTIFOCAL PNEUMONIA. THERE ARE NO EFFUSIONS.; [redacted]20[redacted] (RX DAY 323): CHEST X-RAY: STABLE BILATERAL COVID-19 PNEUMONITIS.; [redacted]20[redacted] (RX DAY 331): CHEST X-RAY: DIFFUSE BILATERAL PULMONARY INFILTRATES, MILDLY IMPROVED COMPARED TO PREVIOUS EXAM. NO PLEURAL EFFUSION OR PNEUMOTHORAX IS SEEN. THE CARDIO MEDIASTINAL SILHOUETTE IS STABLE.

AE Stopped Initial Rx Day	394
Duration of AE	20 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID-19 INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性呼吸不全の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 3.75 年間），潰瘍性大腸炎，前立腺肥大，心室性頻脈及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与375日後＊ ，被験者は急性呼吸不全を発現した。投与394日後＊ ，急性呼吸不全は消失した。

本事象発現前に，被験者は COVID-19 に曝露されており，投与363日後＊ に COVID-19 感染（非重篤）を経験した。被験者は咽頭痛及び息切れがあった。投与729日後＊ ，被験者は COVID-19 の検査で陽性であった。

投与375日後＊，被験者は入院した。被験者は息切れ，最小労作時の呼吸困難，疲労の悪化，発熱，悪寒及び食欲減退があった。被験者の酸素飽和度は低かった。被験者は急性低酸素性呼吸不全と診断され，薬物治療が開始され，回復期血漿の投与及び酸素吸入を受けた。被験者は肺浸潤が悪化したため，デキサメタゾン及びメチルプレドニゾロンの静脈内投与を受けた。入院中，被験者は血便を経験していた。投与394日後＊ ，被験者はプレドニゾロン及び噴霧型気管支拡張薬の投与並びに酸素吸入を受け，安定した状態で退院した。

投与された薬剤は，レムデシビル，デキサメタゾン，アルプラゾラム，メチルプレドニゾロン，エノキサパリン及びアセトアミノフェンであった。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

HUMIRA for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

ENTYVIO for ULCERATIVE COLITIS (20[redacted] -[redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] -[redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] -[redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute respiratory failure (10001053) (Acute respiratory failure (10001053)) [v.24.0] [10001053]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE RESPIRATORY FAILURE

- Investigator: COVID-19 Infection

- AbbVie: Event is more likely a complication of the concurrent COVID-19 infection.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALT:** 41 U/L (normal 16 to 61)

[redacted] **20[redacted] AST:** 40 U/L (normal 15 to 37)

[redacted] **20[redacted] BMI:** 29.1 kg/m2

[redacted] **20[redacted] BUN:** 29 mg/dL (normal 7 to 18)

[redacted] **20[redacted] CALCIUM:** 8.3 mg/dL (normal 8.5 to 10.1)

[redacted] **20[redacted] CHEST X-RAY:** Multifocal interstitial infiltrates identified bilaterally, suspicious for multifocal pneumonia. There are no effusions.

[redacted] **20[redacted] CHEST X-RAY:** Stable bilateral Covid-19 pneumonitis.

[redacted] **20[redacted] CHEST X-RAY:** Diffuse bilateral pulmonary infiltrates, mildly improved compared to previous exam. No pleural effusion or pneumothorax is seen. The cardio mediastinal silhouette is stable.

[redacted] **20[redacted] COVID-19 TEST:** Nasopharyngeal swab: Positive for COVID-19

[redacted] 20[redacted] **COVID-19 TEST:** Nasopharyngeal swab: COVID-19 virus detected and patient presented with acute hypoxemic respiratory failure

[redacted] **20**[redacted] **CREATININE:** 1.13 mg/dL (normal 0.70 to 1.30)

[redacted] **20**[redacted] **HEMOGLOBIN:** 13.1 G/DL (normal 13.5 to 18)

[redacted] **20**[redacted] **RBC:** 4.38 M/uL (normal 4.5 to 6)

[redacted] **20**[redacted] **WBC:** 14.9 K/uL (normal 4.5 to 11)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	5[redacted]	MALE	WHITE

Medical History	Onset Year
ALLERGIC TO ASPIRIN	19[redacted]
ANEMIA	20[redacted]
APPENDICITIS	19[redacted]
ASTHMA	19[redacted]
AXIAL ARTHROPATHY	20[redacted]
CATARACTS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
LOSS OF VISION	20[redacted]
ORAL APTHOUS ULCERS	20[redacted]
PERIPHERAL ARTHROPATHY	20[redacted]
RETINA DETACHMENT	20[redacted]
SEASONAL ALLERGIES	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	19[redacted]
PRIOR PROCEDURES: RETINAL SURGERY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	29	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted] / 1	[redacted] / 45	45

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 g	QD	Y-M: [redacted]
PREDNISONE	60 mg	QD	Y-M: [redacted]
ADALIMUMAB	80.000 mg	ONCE ON DAY 1, THEN @ DAY 15	Y-M: [redacted] / -363
PARACETAMOL	500 mg	PRN	Y-M: [redacted] / -42
BUDESONIDE;FORMOTEROL	90 OTHER: MCG	QD	Y: [redacted]
FLUTICASONE	50 OTHER: MCG	PRN	Y: [redacted]
LORATADINE	10 mg	PRN	Y: [redacted]
MONTELUKAST	10 mg	QD	Y: [redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4.8 g	QD	Y-M: [redacted]	Y-M: [redacted] / 86
PARACETAMOL	500 mg	PRN	Y-M: [redacted] / -42	ONGOING
EMOLLIENTS AND PROTECTIVES	1 OTHER: SOFT GEL	QID	Y-M: [redacted] / 29	ONGOING
PREDNISONE	5 mg	QD	Y-M: [redacted] / 7	Y-M: [redacted] / 11
CEFTRIAXONE	2 g	OTHER: ONCE	Y-M: [redacted] / 41	Y-M: [redacted] / 41
GLYCOPYRRONIUM	0.2 mg	OTHER: ONE TIME	Y-M: [redacted] / 41	Y-M: [redacted] / 41
SODIUM CHLORIDE	1000 mL	OTHER: ONE TIME	Y-M: [redacted] / 41	Y-M: [redacted] / 41
PREDNISONE	40 mg	QD	Y-M: [redacted] / 43	Y-M: [redacted] / 78
HYDROCORTISONE	100 mg	OTHER: EVERY 6 HOURS	Y-M: [redacted] / 45	Y-M: [redacted] / 51

METRONIDAZOLE	500 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 51
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 51
INFLIXIMAB	5 mg/kg	OTHER: AS DIRECTED	Y-M: 20[redacted] / 46	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 51
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 86
PREDNISONE	35 mg	QD	Y-M: 20[redacted] / 79	ONGOING
BUDESONIDE;FORMOTEROL	90 OTHER: MCG	QD	Y: 20[redacted]	ONGOING
FLUTICASONE	50 OTHER: MCG	PRN	Y: 20[redacted]	ONGOING
LORATADINE	10 mg	PRN	Y: 20[redacted]	ONGOING
MONTELUKAST	10 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 93
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 45): Creatinine: 119.344401 [53.041956 - 106.083912] UMOL/L; Leukocytes: 12.52 [4.4 - 10.5] 10^9/L; Lymphocytes/Leukocytes: 12.4 [20.5 - 45] %; Monocytes: 1.38 [0 - 0.8] 10^9/L; NPTST160-CRP INFLAMMATORY: 20.7 [0 - 5] MG/L; NPTST296-INR: 1.17 [0.8 - 1.2] RATIO; NPTST413-PT: 14.5 [11.5 - 14.9] RATIO; Neutrophils: 9.43 [1.5 - 7.5] 10^9/L; Neutrophils/Leukocytes: 76.1 [50 - 70] %; Platelets: 487 [139 - 361] 10^9/L; [redacted]20[redacted] (RX DAY 46): NPTST210-FECES C DIFFICILE AG: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST211-FECES C DIFFICILE TOXIN EIA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST213-FECES LACTOFERRIN: POSITIVE [0 - 0] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 47): NPTST212-FECES CAMPYLOBACTER GRP PCR: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST214-FECES SALMONELLA SPP PCR: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST215-FECES SHIGELLA SPP PCR: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST216-FECES VIBRIO PCR: NOT DETECTED [10 - 100] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 50): Glucose: 6.327798 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.359 [0.369 - 0.485] FRACTION OF 1; Hemoglobin: 120 [126 - 167] G/L; Leukocytes: 10.78 [4.4 - 10.5] 10^9/L; NPTST137-CO2 LVL: 23 [24 - 32] MMOL/L; NPTST159-CRP: 2.1 [0.3 - 5] MG/L; Platelets: 392 [139 - 361] 10^9/L; Potassium: 3.3 [3.5 - 5] MMOL/L; Protein: 58 [65 - 80] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ULCERATIVE COLITIS FLARE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:18
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，虫垂切除，元喫煙者（1 日 0.5 箱を 29 年間），広範囲な潰瘍性大腸炎（全大腸炎型），貧血及び非飲酒者であった。

Event 1 の臨床経過：

投与93日後＊，潰瘍性大腸炎の悪化を発現した。

投与100日後＊，被験者は下痢の増加，1 日 20 回の血便，腹痛，不快感及び悪寒があり，入院した。被験者は，静脈内投与での抗生物質療法，生物学的療法及び副腎皮質ステロイド療法で治療を受けた。投与106日後＊，被験者は退院した。

本事象により，治験薬の投与は完全に中止された。

投与された薬剤は，フラジール，レミケード，ロセフィン，zofran，robinul，prednisone 及び生理食塩水であった。

The patient's past medications include:

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ASPIRIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

---

1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.1] [10009901]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Ulcerative colitis flare

- AbbVie: Event more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT:** Not reported

[redacted] **20[redacted] CO2 LVL:** 23 MMOL/L (normal 24 to 32)

[redacted] **20[redacted] CREATININE:** 1.35 mg/dL (normal 0.60 to 1.20)

[redacted] **20[redacted] CRP:** 2.1 MG/L (normal <5)

[redacted] **20[redacted] CRP INFLAMMATORY:** 20.7 MG/L (normal 0 to 5)

[redacted] **20[redacted] FECES C DIFFICILE AG:** Negative

[redacted] **20[redacted] FECES C DIFFICILE TOXIN EIA:** Negative

[redacted] **20[redacted] FECES CAMPYLOBACTER GRP PCR:** Not Detected

[redacted] **20[redacted] FECES LACTOFERRIN:** Positive

[redacted] **20[redacted] FECES SALMONELLA SPP PCR:** Not Detected

[redacted] 20[redacted] **FECES SHIGELLA SPP PCR:** Not Detected

[redacted] 20[redacted] **FECES VIBRIO PCR:** Not Detected

[redacted] 20[redacted] **GLUCOSE:** 114 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **HEMATOCRIT:** 35.9 % (normal 36.9 to 48.5)

[redacted] 20[redacted] **HEMOGLOBIN:** 12.0 G/DL (normal 12.6 to 16.7)

[redacted] 20[redacted] **INR:** 1.17 RATIO (normal 0.8 to 1.2)

[redacted] 20[redacted] **LYMPHOCYTES %:** 12.4 % (normal 20.5 to 45.0)

[redacted] 20[redacted] **MONOCYTES ABS:** 1.38 X10**3/MCL (normal 0 to 0.80)

[redacted] 20[redacted] **NEUTROPHILS %:** 76.1 %(normal 50.0 to 70.0)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 9.43 X10**3/MCL (normal 1.50 to 7.50)

[redacted] 20[redacted] **PLATELET COUNT:** 487 X10**9/L (normal 139 to 361)

[redacted] 20[redacted] **PLATELET COUNT:** 392 X10**9/L (normal 139 to 361)

[redacted] 20[redacted] **POTASSIUM:** 3.3 MEQ/L (normal 3.5 to 5.0)

[redacted] 20[redacted] **PROTEIN:** 5.8 G/DL (normal 6.5 to 8.0)

[redacted] 20[redacted] **PT:** 14.5 RATIO (normal 11.5 to 14.9)

[redacted] 20[redacted] **WHITE BLOOD CELLS**: 12.52 10^3/uL (normal 4.40 to 10.50)

[redacted] 20[redacted] **WHITE BLOOD CELL:** 10.78 X10**9/L (normal 4.40 to 10.50)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
不安	X			
うつ病	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	3[redacted]	MALE	WHITE

Medical History	Onset Year
ANXIETY	20[redacted]
DEPRESSION	20[redacted]
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 64	64
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 1		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DESVENLAFAXINE	100 mg	QD	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
AMFETAMINE;DEXAMFETAMINE	10 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted] / -199
DICYCLOVERINE	20 mg	OTHER: EVERY 6 HOURS AS NEEDED	Y-M: 20[redacted] / -109

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
DESVENLAFAXINE	100 mg	QD	Y-M: 20[redacted]	Not reported
AMFETAMINE;DEXAMFETAMINE	10 mg	BID	Y-M: 20[redacted]	Not reported
DICYCLOVERINE	20 mg	OTHER: EVERY 6 HOURS AS NEEDED	Y-M: 20[redacted] / -109	Not reported
BREXPIPRAZOLE	2 mg	QD	Y-M: 20[redacted] / 102	Y-M: 20[redacted] / 216
DULOXETINE	30 mg	QD	Y-M: 20[redacted] / 102	Y-M: 20[redacted] / 185
LAMOTRIGINE	25 mg	QD	Y-M: 20[redacted] / 198	Not reported

Event #1: Serious Adverse Event

Event Description	WORSENING ANXIETY, WORSENING DEPRESSION
Preferred term	不安，うつ病
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 249
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day	280
Duration of AE	32 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	IMPROVEMENT IN UC S/S LEADING TO ABILITY TO FOCUS ON TREATMENT FOR HIS ANXIETY/DEPRESSION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted] 20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，不安の悪化及びうつ病の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，不安，うつ病，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与249日後＊，被験者は不安の悪化及びうつ病の悪化を発現した。投与280日後＊，不安の悪化及びうつ病の悪化は消失した。

投与249日後＊，被験者は不安及びうつ病のために入院した。投与280日後＊，被験者は良好な状態で退院した。

治験責任医師によると，被験者には不安及びうつ病の病歴の危険因子があった。

投与された薬剤は，lamotrigone であった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Anxiety aggravated (10048339) (Anxiety (10002855)) [v.24.0] [10048339]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

2) Depression worsened (10012398) (Depression (10012378)) [v.24.0] [10012398]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING ANXIETY

- Investigator: Improvement in UC s/s leading to ability to focus on treatment for his anxiety/depression.

- AbbVie: Events are more likely related to pre-existing anxiety and depression.

Event of WORSENING DEPRESSION

- Investigator: Improvement in UC s/s leading to ability to focus on treatment for his anxiety/depression.

- AbbVie: Events are more likely related to pre-existing anxiety and depression.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY WEIGHT:** 17[redacted] Pounds

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
浸潤性乳癌	X	X		X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
APPENDICITIS	20[redacted]
ASTIGMATISM	20[redacted]
BREAST CYST (LEFT)	20[redacted]
CIATALGIA (SCIATIC NEURITIS)	20[redacted]
LEFT SIDED UC	20[redacted]
MENOPAUSE	20[redacted]
MYOPIA	20[redacted]
OVARIAN CYST (RIGHT)	19[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	20[redacted]
PRIOR PROCEDURES: BOTH BREAST IMPLANT SURGERY	20[redacted]
PRIOR PROCEDURES: BOTH BREAST IMPLANT SURGERY	20[redacted]
PRIOR PROCEDURES: LEFT BREAST CYST REMOVALSURGERY	20[redacted]
PRIOR PROCEDURES: NECK PLASTIC SURGERY	20[redacted]
PRIOR PROCEDURES: NOSE PLASTIC SURGERY	20[redacted]
PRIOR PROCEDURES: OVARIAN CYST REMOVAL SURGERY	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.1 PACK	34	
CIGARS	NEVER			
E-CIGARETTES	NEVER			

PIPES NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 62	62
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 224	224

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1200 mg	BID	Y: 20[redacted]
VEDOLIZUMAB	300.000 mg	EVERY 2 WEEKS (Q2W)	Y: 20[redacted]
BOTULINUM TOXIN TYPE A	50 OTHER: UNITS	OTHER: EVERY 6 MONTHS	Y: 20[redacted]
PYRIDOXINE	100 mg	OTHER: EVERY 6 MONTHS (Q6M)	Y: 20[redacted]
THIAMINE	100 mg	OTHER: EVERY 6 MONTHS (Q6M)	Y: 20[redacted]
VITAMIN B12 NOS	10000 OTHER: MCG	OTHER: EVERY 6 MONTHS	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BOTULINUM TOXIN TYPE A	50 OTHER: UNITS	OTHER: EVERY 6 MONTHS	Y: 20[redacted]	ONGOING
PYRIDOXINE	100 mg	OTHER: EVERY 6 MONTHS (Q6M)	Y: 20[redacted]	ONGOING
THIAMINE	100 mg	OTHER: EVERY 6 MONTHS (Q6M)	Y: 20[redacted]	ONGOING
VITAMIN B12 NOS	10000 OTHER: MCG	OTHER: EVERY 6 MONTHS	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC

Event Description	RIGHT BREAST INVASIVE CARCINOMA
Preferred term	浸潤性乳癌
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 293
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 216): BREAST PHYSICAL EXAMINATION: ABNORMAL: ABNORMAL MASS IN RIGHT BREAST; [redacted]20[redacted] (RX DAY 219): MAMMOGRAPHY`: IRREGULAR MASS RIGHT BREAST, 3 O'CLOCK MIDDLE DEPTH 4 CM FROM THE NIPPLE; RIGHT BREAST ULTRASOUND: IRREGULAR MASS RIGHT BREAST, AT 3 O'CLOCK MIDDLE DEPTH 4 CM FORM THE NIPPLE; ULTRASOUND CORE NEEDLE BIOPSY, RIGHT BREAST, 3 O'CLOCK, 4 CM FROM THE NIPPLE: INVASIVE MAMARY CARCINOMA LARGEST TUMOR FRAGMENT MEASURES 1 CM NOTHINHAM GRADE: 3+2+1=6, GRADE II. ESTROGEN RECEPTOR (ER): POSITIVE 98% PROGESTERONE RECEPTOR (PR): 98% POSITIVE KI-67 PROLIFERATIV E INDEX: 18% HER2: PENDING	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:16:18

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右乳房の浸潤癌の事象を発現した。関連する病歴は，

卵巣嚢胞の切除，右卵巣嚢胞，左乳房嚢胞，左乳房嚢胞の切除，潰瘍性大腸炎，両乳房インプラント，喫煙者（1 日 0.1 箱を 34 年間）及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与293日後＊，被験者は右乳房の浸潤癌を発現した。

投与285日後＊，被験者は乳房の検診で腫瘤を指摘された。投与288日後＊，被験者は超音波検査，乳房撮影，及び右乳房の超音波ガイド下でのコア針生検を受けた。　投与293日後＊，生検の結果，浸潤性乳管癌が陽性であり，被験者は腫瘍科医に紹介された。腫瘍科医は被験者の診断を確認し，腫瘤はステージ 1 に分類された。この時，被験者は体調も良く，関連する症状は認められなかった。被験者は，腫瘤除去術を受けることとなった。

被験者には，叔母 2 人及び姪 3 人の乳癌の家族歴があった。

本事象により，治験薬の投与は中止された。

The patient's past medications include:

MESALAMINE for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Invasive breast carcinoma (10075713) (Invasive breast carcinoma (10075713)) [v.23.1] [10075713]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of RIGHT BREAST INVASIVE CARCINOMA

- Investigator: Not applicable

- AbbVie: Weak temporal relationship to blinded study drug with total cumulative exposure of approximately 9.5 months. Breast cancer is the most frequently diagnosed malignancy in women. Approximately 12.9 percent of women will be diagnosed with female breast cancer at some point during their lifetime.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BREAST PHYSICAL EXAMINATION:** ABNORMAL: MASS IN RIGHT BREAST

[redacted] **20[redacted] MAMMOGRAPHY:** IRREGULAR MASS RIGHT BREAST, 3 O'CLOCK MIDDLE DEPTH 4 CM FROM THE NIPPLE

[redacted] **20[redacted] RIGHT BREAST ULTRASOUND:** IRREGULAR MASS RIGHT BREAST, AT 3 O'CLOCK MIDDLE DEPTH 4 CM FORM THE NIPPLE

[redacted] **20[redacted] ULTRASOUND CORE NEEDLE BIOPSY, RIGHT BREAST: LOCATION:** RIGHT BREAST, 3 O'CLOCK, 4 CM FROM THE NIPPLE. INVASIVE MAMARY CARCINOMA LARGEST TUMOR FRAGMENT MEASURES 1 CM NOTHINHAM GRADE: 3+2+1=6, GRADE II. ESTROGEN RECEPTOR (ER): POSITIVE 98% PROGESTERONE RECEPTOR (PR): 98% POSITIVE KI-67 PROLIFERATIVE INDEX: 18% HER2: PENDING

M14-533 試験

治験の標題： 潰瘍性大腸炎患者を対象としたウパダシチニブ（ABT-494）の安全性及び有効性を評価する第 III 相多施設共同長期継続投与試験
施設数 / 実施国名： 280 施設（アルゼンチン，オーストラリア，オーストリア，ベルギー，ボスニア・ヘルツェゴビナ，ブラジル，カナダ，チリ，中国，コロンビア，クロアチア，チェコ共和国，エストニア，フィンランド，フランス，ドイツ，ギリシャ，ハンガリー，アイルランド，イスラエル，イタリア，日本，韓国，ラトビア，リトアニア，マレーシア，メキシコ，オランダ，ノルウェー，ポーランド，ポルトガル，ロシア，セルビア，スロバキア，南アフリカ，スペイン，スイス，台湾，トルコ，ウクライナ，イギリス及び米国）
治験調整医師： [redacted], MD
公表文献（参考資料）： なし

治験期間：	開発のフェーズ：
最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 データカットオフ日　　：20[redacted] 年 [redacted] 月 [redacted] 日	第 III 相

目的： M14-234 試験 Substudy（以下「SS」）1 の導入療法期間終了時に効果不十分であった潰瘍性大腸炎（以下「UC」）患者，M14-234 試験 SS 3 の維持療法期間中に効果減弱した UC 患者，又は M14-234 試験 SS 3 を完了した UC 患者を対象として，ウパダシチニブの長期安全性及び有効性を評価する。
被験者数（計画時と解析時）： 計画時：950 例，解析時：913 例
診断と主要な組入れ基準： すべての選択基準を満たし，いずれの除外基準にも抵触しない成人男女を本試験へ組み入れた。 主要な選択基準：M14-234 試験 SS 1 の導入療法期間終了時（投与 8 週時）に臨床的改善を達成しなかった被験者，M14-234 試験 SS 3 の維持療法期間中に効果減弱した被験者，又は M14-234 試験 SS 3 を完了した被験者。 主要な除外基準：理由に関わらず，本試験に不適格と治験責任医師が判断した被験者。治験責任医師の臨床評価に基づいて，本試験の被験者候補として不適格と判断された活動性又は再発性の感染症を有する被験者。本試験の投与 0 週時直前の臨床検査で，治験実施計画書に規定された安全性管理ガイドラインの中止基準に抵触している被験者。過去にヤヌスキナーゼ（JAK）阻害剤（トファシチニブ，ルキソリチニブ，バリシチニブ，ペフィシチニブ，アブロシチニブ，フィルゴチニブなど）の投与を受けたことがある被験者。
治験方法： 本試験は，ウパダシチニブの長期安全性及び有効性を評価するために計画された最長 288 週間からなる第 III 相多施設共同長期継続投与試験であった。M14-234 試験 SS 1 の導入療法期間終了時に効果不十分であった UC 患者，M14-234 試験 SS 3 の維持療法期間中に効果減弱した UC 患者，又は M14-234 試験 SS 3 を完了した UC 患者のうち，本試験の選択基準のすべてを満たし，除外基準のいずれも抵触しない約 950 例の被験者が，本試験に移行し，ウパダシチニブの投与を受けることができることとした。本試験は，その科学的な目的及び規制要件に適合するため約 950 例の被験者を組み入れるように計画し，倫理的な観点から不必要に多くの被験者を組み入れないこととした。 本試験への登録のためには，M14-234 試験 SS 1 の投与 8 週時，M14-234 試験 SS 3 の試験期間中に効果減弱が記録された後，及び/又は M14-234 試験 SS 3 の投与 44 週若しくは投与 52 週の完了時，又は M14-234 試験の最終来院時以降 14 日までに，被験者の適格性を評価することとした。初回の長期投与は，本試験の投与 0 週時に実施

した。試験目的のため，「ベースライン」は M14-234 試験又は M14-675 試験で治験薬（ウパダシチニブ又はプラセボ）を初回投与した来院時と定義し，本試験の投与 0 週時は M14-234 試験の最終来院時と同日又は 14 日後までに実施した。

本試験には 2 つのコホートが含まれた。

Cohort 1：

M14-234 試験 SS 1 の導入療法期間終了時に効果不十分であった被験者，又は M14-234 試験 SS 3 の維持療法期間中に効果減弱した被験者約 425 例（計画時）を含めることとした。データカットオフ時点で，Cohort 1 には 562 例の被験者が含まれた。被験者には，投与 0 週時からウパダシチニブ 15 mg 1 日 1 回を非盲検下で投与した。投与 2 週時又はそれ以降，治験責任医師により効果不十分と判断され，安全性の懸念がないことが確認された場合，ウパダシチニブ 30 mg 1 日 1 回に増量できることとした。

Cohort 2：

M14-234 試験 SS 3 を投与 52 週時まで完了したすべての被験者（計画時約 525 例）を Cohort 2 の組入れ対象とした。新型コロナウイルス感染症（以下「COVID-19」）パンデミックの間，M14-234 試験 SS 3 の投与 52 週時の内視鏡検査が欠測となった被験者は Cohort 2 の組入れには不適格としたが，Cohort 1 の組入れは適格とした。データカットオフ時点で，Cohort 2 には 351 例の被験者が含まれた。M14-234 試験 SS 3 の投与 52 週時に臨床的寛解を達成した被験者は，M14-234 試験 SS 3 で割り付けられた元々の用量（プラセボ，ウパダシチニブ 7.5 mg，15 mg 又は 30 mg 1 日 1 回）を投与 0 週時から継続することとした。M14-234 試験 SS 3 の投与 52 週時に臨床的寛解を達成しなかった被験者は，投与 0 週時に盲検下で以下のとおりに投与した。

- 元々プラセボ又はウパダシチニブ 7.5 mg 1 日 1 回に割り付けられた被験者は，ウパダシチニブ 15 mg 1 日 1 回を投与した。
- 元々ウパダシチニブ 15 mg 1 日 1 回に割り付けられた被験者は，ウパダシチニブ 30 mg 1 日 1 回を投与した。
- 元々ウパダシチニブ 30 mg 1 日 1 回に割り付けられた被験者は，同用量を継続した。

被験薬，用量，投与方法及びロット番号：

被験薬	用量	投与方法	バルクロット番号
ウパダシチニブ	7.5 mg	経口	[redacted]
ウパダシチニブ	15 mg	経口	[redacted]
ウパダシチニブ	30 mg	経口	[redacted]

治療期間：

最長 288 週間

対照薬，用量，投与方法及びロット番号：

ウパダシチニブに対応するプラセボの経口フィルムコート錠 バルクロット番号：[redacted]

評価基準：

有効性：

有効性評価項目は，次のとおりとした。

- 投与 0 週時，投与 48 週時及びそれ以降の投与 48 週ごとの評価時点での Adapted Mayo スコアによる臨床的寛解率（Adapted Mayo スコアが 2 以下で，排便回数サブスコア［以下「SFS」］が 1 以下かつベースラインを超えない，直腸出血サブスコア［以下「RBS」］が 0，かつ内視鏡サブスコアが 1 以下）
- 投与 48 週時及びそれ以降の投与 48 週ごとの評価時点で，SFS が 0，RBS が 0，内視鏡サブスコアが 1 以下となった被験者の割合
- 投与 0 週時に Adapted Mayo スコアによる臨床的寛解を達成しており，投与 48 週時及びそれ以降の投与 48 週ごとの評価時点で臨床的寛解を維持した被験者の割合
- 投与 0 週時，投与 48 週時及びそれ以降の投与 48 週ごとの評価時点での Full Mayo スコアによる臨床的寛解率（Full Mayo スコアが 2 以下で，かついずれのサブスコアも 1 を超えない）
- 投与 0 週時に Full Mayo スコアによる臨床的寛解を達成しており，投与 48 週時及びそれ以降の投与 48 週ごとの評価時点で臨床的寛解を維持した被験者の割合
- Cohort 2 でウパダシチニブを増量した被験者での投与 8 週時の Adapted Mayo スコアによる臨床的寛解率
- Cohort 2 でウパダシチニブを増量した被験者での投与 8 週時の Full Mayo スコアによる臨床的寛解率
- Cohort 2 でウパダシチニブを増量した被験者での投与 8 週時の内視鏡的改善率（内視鏡サブスコアが 0 又は 1）
- Cohort 2 でウパダシチニブを増量した被験者での投与 8 週時の内視鏡的寛解率（内視鏡サブスコアが 0）
- 試験期間中の部分的 Mayo スコアによる臨床的寛解率（部分的 Mayo スコアが 2 以下で，かついずれのサブスコアも 1 を超えない）
- 投与 48 週時及びそれ以降の投与 48 週ごとの評価時点で，SFS が 1 以下，RBS が 0，かつ内視鏡サブスコアが 1 以下で脆弱性なしと定義する臨床的寛解を達成した被験者の割合
- 投与 0 週時，投与 48 週時及びそれ以降の投与 48 週ごとの評価時点での Adapted Mayo スコアによる臨床的改善率（Adapted Mayo スコアのベースラインからの減少が 2 以上かつ 30%以上，更に RBS の減少が 1 以上又は RBS が 1 以下）
- 試験期間中の部分的 Mayo スコアによる臨床的改善率（部分的 Mayo スコアのベースラインからの減少が 2 以上かつ 30%以上，更に RBS の減少が 1 以上又は RBS が 1 以下）
- ウパダシチニブを増量した被験者での試験期間中の Adapted Mayo スコアによる臨床的改善率
- ウパダシチニブを増量した被験者での増量後の試験期間中の Adapted Mayo スコアによる臨床的寛解率
- ウパダシチニブを増量した被験者での増量後の試験期間中の Full Mayo スコアによる臨床的寛解率
- 投与 0 週時，投与 48 週時及びそれ以降の投与 48 週ごとの評価時点での内視鏡的改善率
- 投与 0 週時，投与 48 週時及びそれ以降の投与 48 週ごとの評価時点での内視鏡的寛解率
- 投与 0 週時に内視鏡的寛解を達成しており，かつ投与 48 週時及びそれ以降の投与 48 週ごとの評価時点で，内視鏡的寛解を維持した被験者の割合
- ベースラインで副腎皮質ステロイドを投与しており，試験期間中に副腎皮質ステロイドから離脱できた被験者の割合
- ベースラインで副腎皮質ステロイドを投与しており，投与 48 週時及びそれ以降の投与 48 週ごとの評価時点で，副腎皮質ステロイドから離脱し，かつ Adapted Mayo スコアによる臨床的寛解を達成した被験者の割合
- 試験期間中の Inflammatory bowel disease questionnaire（以下「IBDQ」）の改善率（ベースラインと比較して IBDQ スコアの 16 以上の増加）
- 試験期間中の IBDQ の寛解率（IBDQ 合計スコアが 170 以上）
- 試験期間中の腹痛を報告しなかった被験者の割合
- 試験期間中の便意切迫感を報告しなかった被験者の割合
- 試験期間中の高感度 C 反応性タンパク（以下「hsCRP」）のベースラインからの変化量

- 試験期間中の便中カルプロテクチンのベースラインからの変化量
- ベースラインで副腎皮質ステロイドを投与していた被験者での試験期間中の副腎皮質ステロイドの用量のベースラインからの変化量
- 試験期間中の Adapted Mayo スコア，Full Mayo スコア，部分的 Mayo スコア及び Mayo サブスコアのベースラインからの変化量
- 被験者から報告された排便回数（実数）のベースラインからの変化量
- 試験期間中の IBDQ 合計スコア及び IBDQ ドメインスコアのベースラインからの変化量
- 試験期間中の IBDQ 腸症状ドメインの下位項目スコア（Q1，Q5，Q9，Q13，Q17，Q20，Q22，Q24，Q26 及び Q29）のベースラインからの変化量
- 試験期間中の European Quality of Life-5 Dimensions 5 Levels（以下「EQ-5D-5L」）スコアのベースラインからの変化量
- 試験期間中の Work Productivity and Activity Impairment Questionnaire（以下「WPAI」）スコアのベースラインからの変化量
- 試験期間中の 36-item short-form health survey（以下「SF-36」）スコアのベースラインからの変化量
- 試験期間中の Patient Global Impression of Change（以下「PGIC」）分類別の被験者の割合
- 試験期間中の Patient Global Impression of Severity（以下「PGIS」）分類別の被験者の割合
- 試験期間中の Functional assessment of chronic illness therapy fatigue（以下「FACIT-F」）スコアのベースラインからの変化量
- 試験期間中の Ulcerative Colitis Symptoms Questionnaire（以下「UC-SQ」）スコアのベースラインからの変化量
- 試験期間中の医療資源の利用（すべての原因及び UC に関連する入院及び手術）

安全性：

安全性評価について，「ベースライン」は M14-234 試験又は M14-675 試験で治験薬を初回投与した来院時と定義した。

試験期間中の有害事象の発現割合及び 100 人年あたりの発現件数を評価した。バイタルサイン，身体検査所見，臨床検査値のベースラインからの変化を評価した。

統計手法：

有効性：

有効性の解析は，本試験で治験薬を 1 回以上投与したすべての被験者を含む intent to treat（以下「ITT」）集団を対象とした。要約統計量は観察されたデータを基に各来院ごとに示した。連続変数については，データ数，平均値，標準偏差，最小値，第一四分位数，中央値，第三四分位数及び最大値，カテゴリー変数については，頻度及び割合を算出した。

有効性のカテゴリー変数は，規定の来院時に欠測データが出た場合，「未達成例」として取り扱うノンレスポンダーインピュテーション（以下「NRI」）を用いた解析も実施した。

安全性：

安全性の解析は，本試験で治験薬を 1 回以上投与したすべての被験者を含む安全性解析対象集団（以下「SA 集団」）を対象とした。SA 集団のうち，Cohort 1 の被験者を SA1 集団，Cohort 2 の被験者を SA2 集団とした。有害事象の発現割合及び 100 人年あたりの発現件数を投与群ごとに算出した。バイタルサイン，身体検査所見，12 誘導心電図及び臨床検査値の変化を評価した。有害事象は，ICH 国際医薬用語集（MedDRA）version 23.0 を用い，器官別大分類（SOC）別及び基本語（以下「PT」）別に集計した。臨床検査値及びバイタルサインは，ベースラインからの変化量を要約した。

有効性の結果

本試験のデータカットオフまでの結果より，ウパダシチニブ 15 mg 及び 30 mg 1 日 1 回投与は，維持療法試験を完了して本試験に移行した被験者において，UC の徴候及び症状の改善に継続して有効であった。効果減弱し，維持療法試験を中止した被験者では，多くの被験者が，30 mg への増量の有無に関わらず 15 mg の用量で疾患のコントロールを達成できた。

全体として，ウパダシチニブは，疾患活動性及び症状，内視鏡的及び組織学的評価，炎症のバイオマーカー並びに生活の質（以下「QOL」）の改善において，継続して有効又は有効性が維持された。

以上の結果から，ウパダシチニブ 15 mg 及び 30 mg 1 日 1 回投与は，中等症から重症の活動性 UC の長期治療に有効であることが示された。

本試験の有効性評価項目の結果一覧を以下のとおり示す。

M14-533 試験の有効性評価項目の結果一覧（M14-533 試験 CSR）

項目	ITTA1 集団	ITTA2 集団
Adapted Mayo スコアによる臨床的寛解率	TABLE 14.2__1.1.1 TABLE 14.2__1.3.1	TABLE 14.2__1.1.2 TABLE 14.2__1.3.2
副腎皮質ステロイドから離脱した被験者の割合	TABLE 14.2__1.13.1	TABLE 14.2__1.13.2
副腎皮質ステロイドから離脱し，かつ Adapted Mayo スコアによる臨床的寛解を達成した被験者の割合	TABLE 14.2__1.14.1	TABLE 14.2__1.14.2
Full Mayo スコアによる臨床的寛解率	TABLE 14.2__1.4.1 TABLE 14.2__1.5.1	TABLE 14.2__1.4.2 TABLE 14.2__1.5.2
部分的 Mayo スコアによる臨床的寛解率	TABLE 14.2__1.6.1	TABLE 14.2__1.6.2
SFS が 0，RBS が 0，内視鏡サブスコアが 1 以下となった被験者の割合	TABLE 14.2__1.2.1	TABLE 14.2__1.2.2
SFS が 1 以下，RBS が 0，かつ内視鏡サブスコアが 1 以下で脆弱性なしと定義する臨床的寛解を達成した被験者の割合	TABLE 14.2__1.7.1	TABLE 14.2__1.7.2
Adapted Mayo スコアによる臨床的改善率	TABLE 14.2__1.8.1	TABLE 14.2__1.8.2
部分的 Mayo スコアによる臨床的改善率	TABLE 14.2__1.9.1	TABLE 14.2__1.9.2
Adapted Mayo スコア，Full Mayo スコア，部分的 Mayo スコア及び Mayo サブスコアのベースラインからの変化量	TABLE 14.2__1.22.1	TABLE 14.2__1.22.2
腹痛を報告しなかった被験者の割合	TABLE 14.2__1.17.1	TABLE 14.2__1.17.2
便意切迫感を報告しなかった被験者の割合	TABLE 14.2__1.18.1	TABLE 14.2__1.18.2
排便回数のベースラインからの変化量	TABLE 14.2__1.23.1	TABLE 14.2__1.23.2
Cohort 1 でウパダシチニブを増量した被験者での Adapted Mayo スコア又は Full Mayo スコアによる臨床的改善率及び臨床的寛解率	TABLE 14.2__1.41 TABLE 14.2__1.42 TABLE 14.2__1.43	–
Cohort 2 でウパダシチニブを増量した被験者での Adapted Mayo スコア又は Full Mayo スコアによる臨床的寛解率	–	TABLE 14.2__1.37 TABLE 14.2__1.38
内視鏡的改善率	TABLE 14.2__1.10.1	TABLE 14.2__1.10.2

項目	ITTA1 集団	ITTA2 集団
内視鏡的寛解率	TABLE 14.2__1.11.1	TABLE 14.2__1.11.2
	TABLE 14.2__1.12.1	TABLE 14.2__1.12.2
Cohort 2 でウパダシチニブを増量した被験者での内視鏡的改善率及び内視鏡的寛解率	–	TABLE 14.2__1.39
		TABLE 14.2__1.40
hsCRP のベースラインからの変化量	TABLE 14.2__1.19.1	TABLE 14.2__1.19.2
便中カルプロテクチンのベースラインからの変化量	TABLE 14.2__1.20.1	TABLE 14.2__1.20.2
IBDQ の改善率	TABLE 14.2__1.15.1	TABLE 14.2__1.15.2
IBDQ の寛解率	TABLE 14.2__1.16.1	TABLE 14.2__1.16.2
IBDQ 合計スコア及び IBDQ ドメインスコアのベースラインからの変化量	TABLE 14.2__1.24.1	TABLE 14.2__1.24.2
	TABLE 14.2__1.25.1	TABLE 14.2__1.25.2
EQ-5D-5L スコア，WPAI スコア，SF-36 スコア，FACIT-F スコア，UC-SQ スコアのベースラインからの変化量	TABLE 14.2__1.26.1	TABLE 14.2__1.26.2
	TABLE 14.2__1.27.1	TABLE 14.2__1.27.2
	TABLE 14.2__1.28.1	TABLE 14.2__1.28.2
	TABLE 14.2__1.31.1	TABLE 14.2__1.31.2
	TABLE 14.2__1.32.1	TABLE 14.2__1.32.2
PGIC 及び PGIS 分類別の被験者の割合	TABLE 14.2__1.29.1	TABLE 14.2__1.29.2
	TABLE 14.2__1.30.1	TABLE 14.2__1.30.2
UC に関連する入院の発生率及び手術の施行率	TABLE 14.2__1.33.1	TABLE 14.2__1.33.2
	TABLE 14.2__1.34.1	TABLE 14.2__1.34.2
すべての原因による入院の発生率及び手術の施行率	TABLE 14.2__1.35.1	TABLE 14.2__1.35.2
	TABLE 14.2__1.36.1	TABLE 14.2__1.36.2

安全性の結果

SA2 集団では，本試験のデータカットオフまでの重篤な有害事象，治験薬の投与中止に至った有害事象及び特に注目すべき有害事象を含む有害事象の発現頻度，並びに臨床検査値及びバイタルサインの評価において，ウパダシチニブ 15 mg 及び 30 mg 1 日 1 回の長期投与の忍容性は良好であった。ウパダシチニブの他の適応症の臨床開発プログラムで認められたウパダシチニブ 15 mg 及び 30 mg の既知の安全性プロファイルと比較して，新たな重要な安全性リスクは認められなかった。プラセボ 1 日 1 回群（以下「プラセボ群」）の被験者数及び治験薬への曝露は少なかったため，プラセボ群とウパダシチニブ群の直接比較はしなかった。ウパダシチニブ 7.5 mg を投与した被験者は 1 例のみであり，非重篤な膀胱炎が 1 件認められた。

SA1 集団の安全性プロファイルは，SA2 集団で認められた安全性プロファイルとおおむね同様であり，重要な安全性の所見は特定されなかった。

死亡に至った有害事象として，SA2 集団では膵腺癌がウパダシチニブ 30 mg 1 日 1 回群（以下「30 mg 群」）の 1 例に認められ，SA1 集団ではオピオイドの過量投与に伴った脳損傷がウパダシチニブ 15 mg 1 日 1 回群（以下「15 mg 群」）の 1 例に認められた。いずれの死亡に至った有害事象も，治験責任医師により治験薬との因果関係は「関連なし」と判断された。

SA2 集団では，本試験のデータカットオフまでの 100 人年あたりの発現件数が 5 件/100 人年以上であった有害事象は，15 mg 群で上気道感染，潰瘍性大腸炎，COVID-19 及び上咽頭炎であり，30 mg 群で血中クレアチンホスホキナーゼ増加，COVID-19，潰瘍性大腸炎，上咽頭炎，関節痛及び口腔ヘルペスであった。重篤な有害事象の 100 人年あたりの発現件数は，15 mg 群と 30 mg 群で同程度であった。治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，30 mg 群と比較して 15 mg 群の方が多かった。プラセボ群のデータは限定的であるが，治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，ウパダシチニブ群と比較してプラセボ群の方が多かった。

SA1 集団では，本試験のデータカットオフまでの 100 人年あたりの発現件数が 5 件/100 人年以上であった有害事象は，15 mg 群で潰瘍性大腸炎，上咽頭炎，上気道感染，関節痛，血中クレアチンホスホキナーゼ増加及び口腔ヘルペスであり，ウパダシチニブ 15 mg 1 日 1 回投与中に効果不十分と判断され，30 mg 1 日 1 回に増量した群（以下「15 mg/30 mg 群」）では潰瘍性大腸炎，上咽頭炎，関節痛及び血中クレアチンホスホキナーゼ増加であった。SA1 集団の重篤な有害事象及び治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，投与群を通して SA2 集団とおおむね同程度であり，重要な安全性の所見は特定されなかった。

SA2 集団では，いずれかの投与群で 100 人年あたりの発現件数が 5 件/100 人年超であった特に注目すべき有害事象は，重篤な感染症，帯状疱疹，好中球減少症，貧血，リンパ球減少症，クレアチンホスホキナーゼ増加及び薬剤に関連する肝障害であった。

認められた重篤な感染症の種類は，UC 患者集団で予想されるものとおおむね同様であり，現在の COVID-19 パンデミックを反映するもの又はウパダシチニブの投与に関連することが知られているものであった。SA2 集団では，日和見感染又は活動性結核は認められなかった。SA1 集団では，非重篤な日和見感染として口腔真菌感染及びニューモシスチス・イロベチイ感染，並びに活動性結核が 15 mg 群で各 1 例に認められた。SA2 集団では，帯状疱疹の 100 人年あたりの発現件数は，30 mg 群と比較して 15 mg 群の方が数値的に多かった。ほとんどの帯状疱疹は，1 つから 2 つの皮膚分節のみに病変が認められ，非重篤であった。眼球病変が認められた帯状疱疹はなかった。神経系の帯状疱疹感染が 15 mg 群の 1 例に認められたが，治験薬の投与中止には至らず，転帰は回復であった。

SA2 集団では，本試験のデータカットオフまでに，悪性腫瘍はほとんど認められなかった。非黒色腫皮膚癌（以下「NMSC」）を除く悪性腫瘍は，15 mg 群で 1 件（0.9 件/100 人年），30 mg 群で 3 件（2.7 件/100 人年）認められた。NMSC は，30 mg 群で 1 件（ボーエン病）認められた。リンパ腫は認められなかった。NMSC を除く悪性腫瘍の 100 人年あたりの発現件数は，SA2 集団と SA1 集団でおおむね同程度であった。一方，SA1 集団では，NMSC の 100 人年あたりの発現件数は，15 mg 群（0.5 件/100 人年）と比較して 15 mg/30 mg 群（1.6 件/100 人年）の方が多かった。

SA2 集団では，主要心血管事象又は静脈血栓塞栓症は認められなかった。SA1 集団では，主要心血管事象として非致死性心筋梗塞及び非致死性脳卒中が各 1 例に認められ，静脈血栓塞栓症が 5 例に認められた。ほとんどの被験者が組入れ時に心血管の危険因子を有していた。

SA2 集団では，消化管穿孔は認められなかった。SA1 集団では，重篤な有害事象として大腸穿孔が 15 mg 群の 1 例に認められた。治験薬の投与は中止されなかった。大腸穿孔の治験薬との因果関係は，治験責任医師により「関連なし」と判断された。

SA2 集団では，脂肪肝及び肝機能異常（各 1 件）を除き，薬剤に関連する肝障害のすべての PT が臨床検査値の増加（アラニンアミノトランスフェラーゼ増加，アスパラギン酸アミノトランスフェラーゼ増加又は肝酵素上昇など）であった。貧血，好中球減少症又はリンパ球減少症は非重篤で，ほとんどの事象の重症度は軽度又は中等度であった。治験薬の投与中止に至った事象はなかった。SA1 集団では，重篤な有害事象として横紋筋融解症が 1 件認められた。

SA2 集団では，Grade 3 又は 4 の臨床検査値異常及び臨床的な意義があると判断したバイタルサインが認められた被験者の割合は，おおむねまれであった。いずれの集団でも Hy's law と確定された被験者はいなかった。

結論

第 III 相長期継続投与試験である本試験では，ウパダシチニブ 15 mg 及び 30 mg 1 日 1 回投与は，疾患活動性及び症状，内視鏡的及び組織学的評価，炎症のバイオマーカー並びに QOL に関する評価において，継続して有効であった。ウパダシチニブ 15 mg 及び 30 mg 1 日 1 回の長期投与は，おおむね安全であり，忍容性は良好であった。ウパダシチニブの既知の安全性プロファイルと比較して，新たな重要な安全性リスクは特定されなかった。本試験の結果は，中等症から重症の活動性 UC 患者におけるウパダシチニブ 15 mg 及び 30 mg 1 日 1 回の長期投与を裏付けるものであった。

日本人部分集団の有害事象

日本人部分集団の有害事象の発現状況を以下に示す。

SA2 集団

有害事象の 100 人年あたりの発現件数は，15 mg 群（24 例）で 144.2 件/100 人年，30 mg 群（29 例）で 226.5 件/100 人年，プラセボ群（7 例）で 176.5 件/100 人年であった。ウパダシチニブ群で 2 件以上認められた有害事象は，15 mg 群で上咽頭炎，白血球減少症，γ-グルタミルトランスフェラーゼ増加，筋骨格系胸痛及び関節周囲炎，30 mg 群で口腔ヘルペス，上咽頭炎，関節痛，帯状疱疹，好中球減少症及び心室性期外収縮であった。

治験薬と関連ありの有害事象の 100 人年あたりの発現件数は，15 mg 群で 43.3 件/100 人年，30 mg 群で 49.7 件/100 人年，プラセボ群で 88.2 件/100 人年であった。ウパダシチニブ群で 2 件以上認められた治験薬と関連ありの有害事象は，15 mg 群で白血球減少症及び関節周囲炎，30 mg 群で帯状疱疹であった。

高度の有害事象の 100 人年あたりの発現件数は，30 mg 群で 11.0 件/100 人年，プラセボ群で 58.8 件/100 人年であり，15 mg 群では認められなかった。30 mg 群で 2 件以上認められた高度の有害事象はなかった。

死亡に至った有害事象は認められなかった。

重篤な有害事象の 100 人年あたりの発現件数は，30 mg 群で 5.5 件/100 人年，プラセボ群で 29.4 件/100 人年であり，15 mg 群では認められなかった。30 mg 群で 2 件以上認められた重篤な有害事象はなかった。

治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，プラセボ群で 29.4 件/100 人年であり，15 mg 群及び 30 mg 群では認められなかった。

SA1 集団

有害事象の 100 人年あたりの発現件数は，15 mg 群（59 例）で 269.6 件/100 人年，15 mg/30 mg 群（18 例）で 367.0 件/100 人年であった。100 人年あたりの発現件数が 10 件/100 人年以上であった有害事象は，15 mg 群で上咽頭炎及び口腔ヘルペス，15 mg/30 mg 群でクロストリジウム・ディフィシレ感染，上咽頭炎，不眠症，インフルエンザ，湿疹，齲歯，腹部膨満，直腸炎，肺炎及び尿管結石症であった。

治験薬と関連ありの有害事象の 100 人年あたりの発現件数は，15 mg 群で 64.8 件/100 人年，15 mg/30 mg 群で 79.8 件/100 人年であった。15 mg 群で 100 人年あたりの発現件数が 10 件/100 人年以上であった治験薬と関連ありの有害事象はなかった。15 mg/30 mg 群で 100 人年あたりの発現件数が 10 件/100 人年以上であった治験薬と関連ありの有害事象は，肺炎であった。

高度の有害事象の 100 人年あたりの発現件数は，15 mg 群で 3.1 件/100 人年，15 mg/30 mg 群で 5.3 件/100 人年であった。いずれの投与群でも，2 件以上認められた高度の有害事象はなかった。

死亡に至った有害事象は認められなかった。

重篤な有害事象の 100 人年あたりの発現件数は，15 mg 群で 14.6 件/100 人年，15 mg/30 mg 群で 16.0 件/100 人年であった。15 mg 群で 2 件以上認められた重篤な有害事象は，大腸ポリープ，帯状疱疹及び腎結石症であった。15 mg/30 mg 群で 2 件以上認められた重篤な有害事象はなかった。

治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，15 mg 群で 2.1 件/100 人年，15 mg/30 mg 群で 10.6 件/100 人年であった。いずれの投与群でも，2 件以上認められた重篤な有害事象はなかった。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団	日本人部分集団
有害事象の概要（発現割合）	表 1 (TABLE 14.3__1.1.1)	表 11 (TABLE 14.3__1.1.1_J)
有害事象の概要 （100 人年あたりの発現件数）	表 2 (TABLE 14.3__1.1.2)	表 12 (TABLE 14.3__1.1.2_J)
すべての有害事象（発現割合）	表 3 (TABLE 14.3__1.2.1.1)	表 13 (TABLE 14.3__1.2.1.1_J)
すべての有害事象 （100 人年あたりの発現件数）	表 4 (TABLE 14.3__1.2.1.2)	表 14 (TABLE 14.3__1.2.1.2_J)
治験薬と関連ありの有害事象（発現割合）	表 5 (TABLE 14.3__1.3.1.1.1)	表 15 (TABLE 14.3__1.3.1.1.1_J)
治験薬と関連ありの有害事象 （100 人年あたりの発現件数）	表 6 (TABLE 14.3__1.3.1.1.2)	表 16 (TABLE 14.3__1.3.1.1.2_J)
高度の有害事象 （100 人年あたりの発現件数）	表 7 (TABLE 14.3__1.3.3)	表 17 (TABLE 14.3__1.3.3_J)
死亡に至った有害事象 （100 人年あたりの発現件数）	表 8 (TABLE 14.3__2.3.1)	表 18 (TABLE 14.3__2.3.1_J)
重篤な有害事象 （100 人年あたりの発現件数）	表 9 (TABLE 14.3__2.1.1)	表 19 (TABLE 14.3__2.1.1_J)
治験薬の投与中止に至った有害事象 （100 人年あたりの発現件数）	表 10 (TABLE 14.3__2.2.1)	表 20 (TABLE 14.3__2.2.1_J)

表1

[redacted]20[redacted] 14:22 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/0544 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__1.1.1

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All_UPA (N=877) n (%)
Subjects with:								
Any adverse event (AE)	381 (67.8)	140 (63.1)	437 (77.8)	19 (52.8)	1 (100)	71 (52.2)	96 (53.9)	605 (69.0)
Any AE with reasonable possibility of being related to study drug$	169 (30.1)	76 (34.2)	222 (39.5)	9 (25.0)	0	25 (18.4)	34 (19.1)	281 (32.0)
Any severe AE	47 (8.4)	19 (8.6)	66 (11.7)	2 (5.6)	0	8 (5.9)	10 (5.6)	84 (9.6)
Any serious AE	51 (9.1)	27 (12.2)	76 (13.5)	2 (5.6)	0	8 (5.9)	11 (6.2)	95 (10.8)
Any AE leading to discontinuation of study drug	27 (4.8)	20 (9.0)	47 (8.4)	2 (5.6)	0	5 (3.7)	3 (1.7)	55 (6.3)
Any AE leading to death	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
Deaths#	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
Occurring <= 30 days after last dose	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
Occurring > 30 days after last dose	0	0	0	0	0	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.
Includes non treatment emergent deaths.
$ As assessed by investigator.

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表2

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

TABLE 14.3__1.1.2

Overview of Treatment-Emergent Adverse Events and All Deaths per 100 Patient-Years (PYs)
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All_UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
Any treatment-emergent:								
Any adverse event (AE)	1873 (283.6)	663 (269.0)	2536 (279.7)	43 (211.8)	1 (45.5)	256 (240.6)	264 (237.2)	3057 (271.3)
Any AE with reasonable possibility of being related to study drug$	426 (64.5)	177 (71.8)	603 (66.5)	21 (103.4)	0	58 (54.5)	85 (76.4)	746 (66.2)
Any severe AE	56 (8.5)	28 (11.4)	84 (9.3)	2 (9.9)	0	11 (10.3)	10 (9.0)	105 (9.3)
Any serious AE	85 (12.9)	47 (19.1)	132 (14.6)	2 (9.9)	0	11 (10.3)	12 (10.8)	155 (13.8)
Any AE leading to discontinuation of study drug	30 (4.5)	26 (10.5)	56 (6.2)	2 (9.9)	0	6 (5.6)	3 (2.7)	65 (5.8)
Any AE leading to death	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (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 = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.
Includes non treatment emergent deaths.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 14.3 1.1.2

Overview of Treatment-Emergent Adverse Events and All Deaths per 100 Patient-Years (PYs)
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
Deaths#	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
Occurring <= 30 days after last dose	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
Occurring > 30 days after last dose	0	0	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 = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.
Includes non treatment emergent deaths.
$ As assessed by investigator.

Program Source Code: [redacted]

表3

[redacted]20[redacted] 14:27 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/0544 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All_UPA (N=877) n (%)
Any adverse event	381 (67.8)	140 (63.1)	437 (77.8)	19 (52.8)	1 (100)	71 (52.2)	96 (53.9)	605 (69.0)
血液およびリンパ系障害	43 (7.7)	14 (6.3)	56 (10.0)	4 (11.1)	0	8 (5.9)	9 (5.1)	73 (8.3)
貧血	23 (4.1)	3 (1.4)	26 (4.6)	1 (2.8)	0	3 (2.2)	4 (2.2)	33 (3.8)
大球性貧血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
周期性好中球減少症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
内出血発生の増加傾向	1 (0.2)	0	1 (0.2)	1 (2.8)	0	0	1 (0.6)	2 (0.2)
鉄欠乏性貧血	2 (0.4)	2 (0.9)	4 (0.7)	0	0	2 (1.5)	0	6 (0.7)
白血球増加症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
白血球減少症	5 (0.9)	1 (0.5)	6 (1.1)	1 (2.8)	0	1 (0.7)	3 (1.7)	10 (1.1)
リンパ節症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
リンパ球減少症	7 (1.2)	3 (1.4)	9 (1.6)	0	0	1 (0.7)	1 (0.6)	11 (1.3)
小球性貧血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
血液およびリンパ系障害 (Cont.)								
好中球減少症	8 (1.4)	3 (1.4)	11 (2.0)	1 (2.8)	0	1 (0.7)	2 (1.1)	14 (1.6)
汎血球減少症	0	0	0	0	0	0	1 (0.6)	1 (0.1)
網状赤血球増加症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血小板増加症	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
心臓障害	11 (2.0)	1 (0.5)	12 (2.1)	1 (2.8)	0	2 (1.5)	4 (2.2)	18 (2.1)
不安定狭心症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
不整脈	0	0	0	0	0	0	1 (0.6)	1 (0.1)
心房細動	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
第一度房室ブロック	0	0	0	0	0	0	1 (0.6)	1 (0.1)
心拡大	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
冠動脈疾患	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
虚血性心筋症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
心臓障害 (Cont.)								
心筋梗塞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
動悸	2 (0.4)	0	2 (0.4)	1 (2.8)	0	0	0	2 (0.2)
上室性期外収縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
上室性頻脈	0	0	0	0	0	2 (1.5)	0	2 (0.2)
頻脈	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
心室性期外収縮	1 (0.2)	0	1 (0.2)	0	0	0	2 (1.1)	3 (0.3)
心室性頻脈	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
先天性、家族性および遺伝性障害	2 (0.4)	0	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
ジルベール症候群	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
魚鱗癬	0	0	0	0	0	1 (0.7)	0	1 (0.1)
歯原性嚢胞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
耳および迷路障害	9 (1.6)	5 (2.3)	13 (2.3)	0	0	1 (0.7)	4 (2.2)	18 (2.1)
耳痛	3 (0.5)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
外耳の炎症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
内耳障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
メニエール病	0	0	0	0	0	0	1 (0.6)	1 (0.1)
突発性難聴	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
耳鳴	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	2 (1.1)	6 (0.7)
回転性めまい	4 (0.7)	1 (0.5)	5 (0.9)	0	0	1 (0.7)	1 (0.6)	7 (0.8)
内分泌障害	5 (0.9)	2 (0.9)	7 (1.2)	0	0	0	0	7 (0.8)
アジソン病	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
副腎機能不全	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
急性副腎皮質機能不全	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
クッシング様症状	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
内分泌障害 (Cont.)								
甲状腺腫	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
甲状腺機能亢進症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
眼障害	23 (4.1)	6 (2.7)	28 (5.0)	3 (8.3)	0	1 (0.7)	3 (1.7)	32 (3.6)
眼精疲労	0	0	0	1 (2.8)	0	0	0	0
眼瞼炎	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	0	4 (0.5)
眼瞼痙攣	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
白内障	4 (0.7)	0	4 (0.7)	0	0	1 (0.7)	1 (0.6)	6 (0.7)
霰粒腫	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
結膜嚢胞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
結膜出血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
結膜充血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
アレルギー性結膜炎	1 (0.2)	0	1 (0.2)	1 (2.8)	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
眼障害 (Cont.)								
結膜弛緩症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
後天性涙道狭窄	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ドライアイ	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	0	4 (0.5)
上強膜炎	0	0	0	0	0	0	1 (0.6)	1 (0.1)
眼刺激	0	0	0	0	0	0	1 (0.6)	1 (0.1)
眼痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
眼瞼嚢胞	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
緑内障	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
眼充血	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
開放隅角緑内障	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ぶどう膜炎	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
霧視	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
眼障害 (Cont.)								
視力低下	0	0	0	1 (2.8)	0	0	0	0
視力障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
硝子体浮遊物	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
胃腸障害	171 (30.4)	60 (27.0)	208 (37.0)	5 (13.9)	0	25 (18.4)	21 (11.8)	254 (29.0)
腹部不快感	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
腹部膨満	4 (0.7)	2 (0.9)	6 (1.1)	1 (2.8)	0	1 (0.7)	2 (1.1)	9 (1.0)
腹痛	15 (2.7)	3 (1.4)	18 (3.2)	0	0	2 (1.5)	1 (0.6)	21 (2.4)
下腹部痛	6 (1.1)	0	6 (1.1)	0	0	0	0	6 (0.7)
上腹部痛	6 (1.1)	1 (0.5)	7 (1.2)	1 (2.8)	0	1 (0.7)	1 (0.6)	9 (1.0)
腹部圧痛	5 (0.9)	0	5 (0.9)	0	0	0	1 (0.6)	6 (0.7)
裂肛	4 (0.7)	1 (0.5)	5 (0.9)	0	0	0	0	5 (0.6)
痔瘻	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
胃腸障害 (Cont.)								
肛門失禁	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肛門そう痒症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
口角口唇炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
アフタ性潰瘍	4 (0.7)	1 (0.5)	5 (0.9)	0	0	1 (0.7)	0	6 (0.7)
口唇のひび割れ	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
大腸炎	0	2 (0.9)	2 (0.4)	0	0	0	0	2 (0.2)
潰瘍性大腸炎	79 (14.1)	29 (13.1)	101 (18.0)	2 (5.6)	0	7 (5.1)	6 (3.4)	114 (13.0)
結腸異形成	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
便秘	5 (0.9)	2 (0.9)	7 (1.2)	0	0	2 (1.5)	1 (0.6)	10 (1.1)
クローン病	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
便意切迫	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
齲歯	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	0	4 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
胃腸障害 (Cont.)								
歯組織の壊死	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
下痢	17 (3.0)	1 (0.5)	18 (3.2)	0	0	0	1 (0.6)	19 (2.2)
血性下痢	0	0	0	0	0	1 (0.7)	0	1 (0.1)
腸憩室	0	0	0	0	0	0	1 (0.6)	1 (0.1)
十二指腸炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
消化不良	7 (1.2)	5 (2.3)	12 (2.1)	0	0	1 (0.7)	0	13 (1.5)
腸炎	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
おくび	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
軟便	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
大腿ヘルニア	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
鼓腸	7 (1.2)	1 (0.5)	8 (1.4)	0	0	1 (0.7)	0	9 (1.0)
排便回数増加	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
胃腸障害 (Cont.)								
胃障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
胃ポリープ	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
胃炎	4 (0.7)	1 (0.5)	5 (0.9)	1 (2.8)	0	0	0	5 (0.6)
胃腸障害	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
消化管運動障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
胃食道逆流性疾患	7 (1.2)	1 (0.5)	8 (1.4)	1 (2.8)	0	3 (2.2)	1 (0.6)	12 (1.4)
血便排泄	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
痔核	8 (1.4)	3 (1.4)	11 (2.0)	0	0	3 (2.2)	2 (1.1)	16 (1.8)
血栓性痔核	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
裂孔ヘルニア	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
イレウス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
鼠径ヘルニア	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
胃腸障害 (Cont.)								
腸閉塞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
腸管ポリープ	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
過敏性腸症候群	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
大腸穿孔	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
大腸ポリープ	4 (0.7)	1 (0.5)	5 (0.9)	0	0	0	2 (1.1)	7 (0.8)
口唇潰瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
口腔内潰瘍形成	4 (0.7)	1 (0.5)	5 (0.9)	0	0	1 (0.7)	0	6 (0.7)
悪心	21 (3.7)	7 (3.2)	26 (4.6)	1 (2.8)	0	3 (2.2)	3 (1.7)	32 (3.6)
食道運動低下	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
食道痛	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
口腔知覚不全	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
口腔扁平苔癬	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
胃腸障害 (Cont.)								
膵炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
肛門周囲痛	3 (0.5)	0	3 (0.5)	0	0	1 (0.7)	0	4 (0.5)
直腸炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
偽性ポリポーシス	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
直腸異形成	0	0	0	0	0	1 (0.7)	0	1 (0.1)
直腸出血	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	0	4 (0.5)
直腸しぶり	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
口内炎	5 (0.9)	1 (0.5)	6 (1.1)	0	0	0	0	6 (0.7)
舌障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
歯の障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
埋伏歯	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
歯痛	3 (0.5)	4 (1.8)	7 (1.2)	0	0	0	1 (0.6)	8 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
胃腸障害 (Cont.)								
臍ヘルニア	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
嘔吐	12 (2.1)	1 (0.5)	13 (2.3)	1 (2.8)	0	2 (1.5)	1 (0.6)	16 (1.8)
一般・全身障害および投与部位の状態	58 (10.3)	21 (9.5)	74 (13.2)	1 (2.8)	0	6 (4.4)	5 (2.8)	85 (9.7)
無力症	4 (0.7)	0	4 (0.7)	0	0	0	0	4 (0.5)
胸痛	5 (0.9)	4 (1.8)	9 (1.6)	0	0	0	0	9 (1.0)
悪寒	3 (0.5)	1 (0.5)	4 (0.7)	0	0	1 (0.7)	2 (1.1)	7 (0.8)
状態悪化	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
異形成	2 (0.4)	0	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
疲労	16 (2.8)	2 (0.9)	17 (3.0)	0	0	3 (2.2)	1 (0.6)	21 (2.4)
高体温症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
治癒不良	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
インフルエンザ様疾患	9 (1.6)	3 (1.4)	10 (1.8)	0	0	0	1 (0.6)	11 (1.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
一般・全身障害および投与部位の状態 (Cont.)								
医療機器関連損傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
倦怠感	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
末梢性浮腫	4 (0.7)	2 (0.9)	6 (1.1)	0	0	0	0	6 (0.7)
疼痛	4 (0.7)	1 (0.5)	5 (0.9)	0	0	0	0	5 (0.6)
末梢腫脹	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
ポリープ	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
偽ポリープ	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
発熱	17 (3.0)	9 (4.1)	25 (4.4)	1 (2.8)	0	0	1 (0.6)	26 (3.0)
異物感	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
顔面腫脹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ワクチン接種部位反応	0	0	0	0	0	1 (0.7)	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
肝胆道系障害	16 (2.8)	3 (1.4)	19 (3.4)	0	0	2 (1.5)	1 (0.6)	22 (2.5)
胆道ジスキネジア	0	0	0	0	0	1 (0.7)	0	1 (0.1)
胆汁性嚢胞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
硬化性胆管炎	4 (0.7)	0	4 (0.7)	0	0	0	0	4 (0.5)
胆石症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肝嚢胞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肝機能異常	4 (0.7)	1 (0.5)	5 (0.9)	0	0	0	1 (0.6)	6 (0.7)
脂肪肝	3 (0.5)	1 (0.5)	4 (0.7)	0	0	1 (0.7)	0	5 (0.6)
肝細胞損傷	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
肝腫大	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肝障害	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
非アルコール性脂肪性肝疾患	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
免疫系障害	7 (1.2)	4 (1.8)	11 (2.0)	0	0	1 (0.7)	3 (1.7)	15 (1.7)
動物アレルギー	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
アナフィラキシー反応	0	0	0	0	0	0	1 (0.6)	1 (0.1)
薬物過敏症	0	1 (0.5)	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
粉塵アレルギー	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
過敏症	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
ダニアレルギー	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
季節性アレルギー	4 (0.7)	2 (0.9)	6 (1.1)	0	0	1 (0.7)	1 (0.6)	8 (0.9)
感染症および寄生虫症	202 (35.9)	84 (37.8)	269 (47.9)	9 (25.0)	1 (100)	33 (24.3)	48 (27.0)	351 (40.0)
腹部膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
腹壁膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
頚部膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ダニ皮膚炎	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
急性副鼻腔炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
歯槽骨炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肛門膿瘍	0	2 (0.9)	2 (0.4)	0	0	1 (0.7)	1 (0.6)	4 (0.5)
虫垂炎	0	0	0	0	0	0	1 (0.6)	1 (0.1)
無症候性COVID-19	4 (0.7)	0	4 (0.7)	1 (2.8)	0	0	0	4 (0.5)
異型肺炎	0	1 (0.5)	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
細菌感染	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
細菌性膣症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
バルトリン腺炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ブラストシスティス感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
気管支炎	18 (3.2)	4 (1.8)	22 (3.9)	0	0	2 (1.5)	0	24 (2.7)
COVID-19	20 (3.6)	10 (4.5)	30 (5.3)	1 (2.8)	0	8 (5.9)	8 (4.5)	46 (5.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
COVID-19肺炎	1 (0.2)	3 (1.4)	4 (0.7)	0	0	5 (3.7)	2 (1.1)	11 (1.3)
カンピロバクター胃腸炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	1 (0.6)	3 (0.3)
カンピロバクター感染	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
カンジダ感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
蜂巣炎	4 (0.7)	0	4 (0.7)	0	0	2 (1.5)	1 (0.6)	7 (0.8)
感染性胆嚢炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
慢性副鼻腔炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
クロストリジウム・ディフィシレ大腸炎	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
クロストリジウム・ディフィシレ感染	4 (0.7)	4 (1.8)	8 (1.4)	0	0	0	2 (1.1)	10 (1.1)
結腸膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
結膜炎	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
ウイルス性結膜炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
コロナウイルス感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
サイクロスポリジウム感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
膀胱炎	6 (1.1)	1 (0.5)	6 (1.1)	0	1 (100)	3 (2.2)	1 (0.6)	11 (1.3)
毛嚢虫症	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)
感染性皮膚炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
爪の皮膚糸状菌症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
医療機器関連敗血症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
感染性下痢	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	0	3 (0.3)
憩室炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
耳感染	4 (0.7)	1 (0.5)	5 (0.9)	0	0	0	0	5 (0.6)
感染性腸炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
丹毒	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
遊走性紅斑	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
大腸菌感染	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
大腸菌性敗血症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
眼感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
眼瞼感染	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
毛包炎	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
皮膚真菌感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
せつ	0	0	0	0	0	0	2 (1.1)	2 (0.2)
胃腸炎	9 (1.6)	8 (3.6)	17 (3.0)	1 (2.8)	0	0	4 (2.2)	21 (2.4)
ウイルス性胃腸炎	6 (1.1)	1 (0.5)	7 (1.2)	0	0	0	0	7 (0.8)
消化管内細菌過剰増殖	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
消化管感染	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
性器カンジダ症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
陰部ヘルペス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
陰部単純ヘルペス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
歯肉膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
歯肉炎	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
鼠径部膿瘍	1 (0.2)	0	1 (0.2)	1 (2.8)	0	0	0	1 (0.1)
ヘリコバクター性胃炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ヘリコバクター感染	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
単純ヘルペス	6 (1.1)	2 (0.9)	7 (1.2)	0	0	0	0	7 (0.8)
単純ヘルペス性咽頭炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
帯状疱疹	22 (3.9)	12 (5.4)	33 (5.9)	1 (2.8)	0	4 (2.9)	4 (2.2)	41 (4.7)
神経合併症を伴う帯状疱疹感染	0	0	0	0	0	1 (0.7)	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
耳帯状疱疹	0	0	0	0	0	1 (0.7)	0	1 (0.1)
麦粒腫	4 (0.7)	3 (1.4)	7 (1.2)	0	0	0	0	7 (0.8)
膿痂疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
感染性嚢腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
伝染性単核症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
インフルエンザ	19 (3.4)	7 (3.2)	26 (4.6)	1 (2.8)	0	0	0	26 (3.0)
クレブシエラ感染	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
大腸感染	0	0	0	0	0	0	1 (0.6)	1 (0.1)
喉頭炎	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
潜伏結核	5 (0.9)	1 (0.5)	6 (1.1)	0	0	1 (0.7)	2 (1.1)	9 (1.0)
限局性感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
下気道感染	4 (0.7)	0	4 (0.7)	0	0	0	0	4 (0.5)
上咽頭炎	50 (8.9)	22 (9.9)	71 (12.6)	1 (2.8)	0	5 (3.7)	7 (3.9)	83 (9.5)
爪真菌症	4 (0.7)	0	4 (0.7)	0	0	3 (2.2)	0	7 (0.8)
口腔カンジダ症	0	0	0	0	0	0	1 (0.6)	1 (0.1)
口腔真菌感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
口腔ヘルペス	9 (1.6)	6 (2.7)	14 (2.5)	1 (2.8)	0	0	4 (2.2)	18 (2.1)
精巣炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
外耳炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
歯周炎	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
直腸周囲膿瘍	0	0	0	0	0	1 (0.7)	0	1 (0.1)
咽頭炎	2 (0.4)	2 (0.9)	4 (0.7)	0	0	1 (0.7)	1 (0.6)	6 (0.7)
毛巣嚢胞	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
ニューモシスチス・イロベチイ感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肺炎	7 (1.2)	5 (2.3)	12 (2.1)	0	0	0	0	12 (1.4)
細菌性肺炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ウイルス性肺炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
歯髄炎	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
膿疱	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
腎盂腎炎	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
膿尿	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
気道感染	3 (0.5)	2 (0.9)	5 (0.9)	0	0	1 (0.7)	0	6 (0.7)
ウイルス性気道感染	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
鼻炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
根管感染	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
敗血症	0	2 (0.9)	2 (0.4)	0	0	0	0	2 (0.2)
副鼻腔炎	12 (2.1)	6 (2.7)	18 (3.2)	1 (2.8)	0	1 (0.7)	3 (1.7)	22 (2.5)
皮膚感染	1 (0.2)	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ブドウ球菌感染	0	0	0	0	0	1 (0.7)	0	1 (0.1)
レンサ球菌性尿路感染	0	0	0	0	0	1 (0.7)	0	1 (0.1)
皮下組織膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
白癬感染	0	0	0	0	0	0	1 (0.6)	1 (0.1)
足部白癬	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
扁桃炎	0	1 (0.5)	1 (0.2)	0	0	1 (0.7)	1 (0.6)	3 (0.3)
歯膿瘍	2 (0.4)	2 (0.9)	4 (0.7)	0	0	0	2 (1.1)	6 (0.7)
歯感染	2 (0.4)	3 (1.4)	5 (0.9)	0	0	0	0	5 (0.6)
結核	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
上気道感染	36 (6.4)	9 (4.1)	44 (7.8)	0	0	3 (2.2)	2 (1.1)	49 (5.6)
尿路感染	22 (3.9)	1 (0.5)	23 (4.1)	1 (2.8)	0	4 (2.9)	4 (2.2)	31 (3.5)
膣感染	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
水痘	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ウイルス性下痢	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ウイルス感染	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
ウイルス性咽頭炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ウイルス性上気道感染	1 (0.2)	3 (1.4)	4 (0.7)	0	0	0	2 (1.1)	6 (0.7)
外陰部膣カンジダ症	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
外陰膣真菌感染	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
外陰膣炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
傷害、中毒および処置合併症	45 (8.0)	16 (7.2)	60 (10.7)	1 (2.8)	0	5 (3.7)	5 (2.8)	70 (8.0)
動物咬傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
動物による引っかき傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
足関節部骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
節足動物咬傷	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
骨挫傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
第2度熱傷	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
挫傷	7 (1.2)	0	7 (1.2)	0	0	0	0	7 (0.8)
上顎炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
眼外傷	0	0	0	0	0	1 (0.7)	0	1 (0.1)
転倒	7 (1.2)	3 (1.4)	10 (1.8)	0	0	0	0	10 (1.1)
腓骨骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
足骨折	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
傷害、中毒および処置合併症 (Cont.)								
骨折	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
仙骨骨折	0	0	0	0	0	1 (0.7)	0	1 (0.1)
手骨折	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
頭部損傷	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
損傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
企図的過量投与	0	0	0	0	0	1 (0.7)	0	1 (0.1)
関節脱臼	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
関節損傷	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
靱帯断裂	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
靱帯捻挫	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
四肢損傷	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
つち指	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
傷害、中毒および処置合併症 (Cont.)								
半月板損傷	0	0	0	1 (2.8)	0	0	0	0
筋断裂	0	2 (0.9)	2 (0.4)	0	0	0	0	2 (0.2)
肉離れ	5 (0.9)	1 (0.5)	6 (1.1)	0	0	0	1 (0.6)	7 (0.8)
筋骨格内異物	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
過量投与	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
膝蓋骨骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
骨盤骨折	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
処置後血尿	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
処置後出血	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
外傷後頚部症候群	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
外傷後疼痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
術後イレウス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
傷害、中毒および処置合併症 (Cont.)								
処置による腸管穿孔	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
処置による疼痛	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
肺挫傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
橈骨骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肋骨骨折	5 (0.9)	2 (0.9)	7 (1.2)	0	0	0	0	7 (0.8)
交通事故	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
瘢痕	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
陰嚢血腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
皮膚擦過傷	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
皮膚裂傷	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
軟部組織損傷	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ストレス骨折	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	1 (0.6)	5 (0.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
傷害、中毒および処置合併症 (Cont.)								
皮下血腫	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
腱損傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
腱断裂	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
熱傷	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
脛骨骨折	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
歯牙破折	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	0	3 (0.3)
子宮穿孔	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ワクチン接種合併症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
創傷	0	0	0	0	0	1 (0.7)	0	1 (0.1)
創合併症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
手首関節骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
臨床検査	87 (15.5)	34 (15.3)	115 (20.5)	2 (5.6)	0	13 (9.6)	25 (14.0)	153 (17.4)
アラニンアミノトランスフェラーゼ増加	11 (2.0)	2 (0.9)	13 (2.3)	0	0	1 (0.7)	0	14 (1.6)
抗好中球細胞質抗体陽性	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
関節鏡検査	0	1 (0.5)	1 (0.2)	0	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	10 (1.8)	3 (1.4)	13 (2.3)	0	0	0	1 (0.6)	14 (1.6)
細菌検査陽性	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
好塩基球数増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中アルブミン増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中アルカリホスファターゼ増加	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
血中重炭酸塩減少	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
血中ビリルビン増加	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	2 (1.1)	4 (0.5)
血中カルシウム増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中コレステロール減少	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
臨床検査 (Cont.)								
血中コレステロール増加	5 (0.9)	1 (0.5)	6 (1.1)	0	0	1 (0.7)	2 (1.1)	9 (1.0)
血中クレアチン増加	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
血中クレアチンホスホキナーゼMB増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中クレアチンホスホキナーゼ増加	32 (5.7)	15 (6.8)	45 (8.0)	1 (2.8)	0	1 (0.7)	10 (5.6)	56 (6.4)
血中クレアチニン増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中葉酸減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中ブドウ糖減少	0	0	0	0	0	0	1 (0.6)	1 (0.1)
血中ブドウ糖増加	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
血中鉄減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中リン減少	1 (0.2)	0	1 (0.2)	0	0	0	2 (1.1)	3 (0.3)
血中カリウム減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中カリウム増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
臨床検査 (Cont.)								
血圧上昇	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
血中トリグリセリド減少	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
血中トリグリセリド増加	4 (0.7)	0	4 (0.7)	0	0	0	1 (0.6)	5 (0.6)
血中尿素増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
尿中血陽性	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
骨密度減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
クロストリジウム検査陽性	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
凝固時間延長	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
尿中結晶陽性	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
心電図QT延長	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
心電図異常	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
便中カルプロテクチン増加	4 (0.7)	0	4 (0.7)	0	0	0	0	4 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
臨床検査 (Cont.)								
γ-グルタミルトランスフェラーゼ増加	5 (0.9)	1 (0.5)	6 (1.1)	0	0	3 (2.2)	1 (0.6)	10 (1.1)
尿中ブドウ糖陽性	0	0	0	0	0	1 (0.7)	0	1 (0.1)
ヘマトクリット減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ヘモグロビン減少	3 (0.5)	2 (0.9)	5 (0.9)	0	0	0	2 (1.1)	7 (0.8)
肝酵素上昇	4 (0.7)	1 (0.5)	5 (0.9)	0	0	1 (0.7)	1 (0.6)	7 (0.8)
B型肝炎DNA測定陽性	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
高比重リポ蛋白増加	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
ヒト乳頭腫ウイルス検査陽性	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
眼圧上昇	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
臨床検査異常	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
リパーゼ増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肝機能検査異常	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
臨床検査 (Cont.)								
肝機能検査値上昇	2 (0.4)	0	2 (0.4)	0	0	1 (0.7)	1 (0.6)	4 (0.5)
低比重リポ蛋白減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
低比重リポ蛋白増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
リンパ球数減少	6 (1.1)	2 (0.9)	8 (1.4)	0	0	2 (1.5)	3 (1.7)	13 (1.5)
リンパ球百分率減少	0	0	0	0	0	0	1 (0.6)	1 (0.1)
平均赤血球容積増加	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
単球数増加	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
結核菌群検査陽性	0	0	0	0	0	1 (0.7)	0	1 (0.1)
好中球数減少	7 (1.2)	1 (0.5)	8 (1.4)	0	0	4 (2.9)	4 (2.2)	16 (1.8)
好中球数増加	5 (0.9)	0	5 (0.9)	0	0	2 (1.5)	1 (0.6)	8 (0.9)
血小板数減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血小板数増加	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
臨床検査 (Cont.)								
尿中蛋白陽性	2 (0.4)	0	2 (0.4)	0	0	2 (1.5)	0	4 (0.5)
赤血球数減少	4 (0.7)	0	4 (0.7)	0	0	0	2 (1.1)	6 (0.7)
赤血球数増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
網状赤血球数増加	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
尿比重増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
トランスアミナーゼ上昇	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
尿検査異常	0	0	0	0	0	0	1 (0.6)	1 (0.1)
尿中ケトン体陽性	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
尿中白血球エステラーゼ陽性	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
尿量減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ビタミンB12減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
体重減少	0	2 (0.9)	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
臨床検査 (Cont.)								
体重増加	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
白血球数減少	8 (1.4)	1 (0.5)	9 (1.6)	1 (2.8)	0	2 (1.5)	4 (2.2)	15 (1.7)
白血球数増加	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
尿中白血球陽性	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)
代謝および栄養障害	39 (6.9)	10 (4.5)	49 (8.7)	0	0	9 (6.6)	8 (4.5)	66 (7.5)
食欲減退	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
脱水	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
糖尿病	0	0	0	0	0	0	2 (1.1)	2 (0.2)
脂質異常症	2 (0.4)	0	2 (0.4)	0	0	2 (1.5)	0	4 (0.5)
葉酸欠乏	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
耐糖能障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
痛風	0	1 (0.5)	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
代謝および栄養障害 (Cont.)								
ヒスタミン不耐性	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
高コレステロール血症	7 (1.2)	2 (0.9)	9 (1.6)	0	0	2 (1.5)	3 (1.7)	14 (1.6)
高血糖	6 (1.1)	0	6 (1.1)	0	0	1 (0.7)	0	7 (0.8)
高ホモシステイン血症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
高脂血症	6 (1.1)	0	6 (1.1)	0	0	1 (0.7)	1 (0.6)	8 (0.9)
高トリグリセリド血症	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
高尿酸血症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
低アルブミン血症	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
低カリウム血症	2 (0.4)	0	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
低マグネシウム血症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
低ナトリウム血症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
低リン酸血症	3 (0.5)	3 (1.4)	6 (1.1)	0	0	0	0	6 (0.7)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
代謝および栄養障害 (Cont.)								
低蛋白血症	0	0	0	0	0	1 (0.7)	0	1 (0.1)
鉄欠乏	4 (0.7)	1 (0.5)	5 (0.9)	0	0	0	0	5 (0.6)
ラクトース不耐性	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
代謝性アシドーシス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肥満	0	0	0	0	0	0	2 (1.1)	2 (0.2)
過少体重	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ビタミンB群欠乏	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ビタミンB12欠乏	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ビタミンD欠乏	5 (0.9)	1 (0.5)	6 (1.1)	0	0	0	2 (1.1)	8 (0.9)
筋骨格系および結合組織障害	91 (16.2)	40 (18.0)	122 (21.7)	2 (5.6)	0	19 (14.0)	16 (9.0)	157 (17.9)
関節痛	26 (4.6)	17 (7.7)	43 (7.7)	1 (2.8)	0	5 (3.7)	5 (2.8)	53 (6.0)
関節炎	3 (0.5)	2 (0.9)	5 (0.9)	0	0	0	0	5 (0.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
筋骨格系および結合組織障害 (Cont.)								
関節障害	7 (1.2)	1 (0.5)	8 (1.4)	0	0	3 (2.2)	2 (1.1)	13 (1.5)
腋窩腫瘤	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
背部痛	18 (3.2)	8 (3.6)	26 (4.6)	1 (2.8)	0	1 (0.7)	1 (0.6)	28 (3.2)
滑液包炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	1 (0.6)	3 (0.3)
軟骨萎縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
頚部脊柱管狭窄症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
尾骨痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
コンパートメント症候群	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
指炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
腱付着部症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
外骨腫	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
側腹部痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
筋骨格系および結合組織障害 (Cont.)								
単径部痛	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
椎間板変性症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
椎間板障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
椎間板突出	5 (0.9)	2 (0.9)	7 (1.2)	0	0	1 (0.7)	1 (0.6)	9 (1.0)
関節滲出液	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
関節硬直	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
関節腫脹	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
腰部脊柱管狭窄症	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
脛骨内側過労性症候群	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
筋拘縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
筋痙縮	3 (0.5)	3 (1.4)	6 (1.1)	0	0	3 (2.2)	0	9 (1.0)
筋骨格系胸痛	1 (0.2)	1 (0.5)	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
筋骨格系および結合組織障害 (Cont.)								
筋骨格痛	5 (0.9)	4 (1.8)	9 (1.6)	0	0	0	0	9 (1.0)
筋骨格硬直	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	0	4 (0.5)
筋肉痛	12 (2.1)	2 (0.9)	14 (2.5)	0	0	1 (0.7)	2 (1.1)	17 (1.9)
筋膜疼痛症候群	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ミオパチー	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
頚部痛	2 (0.4)	3 (1.4)	5 (0.9)	0	0	0	0	5 (0.6)
変形性関節症	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	0	4 (0.5)
骨端症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
骨壊死	1 (0.2)	1 (0.5)	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
骨減少症	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
骨粗鬆症	1 (0.2)	3 (1.4)	4 (0.7)	0	0	0	0	4 (0.5)
四肢痛	9 (1.6)	7 (3.2)	15 (2.7)	0	0	2 (1.5)	2 (1.1)	19 (2.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
筋骨格系および結合組織障害 (Cont.)								
顎痛	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
膝蓋大腿関節痛症候群	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
関節周囲炎	0	0	0	0	0	1 (0.7)	0	1 (0.1)
足底筋膜炎	4 (0.7)	1 (0.5)	5 (0.9)	0	0	1 (0.7)	0	6 (0.7)
横紋筋融解症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
肩回旋筋腱板症候群	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
軟部組織腫瘤	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
脊柱変形	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
変形性脊椎症	2 (0.4)	2 (0.9)	4 (0.7)	0	0	0	0	4 (0.5)
脊椎炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
脊椎関節障害	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
軟骨下機能不全骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
筋骨格系および結合組織障害 (Cont.)								
滑膜炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
顎関節症候群	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
腱炎	3 (0.5)	0	3 (0.5)	0	0	1 (0.7)	1 (0.6)	5 (0.6)
弾発指	0	0	0	0	0	1 (0.7)	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)	19 (3.4)	7 (3.2)	25 (4.4)	1 (2.8)	0	3 (2.2)	6 (3.4)	34 (3.9)
アクロコルドン	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
結腸腺癌	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
膵腺癌	0	0	0	0	0	0	1 (0.6)	1 (0.1)
基底細胞癌	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	0	3 (0.3)
肺の良性新生物	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
精巣の良性新生物	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ボーエン病	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)								
気管支の良性新生物	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
大腸腺腫	4 (0.7)	0	4 (0.7)	1 (2.8)	0	0	1 (0.6)	5 (0.6)
線維腫	0	0	0	0	0	0	1 (0.6)	1 (0.1)
線維性組織球腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
喉頭扁平上皮癌	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
脂肪腫	0	0	0	0	0	0	1 (0.6)	1 (0.1)
メラノサイト性母斑	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
前立腺癌	0	0	0	0	0	1 (0.7)	0	1 (0.1)
脂漏性角化症	0	0	0	0	0	0	1 (0.6)	1 (0.1)
皮膚乳頭腫	4 (0.7)	2 (0.9)	6 (1.1)	0	0	1 (0.7)	1 (0.6)	8 (0.9)
扁平上皮癌	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
皮膚有棘細胞癌	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)								
子宮頚部扁平上皮癌	0	0	0	0	0	0	1 (0.6)	1 (0.1)
精巣（純粋）セミノーマ	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
精巣癌	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
甲状腺腺腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
子宮平滑筋腫	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
神経系障害	60 (10.7)	20 (9.0)	79 (14.1)	0	0	8 (5.9)	5 (2.8)	92 (10.5)
健忘	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
脳損傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
灼熱感	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
手根管症候群	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	0	3 (0.3)
頚髄神経根障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
注意力障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
神経系障害 (Cont.)								
浮動性めまい	6 (1.1)	3 (1.4)	9 (1.6)	0	0	4 (2.9)	0	13 (1.5)
異常感覚	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
構語障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
頭痛	29 (5.2)	6 (2.7)	35 (6.2)	0	0	3 (2.2)	3 (1.7)	41 (4.7)
知覚過敏	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
感覚鈍麻	3 (0.5)	2 (0.9)	5 (0.9)	0	0	0	0	5 (0.6)
ラクナ梗塞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
記憶障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
片頭痛	7 (1.2)	3 (1.4)	10 (1.8)	0	0	3 (2.2)	0	13 (1.5)
神経痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
神経炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
末梢性ニューロパチー	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
神経系障害 (Cont.)								
後頭神経痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
起立不耐性	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
錯感覚	3 (0.5)	2 (0.9)	5 (0.9)	0	0	0	0	5 (0.6)
睡眠の質低下	0	0	0	0	0	0	1 (0.6)	1 (0.1)
失神寸前の状態	0	1 (0.5)	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
回内筋症候群	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
神経根痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
下肢静止不能症候群	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
坐骨神経痛	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
発作様現象	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
副鼻腔炎に伴う頭痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
失神	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	1 (0.6)	5 (0.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
神経系障害 (Cont.)								
緊張性頭痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
視野欠損	0	0	0	0	0	0	1 (0.6)	1 (0.1)
精神障害	28 (5.0)	7 (3.2)	34 (6.0)	2 (5.6)	0	3 (2.2)	3 (1.7)	40 (4.6)
急性ストレス反応	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
不安	7 (1.2)	0	7 (1.2)	1 (2.8)	0	2 (1.5)	1 (0.6)	10 (1.1)
注意欠如・多動性障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
自閉症スペクトラム障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
うつ病	10 (1.8)	1 (0.5)	11 (2.0)	0	0	2 (1.5)	2 (1.1)	15 (1.7)
全般性不安障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
不眠症	10 (1.8)	4 (1.8)	13 (2.3)	0	0	0	0	13 (1.5)
故意の自傷行為	0	0	0	0	0	0	1 (0.6)	1 (0.1)
気分変化	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
精神障害 (Cont.)								
心的外傷後ストレス障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
落ち着きのなさ	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
睡眠障害	1 (0.2)	0	1 (0.2)	1 (2.8)	0	0	0	1 (0.1)
社交不安障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ストレス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
自殺念慮	0	0	0	0	0	1 (0.7)	0	1 (0.1)
自殺企図	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
腎および尿路障害	28 (5.0)	15 (6.8)	42 (7.5)	2 (5.6)	0	2 (1.5)	2 (1.1)	46 (5.2)
急性腎障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
膀胱タンポナーデ	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
尿路結石	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
非感染性膀胱炎	0	0	0	0	0	1 (0.7)	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
腎および尿路障害 (Cont.)								
排尿困難	7 (1.2)	4 (1.8)	10 (1.8)	0	0	1 (0.7)	0	11 (1.3)
血尿	2 (0.4)	3 (1.4)	5 (0.9)	0	0	0	0	5 (0.6)
緊張性膀胱	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ケトン尿	0	0	0	1 (2.8)	0	0	0	0
腎結石症	4 (0.7)	5 (2.3)	9 (1.6)	0	0	0	0	9 (1.0)
夜間頻尿	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
頻尿	0	0	0	1 (2.8)	0	0	0	0
多尿	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
蛋白尿	6 (1.1)	1 (0.5)	7 (1.2)	1 (2.8)	0	1 (0.7)	2 (1.1)	10 (1.1)
腎萎縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
腎仙痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
腎機能障害	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
腎および尿路障害 (Cont.)								
腎尿細管機能障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
尿管閉塞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
尿管結石症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
生殖系および乳房障害	17 (3.0)	7 (3.2)	24 (4.3)	0	0	3 (2.2)	2 (1.1)	29 (3.3)
無月経	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
萎縮性外陰腟炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
良性前立腺肥大症	2 (0.4)	0	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
乳房障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
乳房腫大	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
乳房腫瘤	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
子宮頚部上皮異形成	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
子宮頚部障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
生殖系および乳房障害 (Cont.)								
子宮頚部の炎症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
勃起不全	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
性器びらん	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
閉経期症状	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
不規則月経	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
不正子宮出血	0	0	0	0	0	1 (0.7)	1 (0.6)	2 (0.2)
卵巣嚢胞	0	0	0	0	0	1 (0.7)	0	1 (0.1)
閉経後出血	0	0	0	0	0	0	1 (0.6)	1 (0.1)
月経前症候群	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
前立腺炎	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	0	3 (0.3)
精液変色	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
子宮ポリープ	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
生殖系および乳房障害 (Cont.)								
子宮脱	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
外陰腟不快感	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
外陰腟の炎症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
外陰腟そう痒症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
呼吸器、胸郭および縦隔障害	58 (10.3)	18 (8.1)	75 (13.3)	0	0	8 (5.9)	5 (2.8)	88 (10.0)
喘息	4 (0.7)	0	4 (0.7)	0	0	0	0	4 (0.5)
無気肺	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
気管支反応性亢進	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
慢性閉塞性肺疾患	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
咳嗽	15 (2.7)	3 (1.4)	18 (3.2)	0	0	4 (2.9)	0	22 (2.5)
発声障害	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
呼吸困難	7 (1.2)	0	7 (1.2)	0	0	0	0	7 (0.8)

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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)								
鼻出血	2 (0.4)	3 (1.4)	5 (0.9)	0	0	3 (2.2)	2 (1.1)	10 (1.1)
鼻閉	2 (0.4)	4 (1.8)	6 (1.1)	0	0	0	0	6 (0.7)
鼻中隔弯曲	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
鼻中隔障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
鼻甲介肥大	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
鼻潰瘍	0	0	0	0	0	1 (0.7)	0	1 (0.1)
口腔咽頭不快感	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
口腔咽頭痛	16 (2.8)	1 (0.5)	17 (3.0)	0	0	2 (1.5)	1 (0.6)	20 (2.3)
呼吸時疼痛	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
胸水	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
胸膜痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
湿性咳嗽	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)								
肺塞栓症	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
肺腫瘤	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
アレルギー性鼻炎	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
鼻漏	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
副鼻腔うっ血	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
副鼻腔痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
睡眠時無呼吸症候群	3 (0.5)	1 (0.5)	4 (0.7)	0	0	1 (0.7)	0	5 (0.6)
咽喉刺激感	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
扁桃肥大	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
上気道うっ血	0	0	0	0	0	0	1 (0.6)	1 (0.1)
上気道の炎症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
上気道咳症候群	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	0	3 (0.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)								
喘鳴	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
皮膚および皮下組織障害	79 (14.1)	33 (14.9)	110 (19.6)	3 (8.3)	0	11 (8.1)	15 (8.4)	136 (15.5)
ざ瘡	11 (2.0)	7 (3.2)	18 (3.2)	0	0	3 (2.2)	3 (1.7)	24 (2.7)
嚢胞性ざ瘡	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
光線角化症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
脱毛症	8 (1.4)	2 (0.9)	10 (1.8)	0	0	0	1 (0.6)	11 (1.3)
水疱	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
皮膚嚢腫	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
皮膚炎	3 (0.5)	1 (0.5)	4 (0.7)	1 (2.8)	0	0	0	4 (0.5)
ざ瘡様皮膚炎	2 (0.4)	0	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
アレルギー性皮膚炎	0	0	0	0	0	0	1 (0.6)	1 (0.1)
接触皮膚炎	4 (0.7)	0	4 (0.7)	0	0	1 (0.7)	0	5 (0.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
皮膚および皮下組織障害 (Cont.)								
剥脱性皮膚炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
薬疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
皮膚乾燥	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
斑状出血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
湿疹	8 (1.4)	5 (2.3)	13 (2.3)	0	0	1 (0.7)	1 (0.6)	15 (1.7)
皮脂欠乏性湿疹	0	0	0	0	0	0	1 (0.6)	1 (0.1)
紅斑	4 (0.7)	0	4 (0.7)	0	0	0	2 (1.1)	6 (0.7)
環状紅斑	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
過角化	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
嵌入爪	0	0	0	0	0	1 (0.7)	0	1 (0.1)
毛孔性角化症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
黒子	0	0	0	0	0	0	1 (0.6)	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
皮膚および皮下組織障害 (Cont.)								
扁平苔癬	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
汗疹	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
爪肥厚	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
寝汗	3 (0.5)	1 (0.5)	4 (0.7)	0	0	1 (0.7)	1 (0.6)	6 (0.7)
爪破損	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
爪甲剥離症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
脂肪織炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
丘疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
口囲皮膚炎	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
点状出血	0	0	0	0	0	1 (0.7)	0	1 (0.1)
そう痒症	7 (1.2)	5 (2.3)	12 (2.1)	0	0	1 (0.7)	1 (0.6)	14 (1.6)
乾癬	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
皮膚および皮下組織障害 (Cont.)								
発疹	16 (2.8)	6 (2.7)	21 (3.7)	1 (2.8)	0	1 (0.7)	2 (1.1)	24 (2.7)
紅斑性皮疹	1 (0.2)	1 (0.5)	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
毛孔性皮疹	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
斑状皮疹	0	1 (0.5)	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
斑状丘疹状皮疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
丘疹性皮疹	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
そう痒性皮疹	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
酒さ	3 (0.5)	2 (0.9)	5 (0.9)	0	0	1 (0.7)	0	6 (0.7)
脂漏性皮膚炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
皮膚変色	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
皮膚剥脱	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
皮膚病変	4 (0.7)	1 (0.5)	5 (0.9)	0	0	0	0	5 (0.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
皮膚および皮下組織障害 (Cont.)								
蕁麻疹	1 (0.2)	1 (0.5)	2 (0.4)	1 (2.8)	0	1 (0.7)	0	3 (0.3)
社会環境	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
閉経	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
外科および内科処置	2 (0.4)	1 (0.5)	3 (0.5)	0	0	1 (0.7)	2 (1.1)	6 (0.7)
植込み型除細動器挿入	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
抜歯	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
智歯抜歯	0	0	0	0	0	1 (0.7)	1 (0.6)	2 (0.2)
血管障害	26 (4.6)	7 (3.2)	33 (5.9)	0	0	5 (3.7)	2 (1.1)	40 (4.6)
大動脈硬化症	0	0	0	0	0	1 (0.7)	0	1 (0.1)
動脈硬化症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
深部静脈血栓症	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
出血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
血管障害 (Cont.)								
ほてり	4 (0.7)	0	4 (0.7)	0	0	0	0	4 (0.5)
高血圧	16 (2.8)	6 (2.7)	22 (3.9)	0	0	3 (2.2)	0	25 (2.9)
高血圧クリーゼ	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
末梢静脈疾患	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
静脈炎	0	0	0	0	0	0	1 (0.6)	1 (0.1)
レイノー現象	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
静脈瘤	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
静脈血栓症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
白衣性高血圧	0	0	0	0	0	0	1 (0.6)	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表4

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

TABLE 14.3__1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All_UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
Any adverse event	1873 (283.6)	663 (269.0)	2536 (279.7)	43 (211.8)	1 (45.5)	256 (240.6)	264 (237.2)	3057 (271.3)
血液およびリンパ系障害	56 (8.5)	16 (6.5)	72 (7.9)	5 (24.6)	0	10 (9.4)	13 (11.7)	95 (8.4)
貧血	24 (3.6)	4 (1.6)	28 (3.1)	1 (4.9)	0	3 (2.8)	4 (3.6)	35 (3.1)
大球性貧血	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
周期性好中球減少症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
内出血発生の増加傾向	1 (0.2)	0	1 (0.1)	1 (4.9)	0	0	1 (0.9)	2 (0.2)
鉄欠乏性貧血	2 (0.3)	2 (0.8)	4 (0.4)	0	0	2 (1.9)	0	6 (0.5)
白血球増加症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
白血球減少症	5 (0.8)	1 (0.4)	6 (0.7)	1 (4.9)	0	2 (1.9)	4 (3.6)	12 (1.1)
リンパ節症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
リンパ球減少症	7 (1.1)	4 (1.6)	11 (1.2)	0	0	1 (0.9)	1 (0.9)	13 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)								
小球性貧血	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
好中球減少症	9 (1.4)	3 (1.2)	12 (1.3)	2 (9.9)	0	1 (0.9)	2 (1.8)	15 (1.3)
汎血球減少症	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
網状赤血球増加症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血小板増加症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
心臓障害	15 (2.3)	1 (0.4)	16 (1.8)	1 (4.9)	0	3 (2.8)	4 (3.6)	23 (2.0)
不安定狭心症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
不整脈	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
心房細動	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
第一度房室ブロック	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
心拡大	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
心臓障害 (Cont.)								
冠動脈疾患	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
虚血性心筋症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
心筋梗塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
動悸	3 (0.5)	0	3 (0.3)	1 (4.9)	0	0	0	3 (0.3)
上室性期外収縮	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
上室性頻脈	0	0	0	0	0	2 (1.9)	0	2 (0.2)
頻脈	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
心室性期外収縮	1 (0.2)	0	1 (0.1)	0	0	0	2 (1.8)	3 (0.3)
心室性頻脈	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
先天性、家族性および遺伝性障害	2 (0.3)	0	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
ジルベール症候群	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
先天性、家族性および遺伝性障害 (Cont.)								
魚鱗癬	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
歯原性嚢胞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
耳および迷路障害	11 (1.7)	5 (2.0)	16 (1.8)	0	0	1 (0.9)	4 (3.6)	21 (1.9)
耳痛	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	0	4 (0.4)
外耳の炎症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
内耳障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
メニエール病	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
突発性難聴	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
耳鳴	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	2 (1.8)	6 (0.5)
回転性めまい	4 (0.6)	1 (0.4)	5 (0.6)	0	0	1 (0.9)	1 (0.9)	7 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
内分泌障害	5 (0.8)	2 (0.8)	7 (0.8)	0	0	0	0	7 (0.6)
アジソン病	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
副腎機能不全	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
急性副腎皮質機能不全	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
クッシング様症状	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
甲状腺腫	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
甲状腺機能亢進症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
眼障害	24 (3.6)	7 (2.8)	31 (3.4)	3 (14.8)	0	1 (0.9)	4 (3.6)	36 (3.2)
眼精疲労	0	0	0	1 (4.9)	0	0	0	0
眼瞼炎	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	0	4 (0.4)
眼瞼痙攣	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
白内障	4 (0.6)	0	4 (0.4)	0	0	1 (0.9)	1 (0.9)	6 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
眼障害 (Cont.)								
霰粒腫	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
結膜嚢胞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
結膜出血	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
結膜充血	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
アレルギー性結膜炎	1 (0.2)	0	1 (0.1)	1 (4.9)	0	0	0	1 (<0.1)
結膜弛緩症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
後天性涙道狭窄	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ドライアイ	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	0	4 (0.4)
上強膜炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
眼刺激	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
眼痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
眼障害 (Cont.)								
眼瞼嚢胞	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
緑内障	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
眼充血	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
開放隅角緑内障	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ぶどう膜炎	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
霧視	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
視力低下	0	0	0	1 (4.9)	0	0	0	0
視力障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
硝子体浮遊物	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
胃腸障害	306 (46.3)	100 (40.6)	406 (44.8)	8 (39.4)	0	38 (35.7)	26 (23.4)	470 (41.7)
腹部不快感	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
腹部膨満	4 (0.6)	3 (1.2)	7 (0.8)	1 (4.9)	0	1 (0.9)	2 (1.8)	10 (0.9)
腹痛	16 (2.4)	3 (1.2)	19 (2.1)	0	0	3 (2.8)	1 (0.9)	23 (2.0)
下腹部痛	6 (0.9)	0	6 (0.7)	0	0	0	0	6 (0.5)
上腹部痛	7 (1.1)	1 (0.4)	8 (0.9)	1 (4.9)	0	1 (0.9)	1 (0.9)	10 (0.9)
腹部圧痛	6 (0.9)	0	6 (0.7)	0	0	0	1 (0.9)	7 (0.6)
裂肛	5 (0.8)	1 (0.4)	6 (0.7)	0	0	0	0	6 (0.5)
痔瘻	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
肛門失禁	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肛門そう痒症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
口角口唇炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
アフタ性潰瘍	5 (0.8)	1 (0.4)	6 (0.7)	0	0	1 (0.9)	0	7 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
口唇のひび割れ	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸炎	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
潰瘍性大腸炎	97 (14.7)	39 (15.8)	136 (15.0)	2 (9.9)	0	9 (8.5)	7 (6.3)	152 (13.5)
結腸異形成	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
便秘	5 (0.8)	2 (0.8)	7 (0.8)	0	0	2 (1.9)	1 (0.9)	10 (0.9)
クローン病	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
便意切迫	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
齲歯	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	0	5 (0.4)
歯組織の壊死	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
下痢	17 (2.6)	1 (0.4)	18 (2.0)	0	0	0	1 (0.9)	19 (1.7)
血性下痢	0	0	0	0	0	1 (0.9)	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
腸憩室	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
十二指腸炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
消化不良	9 (1.4)	5 (2.0)	14 (1.5)	0	0	1 (0.9)	0	15 (1.3)
腸炎	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
おくび	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
軟便	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腿ヘルニア	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
鼓腸	7 (1.1)	1 (0.4)	8 (0.9)	0	0	1 (0.9)	0	9 (0.8)
排便回数増加	1 (0.2)	0	1 (0.1)	0	0	2 (1.9)	0	3 (0.3)
胃障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
胃ポリープ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
胃炎	5 (0.8)	1 (0.4)	6 (0.7)	1 (4.9)	0	0	0	6 (0.5)
胃腸障害	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
消化管運動障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
胃食道逆流性疾患	7 (1.1)	1 (0.4)	8 (0.9)	1 (4.9)	0	3 (2.8)	1 (0.9)	12 (1.1)
血便排泄	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
痔核	8 (1.2)	3 (1.2)	11 (1.2)	0	0	3 (2.8)	2 (1.8)	16 (1.4)
血栓性痔核	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
裂孔ヘルニア	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
イレウス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
鼠径ヘルニア	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
腸閉塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
腸管ポリープ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
過敏性腸症候群	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
大腸穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	8 (1.2)	1 (0.4)	9 (1.0)	0	0	0	2 (1.8)	11 (1.0)
口唇潰瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
口腔内潰瘍形成	4 (0.6)	1 (0.4)	5 (0.6)	0	0	1 (0.9)	0	6 (0.5)
悪心	23 (3.5)	8 (3.2)	31 (3.4)	1 (4.9)	0	3 (2.8)	3 (2.7)	37 (3.3)
食道運動低下	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
食道痛	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
口腔知覚不全	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
口腔扁平苔癬	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
膵炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肛門周囲痛	3 (0.5)	0	3 (0.3)	0	0	1 (0.9)	0	4 (0.4)
直腸炎	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
偽性ポリポーシス	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
直腸異形成	0	0	0	0	0	2 (1.9)	0	2 (0.2)
直腸出血	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	0	5 (0.4)
直腸しぶり	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
口内炎	5 (0.8)	1 (0.4)	6 (0.7)	0	0	0	0	6 (0.5)
舌障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
歯の障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
埋伏歯	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
歯痛	3 (0.5)	4 (1.6)	7 (0.8)	0	0	0	1 (0.9)	8 (0.7)
臍ヘルニア	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
嘔吐	14 (2.1)	1 (0.4)	15 (1.7)	1 (4.9)	0	2 (1.9)	1 (0.9)	18 (1.6)
一般・全身障害および投与部位の状態	81 (12.3)	27 (11.0)	108 (11.9)	1 (4.9)	0	6 (5.6)	7 (6.3)	121 (10.7)
無力症	4 (0.6)	0	4 (0.4)	0	0	0	0	4 (0.4)
胸痛	6 (0.9)	4 (1.6)	10 (1.1)	0	0	0	0	10 (0.9)
悪寒	3 (0.5)	1 (0.4)	4 (0.4)	0	0	1 (0.9)	2 (1.8)	7 (0.6)
状態悪化	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
異形成	2 (0.3)	0	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
疲労	16 (2.4)	2 (0.8)	18 (2.0)	0	0	3 (2.8)	1 (0.9)	22 (2.0)
高体温症	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
治癒不良	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
インフルエンザ様疾患	9 (1.4)	3 (1.2)	12 (1.3)	0	0	0	1 (0.9)	13 (1.2)
医療機器関連損傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
倦怠感	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
末梢性浮腫	4 (0.6)	2 (0.8)	6 (0.7)	0	0	0	0	6 (0.5)
疼痛	4 (0.6)	1 (0.4)	5 (0.6)	0	0	0	0	5 (0.4)
末梢腫脹	2 (0.3)	0	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
ポリープ	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
偽ポリープ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
発熱	23 (3.5)	11 (4.5)	34 (3.7)	1 (4.9)	0	0	2 (1.8)	36 (3.2)
異物感	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
顔面腫脹	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ワクチン接種部位反応	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
肝胆道系障害	21 (3.2)	4 (1.6)	25 (2.8)	0	0	2 (1.9)	1 (0.9)	28 (2.5)
胆道ジスキネジア	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
胆汁性嚢胞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
硬化性胆管炎	4 (0.6)	0	4 (0.4)	0	0	0	0	4 (0.4)
胆石症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
肝嚢胞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肝機能異常	5 (0.8)	1 (0.4)	6 (0.7)	0	0	0	1 (0.9)	7 (0.6)
脂肪肝	3 (0.5)	2 (0.8)	5 (0.6)	0	0	1 (0.9)	0	6 (0.5)
肝細胞損傷	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
肝胆道系障害 (Cont.)								
肝腫大	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肝障害	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
非アルコール性脂肪性肝疾患	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
免疫系障害	7 (1.1)	7 (2.8)	14 (1.5)	0	0	1 (0.9)	3 (2.7)	18 (1.6)
動物アレルギー	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
アナフィラキシー反応	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
薬物過敏症	0	1 (0.4)	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
粉塵アレルギー	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
過敏症	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
ダニアレルギー	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
季節性アレルギー	4 (0.6)	3 (1.2)	7 (0.8)	0	0	1 (0.9)	1 (0.9)	9 (0.8)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症	463 (70.1)	172 (69.8)	635 (70.0)	11 (54.2)	1 (45.5)	64 (60.2)	69 (62.0)	769 (68.3)
腹部膿瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腹壁膿瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頚部膿瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ダニ皮膚炎	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
急性副鼻腔炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
歯槽骨炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肛門膿瘍	0	2 (0.8)	2 (0.2)	0	0	1 (0.9)	1 (0.9)	4 (0.4)
虫垂炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
無症候性COVID-19	4 (0.6)	0	4 (0.4)	1 (4.9)	0	0	0	4 (0.4)
異型肺炎	0	1 (0.4)	1 (0.1)	0	0	1 (0.9)	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
細菌感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
細菌性膣症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
バルトリン腺炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ブラストシスティス感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
気管支炎	24 (3.6)	5 (2.0)	29 (3.2)	0	0	2 (1.9)	0	31 (2.8)
COVID-19	21 (3.2)	10 (4.1)	31 (3.4)	1 (4.9)	0	8 (7.5)	9 (8.1)	48 (4.3)
COVID-19肺炎	1 (0.2)	3 (1.2)	4 (0.4)	0	0	5 (4.7)	2 (1.8)	11 (1.0)
カンピロバクター胃腸炎	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	1 (0.9)	3 (0.3)
カンピロバクター感染	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
カンジダ感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
蜂巣炎	4 (0.6)	0	4 (0.4)	0	0	4 (3.8)	1 (0.9)	9 (0.8)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
感染性胆嚢炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
慢性副鼻腔炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
クロストリジウム・ディフィシレ大腸炎	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
クロストリジウム・ディフィシレ感染	5 (0.8)	8 (3.2)	13 (1.4)	0	0	0	2 (1.8)	15 (1.3)
結腸膿瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
結膜炎	2 (0.3)	0	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
ウイルス性結膜炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
コロナウイルス感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
サイクロスポリジウム感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
膀胱炎	11 (1.7)	3 (1.2)	14 (1.5)	0	1 (45.5)	3 (2.8)	2 (1.8)	20 (1.8)
毛嚢虫症	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	1 (0.9)	4 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
感染性皮膚炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
爪の皮膚糸状菌症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
医療機器関連敗血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
感染性下痢	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (0.3)
憩室炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
耳感染	4 (0.6)	2 (0.8)	6 (0.7)	0	0	0	0	6 (0.5)
感染性腸炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
丹毒	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
遊走性紅斑	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸菌感染	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
大腸菌性敗血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
眼感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
眼瞼感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
毛包炎	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
皮膚真菌感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
せつ	0	0	0	0	0	0	2 (1.8)	2 (0.2)
胃腸炎	9 (1.4)	8 (3.2)	17 (1.9)	1 (4.9)	0	0	4 (3.6)	21 (1.9)
ウイルス性胃腸炎	6 (0.9)	1 (0.4)	7 (0.8)	0	0	0	0	7 (0.6)
消化管内細菌過剰増殖	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
消化管感染	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
性器カンジダ症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
陰部ヘルペス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
陰部単純ヘルペス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
歯肉膿瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
歯肉炎	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
肛径部膿瘍	1 (0.2)	0	1 (0.1)	1 (4.9)	0	0	0	1 (<0.1)
ヘリコバクター性胃炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ヘリコバクター感染	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
単純ヘルペス	10 (1.5)	2 (0.8)	12 (1.3)	0	0	0	0	12 (1.1)
単純ヘルペス性咽頭炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
帯状疱疹	25 (3.8)	12 (4.9)	37 (4.1)	2 (9.9)	0	4 (3.8)	4 (3.6)	45 (4.0)
神経合併症を伴う帯状疱疹感染	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
耳帯状疱疹	0	0	0	0	0	1 (0.9)	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
麦粒腫	4 (0.6)	4 (1.6)	8 (0.9)	0	0	0	0	8 (0.7)
膿痂疹	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
感染性嚢腫	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
伝染性単核症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
インフルエンザ	22 (3.3)	7 (2.8)	29 (3.2)	1 (4.9)	0	0	0	29 (2.6)
クレブシエラ感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸感染	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
喉頭炎	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
潜伏結核	5 (0.8)	1 (0.4)	6 (0.7)	0	0	1 (0.9)	2 (1.8)	9 (0.8)
限局性感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
下気道感染	4 (0.6)	0	4 (0.4)	0	0	0	0	4 (0.4)
上咽頭炎	64 (9.7)	27 (11.0)	91 (10.0)	1 (4.9)	0	6 (5.6)	7 (6.3)	104 (9.2)
爪真菌症	4 (0.6)	0	4 (0.4)	0	0	3 (2.8)	0	7 (0.6)
口腔カンジダ症	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
口腔真菌感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
口腔ヘルペス	34 (5.1)	9 (3.7)	43 (4.7)	1 (4.9)	0	0	6 (5.4)	49 (4.3)
精巣炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
外耳炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
歯周炎	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
直腸周囲膿瘍	0	0	0	0	0	2 (1.9)	0	2 (0.2)
咽頭炎	3 (0.5)	2 (0.8)	5 (0.6)	0	0	1 (0.9)	1 (0.9)	7 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
毛巣嚢胞	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
ニューモシスチス・イロベチイ感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肺炎	9 (1.4)	5 (2.0)	14 (1.5)	0	0	0	0	14 (1.2)
細菌性肺炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ウイルス性肺炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
歯髄炎	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
膿疱	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
腎盂腎炎	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
膿尿	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
気道感染	3 (0.5)	2 (0.8)	5 (0.6)	0	0	1 (0.9)	0	6 (0.5)
ウイルス性気道感染	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
鼻炎	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
根管感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
敗血症	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
副鼻腔炎	14 (2.1)	6 (2.4)	20 (2.2)	1 (4.9)	0	1 (0.9)	3 (2.7)	24 (2.1)
皮膚感染	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
ブドウ球菌感染	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
レンサ球菌性尿路感染	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
皮下組織膿瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
白癬感染	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
足部白癬	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
扁桃炎	0	1 (0.4)	1 (0.1)	0	0	1 (0.9)	1 (0.9)	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
歯膿瘍	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	2 (1.8)	6 (0.5)
歯感染	2 (0.3)	3 (1.2)	5 (0.6)	0	0	0	0	5 (0.4)
結核	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
上気道感染	55 (8.3)	12 (4.9)	67 (7.4)	0	0	10 (9.4)	2 (1.8)	79 (7.0)
尿路感染	25 (3.8)	1 (0.4)	26 (2.9)	1 (4.9)	0	4 (3.8)	4 (3.6)	34 (3.0)
腟感染	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
水痘	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ウイルス性下痢	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ウイルス感染	2 (0.3)	0	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
ウイルス性咽頭炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ウイルス性上気道感染	1 (0.2)	3 (1.2)	4 (0.4)	0	0	0	2 (1.8)	6 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
外陰部腟カンジダ症	2 (0.3)	0	2 (0.2)	0	0	0	2 (1.8)	4 (0.4)
外陰腟真菌感染	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
外陰腟炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
傷害、中毒および処置合併症	78 (11.8)	31 (12.6)	109 (12.0)	1 (4.9)	0	5 (4.7)	6 (5.4)	120 (10.7)
動物咬傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
動物による引っかき傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
足関節部骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
節足動物咬傷	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
骨挫傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
第2度熱傷	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
挫傷	7 (1.1)	0	7 (0.8)	0	0	0	0	7 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
上顎炎	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
眼外傷	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
転倒	8 (1.2)	5 (2.0)	13 (1.4)	0	0	0	0	13 (1.2)
腓骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
足骨折	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
骨折	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
仙骨骨折	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
手骨折	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
頭部損傷	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
損傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
企図的過量投与	0	0	0	0	0	1 (0.9)	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
関節脱臼	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
関節損傷	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
靭帯断裂	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
靭帯捻挫	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
四肢損傷	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
つち指	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
半月板損傷	0	0	0	1 (4.9)	0	0	0	0
筋断裂	0	3 (1.2)	3 (0.3)	0	0	0	0	3 (0.3)
肉離れ	5 (0.8)	1 (0.4)	6 (0.7)	0	0	0	1 (0.9)	7 (0.6)
筋骨格内異物	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
過量投与	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
膝蓋骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
骨盤骨折	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
処置後血尿	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
処置後出血	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
外傷後頚部症候群	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
外傷後疼痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
術後イレウス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
処置による腸管穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
処置による疼痛	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
肺挫傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
橈骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
肋骨骨折	5 (0.8)	2 (0.8)	7 (0.8)	0	0	0	0	7 (0.6)
交通事故	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
瘢痕	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
陰嚢血腫	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚擦過傷	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
皮膚裂傷	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
軟部組織損傷	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ストレス骨折	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
皮下血腫	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
腱損傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腱断裂	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
熱傷	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
脛骨骨折	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
歯牙破折	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (0.3)
子宮穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ワクチン接種合併症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
創傷	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
創合併症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
手首関節骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
臨床検査	185 (28.0)	51 (20.7)	236 (26.0)	2 (9.9)	0	27 (25.4)	50 (44.9)	313 (27.8)
アラニンアミノトランスフェラーゼ増加	12 (1.8)	2 (0.8)	14 (1.5)	0	0	1 (0.9)	0	15 (1.3)
抗好中球細胞質抗体陽性	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
関節鏡検査	0	1 (0.4)	1 (0.1)	0	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	11 (1.7)	3 (1.2)	14 (1.5)	0	0	0	1 (0.9)	15 (1.3)
細菌検査陽性	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
好塩基球数増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中アルブミン増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中アルカリホスファターゼ増加	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
血中重炭酸塩減少	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
血中ビリルビン増加	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	4 (3.6)	6 (0.5)
血中カルシウム増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中コレステロール減少	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
血中コレステロール増加	5 (0.8)	1 (0.4)	6 (0.7)	0	0	1 (0.9)	2 (1.8)	9 (0.8)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
血中クレアチン増加	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
血中クレアチンホスホキナーゼMB増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中クレアチンホスホキナーゼ増加	36 (5.5)	18 (7.3)	54 (6.0)	1 (4.9)	0	1 (0.9)	10 (9.0)	65 (5.8)
血中クレアチニン増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中葉酸減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中ブドウ糖減少	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
血中ブドウ糖増加	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
血中鉄減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中リン減少	1 (0.2)	0	1 (0.1)	0	0	0	2 (1.8)	3 (0.3)
血中カリウム減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中カリウム増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
血圧上昇	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
血中トリグリセリド減少	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
血中トリグリセリド増加	4 (0.6)	0	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
血中尿素増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
尿中血陽性	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
骨密度減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
クロストリジウム検査陽性	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
凝固時間延長	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
尿中結晶陽性	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
心電図QT延長	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
心電図異常	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
便中カルプロテクチン増加	4 (0.6)	0	4 (0.4)	0	0	0	0	4 (0.4)
γ-グルタミルトランスフェラーゼ増加	6 (0.9)	1 (0.4)	7 (0.8)	0	0	4 (3.8)	1 (0.9)	12 (1.1)
尿中ブドウ糖陽性	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
ヘマトクリット減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ヘモグロビン減少	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	2 (1.8)	7 (0.6)
肝酵素上昇	5 (0.8)	1 (0.4)	6 (0.7)	0	0	1 (0.9)	1 (0.9)	8 (0.7)
B型肝炎DNA測定陽性	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
高比重リポ蛋白増加	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
ヒト乳頭腫ウイルス検査陽性	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
眼圧上昇	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
臨床検査異常	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
リパーゼ増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肝機能検査異常	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肝機能検査値上昇	2 (0.3)	0	2 (0.2)	0	0	1 (0.9)	1 (0.9)	4 (0.4)
低比重リポ蛋白減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
低比重リポ蛋白増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
リンパ球数減少	7 (1.1)	2 (0.8)	9 (1.0)	0	0	2 (1.9)	3 (2.7)	14 (1.2)
リンパ球百分率減少	0	0	0	0	0	0	2 (1.8)	2 (0.2)
平均赤血球容積増加	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
単球数増加	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
結核菌群検査陽性	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
好中球数減少	8 (1.2)	1 (0.4)	9 (1.0)	0	0	5 (4.7)	5 (4.5)	19 (1.7)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
好中球数増加	5 (0.8)	0	5 (0.6)	0	0	2 (1.9)	1 (0.9)	8 (0.7)
血小板数減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血小板数増加	2 (0.3)	0	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
尿中蛋白陽性	3 (0.5)	0	3 (0.3)	0	0	2 (1.9)	0	5 (0.4)
赤血球数減少	4 (0.6)	0	4 (0.4)	0	0	0	2 (1.8)	6 (0.5)
赤血球数増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
網状赤血球数増加	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
尿比重増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
トランスアミナーゼ上昇	2 (0.3)	0	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
尿検査異常	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
尿中ケトン体陽性	3 (0.5)	0	3 (0.3)	0	0	0	1 (0.9)	4 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
尿中白血球エステラーゼ陽性	4 (0.6)	0	4 (0.4)	0	0	0	0	4 (0.4)
尿量減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ビタミンB12減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
体重減少	0	2 (0.8)	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
体重増加	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
白血球数減少	8 (1.2)	1 (0.4)	9 (1.0)	1 (4.9)	0	3 (2.8)	4 (3.6)	16 (1.4)
白血球数増加	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
尿中白血球陽性	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
代謝および栄養障害	54 (8.2)	13 (5.3)	67 (7.4)	0	0	10 (9.4)	11 (9.9)	88 (7.8)
食欲減退	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
脱水	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
糖尿病	0	0	0	0	0	0	2 (1.8)	2 (0.2)
脂質異常症	2 (0.3)	0	2 (0.2)	0	0	2 (1.9)	0	4 (0.4)
葉酸欠乏	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
耐糖能障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
痛風	0	1 (0.4)	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
ヒスタミン不耐性	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
高コレステロール血症	7 (1.1)	2 (0.8)	9 (1.0)	0	0	2 (1.9)	3 (2.7)	14 (1.2)
高血糖	6 (0.9)	0	6 (0.7)	0	0	2 (1.9)	0	8 (0.7)
高ホモシステイン血症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
高脂血症	6 (0.9)	0	6 (0.7)	0	0	1 (0.9)	2 (1.8)	9 (0.8)
高トリグリセリド血症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
高尿酸血症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
低アルブミン血症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
低カリウム血症	2 (0.3)	0	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
低マグネシウム血症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
低ナトリウム血症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
低リン酸血症	3 (0.5)	4 (1.6)	7 (0.8)	0	0	0	0	7 (0.6)
低蛋白血症	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
鉄欠乏	4 (0.6)	1 (0.4)	5 (0.6)	0	0	0	0	5 (0.4)
ラクトース不耐性	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
代謝性アシドーシス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肥満	0	0	0	0	0	0	2 (1.8)	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
過少体重	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ビタミンB群欠乏	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ビタミンB12欠乏	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ビタミンD欠乏	5 (0.8)	1 (0.4)	6 (0.7)	0	0	0	2 (1.8)	8 (0.7)
筋骨格系および結合組織障害	154 (23.3)	70 (28.4)	224 (24.7)	2 (9.9)	0	26 (24.4)	18 (16.2)	268 (23.8)
関節痛	35 (5.3)	19 (7.7)	54 (6.0)	1 (4.9)	0	5 (4.7)	6 (5.4)	65 (5.8)
関節炎	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	0	5 (0.4)
関節障害	7 (1.1)	1 (0.4)	8 (0.9)	0	0	3 (2.8)	2 (1.8)	13 (1.2)
腋窩腫瘤	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
背部痛	21 (3.2)	9 (3.7)	30 (3.3)	1 (4.9)	0	1 (0.9)	1 (0.9)	32 (2.8)
滑液包炎	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	1 (0.9)	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
軟骨萎縮	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頚部脊柱管狭窄症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
尾骨痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
コンパートメント症候群	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
指炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腱付着部症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
外骨腫	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
側腹部痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
鼡径部痛	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
椎間板変性症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
椎間板障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
椎間板突出	5 (0.8)	2 (0.8)	7 (0.8)	0	0	1 (0.9)	1 (0.9)	9 (0.8)
関節滲出液	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
関節硬直	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
関節腫脹	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
腰部脊柱管狭窄症	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
脛骨内側過労性症候群	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
筋拘縮	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
筋痙縮	3 (0.5)	3 (1.2)	6 (0.7)	0	0	3 (2.8)	0	9 (0.8)
筋骨格系胸痛	1 (0.2)	1 (0.4)	2 (0.2)	0	0	2 (1.9)	0	4 (0.4)
筋骨格痛	5 (0.8)	4 (1.6)	9 (1.0)	0	0	0	0	9 (0.8)
筋骨格硬直	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	0	4 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
筋肉痛	12 (1.8)	2 (0.8)	14 (1.5)	0	0	1 (0.9)	2 (1.8)	17 (1.5)
筋膜疼痛症候群	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ミオパチー	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頚部痛	2 (0.3)	3 (1.2)	5 (0.6)	0	0	0	0	5 (0.4)
変形性関節症	4 (0.6)	1 (0.4)	5 (0.6)	0	0	0	0	5 (0.4)
骨端症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
骨壊死	1 (0.2)	1 (0.4)	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
骨減少症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
骨粗鬆症	1 (0.2)	3 (1.2)	4 (0.4)	0	0	0	0	4 (0.4)
四肢痛	9 (1.4)	8 (3.2)	17 (1.9)	0	0	2 (1.9)	2 (1.8)	21 (1.9)
顎痛	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) 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	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
関節周囲炎	0	0	0	0	0	2 (1.9)	0	2 (0.2)
足底筋膜炎	4 (0.6)	1 (0.4)	5 (0.6)	0	0	1 (0.9)	0	6 (0.5)
横紋筋融解症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
肩回旋筋腱板症候群	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
軟部組織腫瘤	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
脊柱変形	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
変形性脊椎症	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	0	4 (0.4)
脊椎炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脊椎関節障害	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
軟骨下機能不全骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
滑膜炎	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
顎関節症候群	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
腱炎	3 (0.5)	0	3 (0.3)	0	0	1 (0.9)	1 (0.9)	5 (0.4)
弾発指	0	0	0	0	0	1 (0.9)	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）	21 (3.2)	10 (4.1)	31 (3.4)	1 (4.9)	0	3 (2.8)	8 (7.2)	42 (3.7)
アクロコルドン	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
結腸腺癌	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
膵腺癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
基底細胞癌	1 (0.2)	3 (1.2)	4 (0.4)	0	0	0	0	4 (0.4)
肺の良性新生物	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
精巣の良性新生物	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) 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.)								
ボーエン病	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
気管支の良性新生物	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
大腸腺腫	4 (0.6)	0	4 (0.4)	1 (4.9)	0	0	1 (0.9)	5 (0.4)
線維腫	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
線維性組織球腫	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
喉頭扁平上皮癌	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脂肪腫	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
メラノサイト性母斑	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
前立腺癌	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
脂漏性角化症	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
皮膚乳頭腫	4 (0.6)	2 (0.8)	6 (0.7)	0	0	1 (0.9)	1 (0.9)	8 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) 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.)								
扁平上皮癌	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚有棘細胞癌	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
子宮頚部扁平上皮癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
精巣（純粋）セミノーマ	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
精巣癌	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
甲状腺腺腫	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
子宮平滑筋腫	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
神経系障害	74 (11.2)	29 (11.8)	103 (11.4)	0	0	12 (11.3)	7 (6.3)	122 (10.8)
健忘	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
脳損傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
灼熱感	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
神経系障害 (Cont.)								
手根管症候群	1 (0.2)	3 (1.2)	4 (0.4)	0	0	0	0	4 (0.4)
頚髄神経根障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
注意力障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
浮動性めまい	7 (1.1)	3 (1.2)	10 (1.1)	0	0	4 (3.8)	0	14 (1.2)
異常感覚	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
構語障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頭痛	32 (4.8)	6 (2.4)	38 (4.2)	0	0	4 (3.8)	3 (2.7)	45 (4.0)
知覚過敏	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
感覚鈍麻	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	0	5 (0.4)
ラクナ梗塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
記憶障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
神経系障害 (Cont.)								
片頭痛	7 (1.1)	3 (1.2)	10 (1.1)	0	0	4 (3.8)	0	14 (1.2)
神経痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
神経炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
末梢性ニューロパチー	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
後頭神経痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
起立不耐性	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
錯感覚	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	0	5 (0.4)
睡眠の質低下	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
失神寸前の状態	0	1 (0.4)	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
回内筋症候群	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
神経根痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
神経系障害 (Cont.)								
下肢静止不能症候群	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
坐骨神経痛	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
発作様現象	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
副鼻腔炎に伴う頭痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
失神	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
緊張性頭痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
視野欠損	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
精神障害	36 (5.5)	10 (4.1)	46 (5.1)	2 (9.9)	0	6 (5.6)	4 (3.6)	56 (5.0)
急性ストレス反応	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
不安	7 (1.1)	0	7 (0.8)	1 (4.9)	0	2 (1.9)	1 (0.9)	10 (0.9)
注意欠如・多動性障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
精神障害 (Cont.)								
自閉症スペクトラム障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
うつ病	10 (1.5)	1 (0.4)	11 (1.2)	0	0	2 (1.9)	2 (1.8)	15 (1.3)
全般性不安障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
不眠症	10 (1.5)	6 (2.4)	16 (1.8)	0	0	0	0	16 (1.4)
故意の自傷行為	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
気分変化	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
心的外傷後ストレス障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
落ち着きのなさ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
睡眠障害	2 (0.3)	0	2 (0.2)	1 (4.9)	0	0	0	2 (0.2)
社交不安障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ストレス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
精神障害 (Cont.)								
自殺念慮	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
自殺企図	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
腎および尿路障害	33 (5.0)	20 (8.1)	53 (5.8)	3 (14.8)	0	4 (3.8)	2 (1.8)	59 (5.2)
急性腎障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
膀胱タンポナーデ	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
尿路結石	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
非感染性膀胱炎	0	0	0	0	0	2 (1.9)	0	2 (0.2)
排尿困難	8 (1.2)	5 (2.0)	13 (1.4)	0	0	1 (0.9)	0	14 (1.2)
血尿	2 (0.3)	3 (1.2)	5 (0.6)	0	0	0	0	5 (0.4)
緊張性膀胱	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ケトン尿	0	0	0	1 (4.9)	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
腎および尿路障害 (Cont.)								
腎結石症	5 (0.8)	6 (2.4)	11 (1.2)	0	0	0	0	11 (1.0)
夜間頻尿	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
頻尿	0	0	0	1 (4.9)	0	0	0	0
多尿	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
蛋白尿	6 (0.9)	1 (0.4)	7 (0.8)	1 (4.9)	0	1 (0.9)	2 (1.8)	10 (0.9)
腎萎縮	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腎仙痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腎機能障害	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
腎尿細管機能障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
尿管閉塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
尿管結石症	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
生殖系および乳房障害	20 (3.0)	8 (3.2)	28 (3.1)	0	0	3 (2.8)	2 (1.8)	33 (2.9)
無月経	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
萎縮性外陰腟炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
良性前立腺肥大症	2 (0.3)	0	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
乳房障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
乳房腫大	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
乳房腫瘤	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
子宮頚部上皮異形成	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
子宮頚部障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
子宮頚部の炎症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
勃起不全	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)								
性器びらん	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
閉経期症状	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
不規則月経	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
不正子宮出血	0	0	0	0	0	1 (0.9)	1 (0.9)	2 (0.2)
卵巣嚢胞	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
閉経後出血	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
月経前症候群	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
前立腺炎	1 (0.2)	3 (1.2)	4 (0.4)	0	0	0	0	4 (0.4)
精液変色	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
子宮ポリープ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
子宮脱	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)								
外陰腟不快感	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
外陰腟の炎症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
外陰腟そう痒症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	85 (12.9)	24 (9.7)	109 (12.0)	0	0	13 (12.2)	5 (4.5)	127 (11.3)
喘息	6 (0.9)	0	6 (0.7)	0	0	0	0	6 (0.5)
無気肺	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
気管支反応性亢進	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
慢性閉塞性肺疾患	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
咳嗽	17 (2.6)	4 (1.6)	21 (2.3)	0	0	4 (3.8)	0	25 (2.2)
発声障害	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
呼吸困難	8 (1.2)	0	8 (0.9)	0	0	0	0	8 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
鼻出血	2 (0.3)	3 (1.2)	5 (0.6)	0	0	3 (2.8)	2 (1.8)	10 (0.9)
鼻閉	2 (0.3)	5 (2.0)	7 (0.8)	0	0	0	0	7 (0.6)
鼻中隔弯曲	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
鼻中隔障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
鼻甲介肥大	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
鼻潰瘍	0	0	0	0	0	2 (1.9)	0	2 (0.2)
口腔咽頭不快感	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
口腔咽頭痛	18 (2.7)	1 (0.4)	19 (2.1)	0	0	2 (1.9)	1 (0.9)	22 (2.0)
呼吸時疼痛	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
胸水	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
胸膜痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
湿性咳嗽	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	1 (0.9)	4 (0.4)
肺塞栓症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
肺腫瘤	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
アレルギー性鼻炎	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
鼻漏	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
副鼻腔うっ血	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	0	4 (0.4)
副鼻腔痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
睡眠時無呼吸症候群	3 (0.5)	1 (0.4)	4 (0.4)	0	0	1 (0.9)	0	5 (0.4)
咽喉刺激感	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
扁桃肥大	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
上気道うっ血	0	0	0	0	0	0	1 (0.9)	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
上気道の炎症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
上気道咳症候群	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (0.3)
喘鳴	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
皮膚および皮下組織障害	109 (16.5)	46 (18.7)	155 (17.1)	3 (14.8)	0	14 (13.2)	16 (14.4)	185 (16.4)
ざ瘡	12 (1.8)	7 (2.8)	19 (2.1)	0	0	3 (2.8)	3 (2.7)	25 (2.2)
嚢胞性ざ瘡	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
光線角化症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
脱毛症	9 (1.4)	2 (0.8)	11 (1.2)	0	0	0	1 (0.9)	12 (1.1)
水疱	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚嚢腫	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
皮膚炎	3 (0.5)	1 (0.4)	4 (0.4)	1 (4.9)	0	0	0	4 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
ざ瘡様皮膚炎	2 (0.3)	0	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
アレルギー性皮膚炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
接触皮膚炎	4 (0.6)	0	4 (0.4)	0	0	1 (0.9)	0	5 (0.4)
剥脱性皮膚炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
薬疹	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚乾燥	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
斑状出血	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
湿疹	9 (1.4)	5 (2.0)	14 (1.5)	0	0	1 (0.9)	1 (0.9)	16 (1.4)
皮脂欠乏性湿疹	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
紅斑	4 (0.6)	0	4 (0.4)	0	0	0	2 (1.8)	6 (0.5)
環状紅斑	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
過角化	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
嵌入爪	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
毛孔性角化症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
黒子	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
扁平苔癬	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
汗疹	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
爪肥厚	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
寝汗	4 (0.6)	1 (0.4)	5 (0.6)	0	0	1 (0.9)	1 (0.9)	7 (0.6)
爪破損	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
爪甲剥離症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脂肪織炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
丘疹	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
口囲皮膚炎	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
点状出血	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
そう痒症	9 (1.4)	5 (2.0)	14 (1.5)	0	0	1 (0.9)	1 (0.9)	16 (1.4)
乾癬	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
発疹	18 (2.7)	8 (3.2)	26 (2.9)	1 (4.9)	0	1 (0.9)	2 (1.8)	29 (2.6)
紅斑性皮疹	1 (0.2)	1 (0.4)	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
毛孔性皮疹	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
斑状皮疹	0	1 (0.4)	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
斑状丘疹状皮疹	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
丘疹性皮疹	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
そう痒性皮疹	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
酒さ	3 (0.5)	2 (0.8)	5 (0.6)	0	0	1 (0.9)	0	6 (0.5)
脂漏性皮膚炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚変色	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚剥脱	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚病変	4 (0.6)	1 (0.4)	5 (0.6)	0	0	0	0	5 (0.4)
蕁麻疹	1 (0.2)	1 (0.4)	2 (0.2)	1 (4.9)	0	1 (0.9)	0	3 (0.3)
社会環境	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
閉経	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
外科および内科処置	2 (0.3)	1 (0.4)	3 (0.3)	0	0	1 (0.9)	2 (1.8)	6 (0.5)
植込み型除細動器挿入	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
外科および内科処置 (Cont.)								
抜歯	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
智歯抜歯	0	0	0	0	0	1 (0.9)	1 (0.9)	2 (0.2)
血管障害	31 (4.7)	8 (3.2)	39 (4.3)	0	0	5 (4.7)	2 (1.8)	46 (4.1)
大動脈硬化症	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
動脈硬化症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
深部静脈血栓症	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
出血	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ほてり	4 (0.6)	0	4 (0.4)	0	0	0	0	4 (0.4)
高血圧	18 (2.7)	7 (2.8)	25 (2.8)	0	0	3 (2.8)	0	28 (2.5)
高血圧クリーゼ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
末梢静脈疾患	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
血管障害 (Cont.)								
静脈炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
レイノー現象	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
静脈瘤	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
静脈血栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
白衣性高血圧	0	0	0	0	0	0	1 (0.9)	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表5

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

TABLE 14.3__1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All_UPA (N=877) n (%)
Any adverse event	169 (30.1)	76 (34.2)	222 (39.5)	9 (25.0)	0	25 (18.4)	34 (19.1)	281 (32.0)
血液およびリンパ系障害	17 (3.0)	9 (4.1)	25 (4.4)	3 (8.3)	0	5 (3.7)	5 (2.8)	35 (4.0)
貧血	6 (1.1)	0	6 (1.1)	1 (2.8)	0	1 (0.7)	2 (1.1)	9 (1.0)
周期性好中球減少症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
鉄欠乏性貧血	0	0	0	0	0	1 (0.7)	0	1 (0.1)
白血球増加症	0	1 (0.5)	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
白血球減少症	5 (0.9)	1 (0.5)	6 (1.1)	1 (2.8)	0	1 (0.7)	3 (1.7)	10 (1.1)
リンパ球減少症	6 (1.1)	3 (1.4)	8 (1.4)	0	0	1 (0.7)	1 (0.6)	10 (1.1)
好中球減少症	7 (1.2)	3 (1.4)	10 (1.8)	1 (2.8)	0	1 (0.7)	1 (0.6)	12 (1.4)
汎血球減少症	0	0	0	0	0	0	1 (0.6)	1 (0.1)
網状赤血球増加症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
心臓障害	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
第一度房室ブロック	0	0	0	0	0	0	1 (0.6)	1 (0.1)
動悸	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
頻脈	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
耳および迷路障害	3 (0.5)	2 (0.9)	5 (0.9)	0	0	0	1 (0.6)	6 (0.7)
耳痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
外耳の炎症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
内耳障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
メニエール病	0	0	0	0	0	0	1 (0.6)	1 (0.1)
耳鳴	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
回転性めまい	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
内分泌障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
クッシング様症状	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
眼障害	0	1 (0.5)	1 (0.2)	1 (2.8)	0	0	0	1 (0.1)
眼精疲労	0	0	0	1 (2.8)	0	0	0	0
眼瞼炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
胃腸障害	30 (5.3)	14 (6.3)	42 (7.5)	4 (11.1)	0	4 (2.9)	4 (2.2)	50 (5.7)
腹部膨満	1 (0.2)	0	1 (0.2)	1 (2.8)	0	0	0	1 (0.1)
腹痛	0	0	0	0	0	1 (0.7)	0	1 (0.1)
下腹部痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
腹部圧痛	0	0	0	0	0	0	1 (0.6)	1 (0.1)
口角口唇炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
アフタ性潰瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
大腸炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
潰瘍性大腸炎	12 (2.1)	6 (2.7)	17 (3.0)	2 (5.6)	0	1 (0.7)	1 (0.6)	19 (2.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
胃腸障害 (Cont.)								
結腸異形成	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
便秘	0	1 (0.5)	1 (0.2)	0	0	2 (1.5)	1 (0.6)	4 (0.5)
便意切迫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
下痢	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	0	4 (0.5)
鼓腸	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
胃炎	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
胃食道逆流性疾患	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
痔核	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
腸閉塞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
大腸ポリープ	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
口腔内潰瘍形成	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
悪心	3 (0.5)	0	3 (0.5)	1 (2.8)	0	0	0	3 (0.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
胃腸障害 (Cont.)								
膵炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
直腸出血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
口内炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
嘔吐	2 (0.4)	0	2 (0.4)	1 (2.8)	0	0	1 (0.6)	3 (0.3)
一般・全身障害および投与部位の状態	14 (2.5)	6 (2.7)	20 (3.6)	0	0	1 (0.7)	2 (1.1)	23 (2.6)
無力症	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
悪寒	1 (0.2)	1 (0.5)	2 (0.4)	0	0	1 (0.7)	1 (0.6)	4 (0.5)
疲労	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
治癒不良	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
インフルエンザ様疾患	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	1 (0.6)	5 (0.6)
倦怠感	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
疼痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
一般・全身障害および投与部位の状態 (Cont.)								
末梢腫脹	0	0	0	0	0	0	1 (0.6)	1 (0.1)
発熱	4 (0.7)	4 (1.8)	8 (1.4)	0	0	0	0	8 (0.9)
肝胆道系障害	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	0	4 (0.5)
硬化性胆管炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
脂肪肝	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
肝障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
非アルコール性脂肪性肝疾患	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
免疫系障害	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
過敏症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
感染症および寄生虫症	86 (15.3)	33 (14.9)	114 (20.3)	4 (11.1)	0	12 (8.8)	15 (8.4)	141 (16.1)
腹壁膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
肛門膿瘍	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD n (%)	SA 1 Population Total n (%)	SA 2 Population Placebo n (%)	SA 2 Population UPA 7.5 mg QD n (%)	SA 2 Population UPA 15 mg QD n (%)	SA 2 Population UPA 30 mg QD n (%)	SA UPA All UPA n (%)
	(N=562)	(N=222)	(N=562)	(N=36)	(N=1)	(N=136)	(N=178)	(N=877)
感染症および寄生虫症 (Cont.)								
無症候性COVID-19	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
細菌感染	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
細菌性膣症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
気管支炎	6 (1.1)	2 (0.9)	8 (1.4)	0	0	1 (0.7)	0	9 (1.0)
COVID-19	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
COVID-19肺炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	1 (0.6)	3 (0.3)
カンジダ感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
蜂巣炎	1 (0.2)	0	1 (0.2)	0	0	2 (1.5)	0	3 (0.3)
感染性胆嚢炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
クロストリジウム・ディフィシレ感染	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	1 (0.6)	5 (0.6)
結膜炎	0	0	0	0	0	0	1 (0.6)	1 (0.1)
ウイルス性結膜炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
毛嚢虫症	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)
爪の皮膚糸状菌症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
感染性下痢	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
耳感染	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
丹毒	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
眼感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
毛包炎	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
せつ	0	0	0	0	0	0	1 (0.6)	1 (0.1)
胃腸炎	0	2 (0.9)	2 (0.4)	1 (2.8)	0	0	0	2 (0.2)
ウイルス性胃腸炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
性器カンジダ症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
陰部ヘルペス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
陰部単純ヘルペス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
歯肉炎	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
肛径部膿瘍	1 (0.2)	0	1 (0.2)	1 (2.8)	0	0	0	1 (0.1)
単純ヘルペス	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
単純ヘルペス性咽頭炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
帯状疱疹	19 (3.4)	8 (3.6)	27 (4.8)	1 (2.8)	0	3 (2.2)	4 (2.2)	34 (3.9)
耳帯状疱疹	0	0	0	0	0	1 (0.7)	0	1 (0.1)
麦粒腫	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
伝染性単核症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
インフルエンザ	5 (0.9)	1 (0.5)	6 (1.1)	1 (2.8)	0	0	0	6 (0.7)
潜伏結核	3 (0.5)	0	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)
限局性感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
下気道感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
上咽頭炎	10 (1.8)	8 (3.6)	18 (3.2)	0	0	1 (0.7)	1 (0.6)	20 (2.3)
爪真菌症	2 (0.4)	0	2 (0.4)	0	0	2 (1.5)	0	4 (0.5)
口腔カンジダ症	0	0	0	0	0	0	1 (0.6)	1 (0.1)
口腔ヘルペス	3 (0.5)	3 (1.4)	6 (1.1)	1 (2.8)	0	0	1 (0.6)	7 (0.8)
直腸周囲膿瘍	0	0	0	0	0	1 (0.7)	0	1 (0.1)
咽頭炎	0	2 (0.9)	2 (0.4)	0	0	0	0	2 (0.2)
肺炎	4 (0.7)	3 (1.4)	7 (1.2)	0	0	0	0	7 (0.8)
膿疱	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
腎盂腎炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
気道感染	1 (0.2)	0	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
鼻炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
根管感染	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
敗血症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
副鼻腔炎	5 (0.9)	1 (0.5)	6 (1.1)	0	0	0	0	6 (0.7)
皮膚感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
足部白癬	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
扁桃炎	0	1 (0.5)	1 (0.2)	0	0	1 (0.7)	0	2 (0.2)
歯膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
歯感染	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
結核	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
上気道感染	25 (4.4)	5 (2.3)	30 (5.3)	0	0	1 (0.7)	0	31 (3.5)
尿路感染	8 (1.4)	0	8 (1.4)	0	0	2 (1.5)	0	10 (1.1)
腟感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
感染症および寄生虫症 (Cont.)								
水痘	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ウイルス性上気道感染	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
外陰部腟カンジダ症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
外陰腟真菌感染	0	0	0	0	0	0	1 (0.6)	1 (0.1)
傷害、中毒および処置合併症	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
筋断裂	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
皮膚裂傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
皮下血腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
臨床検査	51 (9.1)	21 (9.5)	69 (12.3)	2 (5.6)	0	4 (2.9)	14 (7.9)	87 (9.9)
アラニンアミノトランスフェラーゼ増加	8 (1.4)	2 (0.9)	10 (1.8)	0	0	0	0	10 (1.1)
アスパラギン酸アミノトランスフェラーゼ増加	7 (1.2)	3 (1.4)	10 (1.8)	0	0	0	1 (0.6)	11 (1.3)
血中アルカリホスファターゼ増加	0	0	0	0	0	0	1 (0.6)	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
臨床検査 (Cont.)								
血中ビリルビン増加	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
血中コレステロール増加	3 (0.5)	1 (0.5)	4 (0.7)	0	0	0	1 (0.6)	5 (0.6)
血中クレアチンホスホキナーゼ増加	23 (4.1)	12 (5.4)	33 (5.9)	1 (2.8)	0	1 (0.7)	6 (3.4)	40 (4.6)
血中クレアチニン増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血中葉酸減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血圧上昇	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
血中トリグリセリド増加	3 (0.5)	0	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)
凝固時間延長	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
γ-グルタミルトランスフェラーゼ増加	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
ヘマトクリット減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ヘモグロビン減少	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)
肝酵素上昇	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
臨床検査 (Cont.)								
高比重リポ蛋白増加	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
臨床検査異常	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
肝機能検査異常	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
肝機能検査値上昇	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
低比重リポ蛋白増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
リンパ球数減少	4 (0.7)	2 (0.9)	6 (1.1)	0	0	2 (1.5)	3 (1.7)	11 (1.3)
リンパ球百分率減少	0	0	0	0	0	0	1 (0.6)	1 (0.1)
好中球数減少	6 (1.1)	0	6 (1.1)	0	0	3 (2.2)	2 (1.1)	11 (1.3)
好中球数増加	2 (0.4)	0	2 (0.4)	0	0	2 (1.5)	1 (0.6)	5 (0.6)
血小板数減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
血小板数増加	0	0	0	0	0	0	1 (0.6)	1 (0.1)
赤血球数減少	2 (0.4)	0	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
臨床検査 (Cont.)								
網状赤血球数増加	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
トランスアミナーゼ上昇	0	0	0	0	0	0	1 (0.6)	1 (0.1)
尿中ケトン体陽性	0	0	0	0	0	0	1 (0.6)	1 (0.1)
尿中白血球エステラーゼ陽性	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
体重増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
白血球数減少	6 (1.1)	0	6 (1.1)	1 (2.8)	0	2 (1.5)	1 (0.6)	9 (1.0)
尿中白血球陽性	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	1 (0.6)	3 (0.3)
代謝および栄養障害	8 (1.4)	2 (0.9)	10 (1.8)	0	0	2 (1.5)	2 (1.1)	14 (1.6)
脂質異常症	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
高コレステロール血症	3 (0.5)	1 (0.5)	4 (0.7)	0	0	1 (0.7)	1 (0.6)	6 (0.7)
高血糖	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
高脂血症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
代謝および栄養障害 (Cont.)								
低リン酸血症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
低蛋白血症	0	0	0	0	0	1 (0.7)	0	1 (0.1)
肥満	0	0	0	0	0	0	1 (0.6)	1 (0.1)
筋骨格系および結合組織障害	14 (2.5)	6 (2.7)	20 (3.6)	0	0	3 (2.2)	2 (1.1)	25 (2.9)
関節痛	3 (0.5)	3 (1.4)	6 (1.1)	0	0	1 (0.7)	0	7 (0.8)
関節障害	2 (0.4)	0	2 (0.4)	0	0	1 (0.7)	0	3 (0.3)
背部痛	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
指炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
筋拘縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
筋痙縮	0	0	0	0	0	1 (0.7)	0	1 (0.1)
筋骨格系胸痛	0	0	0	0	0	1 (0.7)	0	1 (0.1)
筋骨格痛	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
筋骨格系および結合組織障害 (Cont.)								
筋骨格硬直	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
筋肉痛	3 (0.5)	2 (0.9)	5 (0.9)	0	0	0	1 (0.6)	6 (0.7)
四肢痛	1 (0.2)	0	1 (0.2)	0	0	0	2 (1.1)	3 (0.3)
顎痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
関節周囲炎	0	0	0	0	0	1 (0.7)	0	1 (0.1)
横紋筋融解症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
腱炎	0	0	0	0	0	1 (0.7)	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）	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	1 (0.6)	4 (0.5)
基底細胞癌	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
ボーエン病	0	0	0	0	0	0	1 (0.6)	1 (0.1)
皮膚乳頭腫	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
皮膚有棘細胞癌	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
神経系障害	8 (1.4)	2 (0.9)	10 (1.8)	0	0	1 (0.7)	1 (0.6)	12 (1.4)
灼熱感	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
構語障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
頭痛	5 (0.9)	1 (0.5)	6 (1.1)	0	0	1 (0.7)	1 (0.6)	8 (0.9)
知覚過敏	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
片頭痛	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
視野欠損	0	0	0	0	0	0	1 (0.6)	1 (0.1)
精神障害	2 (0.4)	0	2 (0.4)	1 (2.8)	0	0	1 (0.6)	3 (0.3)
不安	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
うつ病	0	0	0	0	0	0	1 (0.6)	1 (0.1)
睡眠障害	0	0	0	1 (2.8)	0	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
腎および尿路障害	7 (1.2)	4 (1.8)	10 (1.8)	1 (2.8)	0	0	2 (1.1)	12 (1.4)
急性腎障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
排尿困難	1 (0.2)	2 (0.9)	2 (0.4)	0	0	0	0	2 (0.2)
血尿	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
ケトン尿	0	0	0	1 (2.8)	0	0	0	0
腎結石症	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
蛋白尿	2 (0.4)	1 (0.5)	3 (0.5)	1 (2.8)	0	0	2 (1.1)	5 (0.6)
腎機能障害	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)
生殖系および乳房障害	5 (0.9)	4 (1.8)	9 (1.6)	0	0	0	0	9 (1.0)
良性前立腺肥大症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
勃起不全	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
性器びらん	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
不規則月経	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
生殖系および乳房障害 (Cont.)								
前立腺炎	1 (0.2)	2 (0.9)	3 (0.5)	0	0	0	0	3 (0.3)
精液変色	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
外陰腟そう痒症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
呼吸器、胸郭および縦隔障害	13 (2.3)	4 (1.8)	17 (3.0)	0	0	0	2 (1.1)	19 (2.2)
咳嗽	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
鼻出血	0	0	0	0	0	0	1 (0.6)	1 (0.1)
鼻閉	0	2 (0.9)	2 (0.4)	0	0	0	0	2 (0.2)
口腔咽頭痛	7 (1.2)	0	7 (1.2)	0	0	0	0	7 (0.8)
湿性咳嗽	0	0	0	0	0	0	1 (0.6)	1 (0.1)
肺塞栓症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
アレルギー性鼻炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
鼻漏	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	SA 1 Population Total (N=562) n (%)	SA 2 Population Placebo (N=36) n (%)	SA 2 Population UPA 7.5 mg QD (N=1) n (%)	SA 2 Population UPA 15 mg QD (N=136) n (%)	SA 2 Population UPA 30 mg QD (N=178) n (%)	SA UPA All UPA (N=877) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)								
副鼻腔うっ血	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
上気道咳症候群	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
皮膚および皮下組織障害	19 (3.4)	14 (6.3)	33 (5.9)	0	0	2 (1.5)	7 (3.9)	42 (4.8)
ざ瘡	2 (0.4)	3 (1.4)	5 (0.9)	0	0	2 (1.5)	1 (0.6)	8 (0.9)
嚢胞性ざ瘡	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
脱毛症	3 (0.5)	2 (0.9)	5 (0.9)	0	0	0	0	5 (0.6)
アレルギー性皮膚炎	0	0	0	0	0	0	1 (0.6)	1 (0.1)
剥脱性皮膚炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
皮膚乾燥	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
湿疹	0	1 (0.5)	1 (0.2)	0	0	0	1 (0.6)	2 (0.2)
紅斑	0	0	0	0	0	0	1 (0.6)	1 (0.1)
環状紅斑	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
皮膚および皮下組織障害 (Cont.)								
丘疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
そう痒症	2 (0.4)	2 (0.9)	4 (0.7)	0	0	0	0	4 (0.5)
発疹	6 (1.1)	2 (0.9)	8 (1.4)	0	0	0	2 (1.1)	10 (1.1)
紅斑性皮疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
毛孔性皮疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
斑状皮疹	0	0	0	0	0	0	1 (0.6)	1 (0.1)
丘疹性皮疹	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
そう痒性皮疹	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
酒さ	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
脂漏性皮膚炎	0	1 (0.5)	1 (0.2)	0	0	0	0	1 (0.1)
皮膚剥脱	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
皮膚病変	2 (0.4)	0	2 (0.4)	0	0	0	0	2 (0.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=222) n (%)	Total (N=562) n (%)	Placebo (N=36) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=136) n (%)	UPA 30 mg QD (N=178) n (%)	All UPA (N=877) n (%)
血管障害	7 (1.2)	2 (0.9)	9 (1.6)	0	0	0	0	9 (1.0)
深部静脈血栓症	1 (0.2)	1 (0.5)	2 (0.4)	0	0	0	0	2 (0.2)
ほてり	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
高血圧	2 (0.4)	1 (0.5)	3 (0.5)	0	0	0	0	3 (0.3)
高血圧クリーゼ	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
レイノー現象	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)
静脈血栓症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (0.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表6

[redacted]20[redacted] 14:27 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/0544 - CLINICAL/STATISTICAL

TABLE 14.3__1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All_UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
Any adverse event	426 (64.5)	177 (71.8)	603 (66.5)	21 (103.4)	0	58 (54.5)	85 (76.4)	746 (66.2)
血液およびリンパ系障害	26 (3.9)	10 (4.1)	36 (4.0)	4 (19.7)	0	7 (6.6)	9 (8.1)	52 (4.6)
貧血	6 (0.9)	0	6 (0.7)	1 (4.9)	0	1 (0.9)	2 (1.8)	9 (0.8)
周期性好中球減少症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
鉄欠乏性貧血	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
白血球増加症	0	1 (0.4)	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
白血球減少症	5 (0.8)	1 (0.4)	6 (0.7)	1 (4.9)	0	2 (1.9)	4 (3.6)	12 (1.1)
リンパ球減少症	6 (0.9)	4 (1.6)	10 (1.1)	0	0	1 (0.9)	1 (0.9)	12 (1.1)
好中球減少症	8 (1.2)	3 (1.2)	11 (1.2)	2 (9.9)	0	1 (0.9)	1 (0.9)	13 (1.2)
汎血球減少症	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
網状赤血球増加症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
心臓障害	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
第一度房室ブロック	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
動悸	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頻脈	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
耳および迷路障害	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	1 (0.9)	6 (0.5)
耳痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
外耳の炎症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
内耳障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
メニエール病	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
耳鳴	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
回転性めまい	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
内分泌障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
クッシング様症状	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
眼障害	0	1 (0.4)	1 (0.1)	1 (4.9)	0	0	0	1 (<0.1)
眼精疲労	0	0	0	1 (4.9)	0	0	0	0
眼瞼炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
胃腸障害	35 (5.3)	16 (6.5)	51 (5.6)	5 (24.6)	0	5 (4.7)	5 (4.5)	61 (5.4)
腹部膨満	1 (0.2)	0	1 (0.1)	1 (4.9)	0	0	0	1 (<0.1)
腹痛	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
下腹部痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腹部圧痛	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
口角口唇炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
アフタ性潰瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
大腸炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
潰瘍性大腸炎	13 (2.0)	8 (3.2)	21 (2.3)	2 (9.9)	0	2 (1.9)	1 (0.9)	24 (2.1)
結腸異形成	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
便秘	0	1 (0.4)	1 (0.1)	0	0	2 (1.9)	1 (0.9)	4 (0.4)
便意切迫	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
下痢	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	0	4 (0.4)
鼓腸	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
胃炎	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
胃食道逆流性疾患	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
痔核	2 (0.3)	0	2 (0.2)	0	0	0	1 (0.9)	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
腸閉塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
口腔内潰瘍形成	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
悪心	4 (0.6)	0	4 (0.4)	1 (4.9)	0	0	0	4 (0.4)
膵炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
直腸出血	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
口内炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
嘔吐	2 (0.3)	0	2 (0.2)	1 (4.9)	0	0	1 (0.9)	3 (0.3)
一般・全身障害および投与部位の状態	16 (2.4)	7 (2.8)	23 (2.5)	0	0	1 (0.9)	3 (2.7)	27 (2.4)
無力症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
悪寒	1 (0.2)	1 (0.4)	2 (0.2)	0	0	1 (0.9)	1 (0.9)	4 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
疲労	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
治癒不良	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
インフルエンザ様疾患	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
倦怠感	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
疼痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
末梢腫脹	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
発熱	4 (0.6)	5 (2.0)	9 (1.0)	0	0	0	0	9 (0.8)
肝胆道系障害	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	0	4 (0.4)
硬化性胆管炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脂肪肝	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肝障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
肝胆道系障害 (Cont.)								
非アルコール性脂肪性肝疾患	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
免疫系障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
過敏症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
感染症および寄生虫症	155 (23.5)	58 (23.5)	213 (23.5)	6 (29.6)	0	20 (18.8)	16 (14.4)	249 (22.1)
腹壁膿瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肛門膿瘍	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
無症候性COVID-19	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
細菌感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
細菌性膣症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
気管支炎	7 (1.1)	2 (0.8)	9 (1.0)	0	0	1 (0.9)	0	10 (0.9)
COVID-19	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
COVID-19肺炎	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	1 (0.9)	3 (0.3)
カンジダ感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
蜂巣炎	1 (0.2)	0	1 (0.1)	0	0	4 (3.8)	0	5 (0.4)
感染性胆嚢炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
クロストリジウム・ディフィシレ感染	4 (0.6)	1 (0.4)	5 (0.6)	0	0	0	1 (0.9)	6 (0.5)
結膜炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
ウイルス性結膜炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
毛嚢虫症	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	1 (0.9)	4 (0.4)
爪の皮膚糸状菌症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
感染性下痢	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
耳感染	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
丹毒	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
眼感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
毛包炎	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
せつ	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
胃腸炎	0	2 (0.8)	2 (0.2)	1 (4.9)	0	0	0	2 (0.2)
ウイルス性胃腸炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
性器カンジダ症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
陰部ヘルペス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
陰部単純ヘルペス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
歯肉炎	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
単径部膿瘍	1 (0.2)	0	1 (0.1)	1 (4.9)	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
単純ヘルペス	5 (0.8)	1 (0.4)	6 (0.7)	0	0	0	0	6 (0.5)
単純ヘルペス性咽頭炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
帯状疱疹	22 (3.3)	8 (3.2)	30 (3.3)	2 (9.9)	0	3 (2.8)	4 (3.6)	37 (3.3)
耳帯状疱疹	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
麦粒腫	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
伝染性単核症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
インフルエンザ	5 (0.8)	1 (0.4)	6 (0.7)	1 (4.9)	0	0	0	6 (0.5)
潜伏結核	3 (0.5)	0	3 (0.3)	0	0	0	1 (0.9)	4 (0.4)
限局性感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
下気道感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
上咽頭炎	10 (1.5)	9 (3.7)	19 (2.1)	0	0	2 (1.9)	1 (0.9)	22 (2.0)

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
爪真菌症	2 (0.3)	0	2 (0.2)	0	0	2 (1.9)	0	4 (0.4)
口腔カンジダ症	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
口腔ヘルペス	8 (1.2)	5 (2.0)	13 (1.4)	1 (4.9)	0	0	1 (0.9)	14 (1.2)
直腸周囲膿瘍	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
咽頭炎	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
肺炎	5 (0.8)	3 (1.2)	8 (0.9)	0	0	0	0	8 (0.7)
膿疱	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腎盂腎炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
気道感染	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
鼻炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
根管感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
敗血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
副鼻腔炎	6 (0.9)	1 (0.4)	7 (0.8)	0	0	0	0	7 (0.6)
皮膚感染	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
足部白癬	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
扁桃炎	0	1 (0.4)	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
歯膿瘍	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
歯感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
結核	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
上気道感染	31 (4.7)	7 (2.8)	38 (4.2)	0	0	1 (0.9)	0	39 (3.5)
尿路感染	9 (1.4)	0	9 (1.0)	0	0	2 (1.9)	0	11 (1.0)
腟感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
水痘	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ウイルス性上気道感染	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
外陰部腟カンジダ症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
外陰腟真菌感染	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
傷害、中毒および処置合併症	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	0	4 (0.4)
筋断裂	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
皮膚裂傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮下血腫	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
臨床検査	89 (13.5)	28 (11.4)	117 (12.9)	2 (9.9)	0	12 (11.3)	30 (27.0)	159 (14.1)
アラニンアミノトランスフェラーゼ増加	8 (1.2)	2 (0.8)	10 (1.1)	0	0	0	0	10 (0.9)
アスパラギン酸アミノトランスフェラーゼ増加	7 (1.1)	3 (1.2)	10 (1.1)	0	0	0	1 (0.9)	11 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
血中アルカリホスファターゼ増加	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
血中ビリルビン増加	1 (0.2)	0	1 (0.1)	0	0	0	2 (1.8)	3 (0.3)
血中コレステロール増加	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
血中クレアチンホスホキナーゼ増加	25 (3.8)	14 (5.7)	39 (4.3)	1 (4.9)	0	1 (0.9)	6 (5.4)	46 (4.1)
血中クレアチニン増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中葉酸減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血圧上昇	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
血中トリグリセリド増加	3 (0.5)	0	3 (0.3)	0	0	0	1 (0.9)	4 (0.4)
凝固時間延長	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
γ-グルタミルトランスフェラーゼ増加	2 (0.3)	0	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
ヘマトクリット減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
ヘモグロビン減少	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	1 (0.9)	4 (0.4)
肝酵素上昇	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
高比重リポ蛋白増加	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
臨床検査異常	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肝機能検査異常	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肝機能検査値上昇	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
低比重リポ蛋白増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
リンパ球数減少	5 (0.8)	2 (0.8)	7 (0.8)	0	0	2 (1.9)	3 (2.7)	12 (1.1)
リンパ球百分率減少	0	0	0	0	0	0	2 (1.8)	2 (0.2)
好中球数減少	6 (0.9)	0	6 (0.7)	0	0	4 (3.8)	3 (2.7)	13 (1.2)
好中球数増加	2 (0.3)	0	2 (0.2)	0	0	2 (1.9)	1 (0.9)	5 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
臨床検査 (Cont.)								
血小板数減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血小板数増加	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
赤血球数減少	2 (0.3)	0	2 (0.2)	0	0	0	1 (0.9)	3 (0.3)
網状赤血球数増加	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
トランスアミナーゼ上昇	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
尿中ケトン体陽性	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
尿中白血球エステラーゼ陽性	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
体重増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
白血球数減少	6 (0.9)	0	6 (0.7)	1 (4.9)	0	3 (2.8)	1 (0.9)	10 (0.9)
尿中白血球陽性	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	1 (0.9)	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
代謝および栄養障害	8 (1.2)	3 (1.2)	11 (1.2)	0	0	2 (1.9)	2 (1.8)	15 (1.3)
脂質異常症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
高コレステロール血症	3 (0.5)	1 (0.4)	4 (0.4)	0	0	1 (0.9)	1 (0.9)	6 (0.5)
高血糖	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
高脂血症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
低リン酸血症	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (0.3)
低蛋白血症	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
肥満	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
筋骨格系および結合組織障害	14 (2.1)	9 (3.7)	23 (2.5)	0	0	7 (6.6)	3 (2.7)	33 (2.9)
関節痛	3 (0.5)	3 (1.2)	6 (0.7)	0	0	1 (0.9)	0	7 (0.6)
関節障害	2 (0.3)	0	2 (0.2)	0	0	1 (0.9)	0	3 (0.3)
背部痛	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
指炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
筋拘縮	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
筋痙縮	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
筋骨格系胸痛	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
筋骨格痛	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
筋骨格硬直	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
筋肉痛	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	1 (0.9)	6 (0.5)
四肢痛	1 (0.2)	0	1 (0.1)	0	0	0	2 (1.8)	3 (0.3)
顎痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
関節周囲炎	0	0	0	0	0	2 (1.9)	0	2 (0.2)
横紋筋融解症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
腱炎	0	0	0	0	0	1 (0.9)	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）	1 (0.2)	3 (1.2)	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
基底細胞癌	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
ボーエン病	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
皮膚乳頭腫	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚有棘細胞癌	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
神経系障害	10 (1.5)	2 (0.8)	12 (1.3)	0	0	2 (1.9)	2 (1.8)	16 (1.4)
灼熱感	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
構語障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頭痛	6 (0.9)	1 (0.4)	7 (0.8)	0	0	2 (1.9)	1 (0.9)	10 (0.9)
知覚過敏	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
神経系障害 (Cont.)								
片頭痛	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
視野欠損	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
精神障害	2 (0.3)	0	2 (0.2)	1 (4.9)	0	0	1 (0.9)	3 (0.3)
不安	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
うつ病	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
睡眠障害	0	0	0	1 (4.9)	0	0	0	0
腎および尿路障害	8 (1.2)	4 (1.6)	12 (1.3)	2 (9.9)	0	0	2 (1.8)	14 (1.2)
急性腎障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
排尿困難	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	0	4 (0.4)
血尿	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ケトン尿	0	0	0	1 (4.9)	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
腎および尿路障害 (Cont.)								
腎結石症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
蛋白尿	2 (0.3)	1 (0.4)	3 (0.3)	1 (4.9)	0	0	2 (1.8)	5 (0.4)
腎機能障害	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
生殖系および乳房障害	5 (0.8)	4 (1.6)	9 (1.0)	0	0	0	0	9 (0.8)
良性前立腺肥大症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
勃起不全	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
性器びらん	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
不規則月経	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
前立腺炎	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (0.3)
精液変色	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
外陰腟そう痒症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害	16 (2.4)	6 (2.4)	22 (2.4)	0	0	0	2 (1.8)	24 (2.1)
咳嗽	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
鼻出血	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
鼻閉	0	3 (1.2)	3 (0.3)	0	0	0	0	3 (0.3)
口腔咽頭痛	7 (1.1)	0	7 (0.8)	0	0	0	0	7 (0.6)
湿性咳嗽	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
肺塞栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
アレルギー性鼻炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
鼻漏	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
副鼻腔うっ血	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	0	4 (0.4)
上気道咳症候群	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
皮膚および皮下組織障害	24 (3.6)	17 (6.9)	41 (4.5)	0	0	2 (1.9)	7 (6.3)	50 (4.4)
ざ瘡	2 (0.3)	3 (1.2)	5 (0.6)	0	0	2 (1.9)	1 (0.9)	8 (0.7)
嚢胞性ざ瘡	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脱毛症	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	0	5 (0.4)
アレルギー性皮膚炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
剥脱性皮膚炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚乾燥	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
湿疹	0	1 (0.4)	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
紅斑	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
環状紅斑	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
丘疹	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
そう痒症	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	0	4 (0.4)
発疹	6 (0.9)	4 (1.6)	10 (1.1)	0	0	0	2 (1.8)	12 (1.1)
紅斑性皮疹	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
毛孔性皮疹	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
斑状皮疹	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
丘疹性皮疹	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
そう痒性皮疹	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
酒さ	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
脂漏性皮膚炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚剥脱	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚病変	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
血管障害	7 (1.1)	2 (0.8)	9 (1.0)	0	0	0	0	9 (0.8)
深部静脈血栓症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
ほてり	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
高血圧	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
高血圧クリーゼ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
レイノー現象	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
静脈血栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3__1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All_UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
Any adverse event	56 (8.5)	28 (11.4)	84 (9.3)	2 (9.9)	0	11 (10.3)	10 (9.0)	105 (9.3)
血液およびリンパ系障害	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
リンパ球減少症	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
好中球減少症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
心臓障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
心房細動	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
耳および迷路障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
突発性難聴	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
胃腸障害	19 (2.9)	5 (2.0)	24 (2.6)	1 (4.9)	0	1 (0.9)	0	25 (2.2)
腹痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
裂肛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
潰瘍性大腸炎	15 (2.3)	3 (1.2)	18 (2.0)	1 (4.9)	0	1 (0.9)	0	19 (1.7)
結腸異形成	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
膵炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
一般・全身障害および投与部位の状態	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
疲労	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
疼痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
発熱	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
感染症および寄生虫症	7 (1.1)	12 (4.9)	19 (2.1)	1 (4.9)	0	4 (3.8)	3 (2.7)	26 (2.3)
COVID-19	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
COVID-19肺炎	0	2 (0.8)	2 (0.2)	0	0	2 (1.9)	1 (0.9)	5 (0.4)
蜂巣炎	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
感染性胆嚢炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
クロストリジウム・ディフィシレ感染	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
医療機器関連敗血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸菌感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸菌性敗血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
消化管感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
帯状疱疹	1 (0.2)	1 (0.4)	2 (0.2)	1 (4.9)	0	0	1 (0.9)	3 (0.3)
耳帯状疱疹	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
毛巣嚢胞	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
肺炎	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
細菌性肺炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ウイルス性肺炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
敗血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
傷害、中毒および処置合併症	5 (0.8)	0	5 (0.6)	0	0	2 (1.9)	0	7 (0.6)
腓骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
企図的過量投与	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
処置による腸管穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肋骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脛骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
子宮穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
創傷	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
臨床検査	4 (0.6)	0	4 (0.4)	0	0	1 (0.9)	2 (1.8)	7 (0.6)
血中クレアチンホスホキナーゼ増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血中トリグリセリド増加	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肝酵素上昇	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
肝機能検査値上昇	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
リンパ球数減少	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
好中球数減少	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (0.2)
代謝および栄養障害	2 (0.3)	2 (0.8)	4 (0.4)	0	0	0	0	4 (0.4)
高血糖	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
低リン酸血症	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
過少体重	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
筋骨格系および結合組織障害	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	1 (0.9)	5 (0.4)
関節痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
背部痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
滑液包炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
四肢痛	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肩回旋筋腱板症候群	1 (0.2)	0	1 (0.1)	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）	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	2 (1.8)	4 (0.4)
膵腺癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
子宮頚部扁平上皮癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
精巣（純粋）セミノーマ	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) 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.)								
精巣癌	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
神経系障害	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	0	5 (0.4)
脳損傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頭痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
片頭痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
神経炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
坐骨神経痛	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
精神障害	1 (0.2)	0	1 (0.1)	0	0	3 (2.8)	1 (0.9)	5 (0.4)
不安	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
うつ病	0	0	0	0	0	1 (0.9)	1 (0.9)	2 (0.2)
自殺念慮	0	0	0	0	0	1 (0.9)	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
精神障害 (Cont.)								
自殺企図	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腎および尿路障害	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (0.3)
排尿困難	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腎結石症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
尿管結石症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
生殖系および乳房障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
子宮頚部の炎症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	2 (0.3)	1 (0.4)	3 (0.3)	0	0	0	0	3 (0.3)
喘息	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肺塞栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
睡眠時無呼吸症候群	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.3

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
皮膚および皮下組織障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ざ瘡	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
血管障害	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
深部静脈血栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
静脈血栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表8

[redacted]20[redacted] 14:27 [redacted]

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

TABLE 14.3__2.3.1

Treatment-Emergent Adverse Events Leading to Death per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All_UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
Any adverse event	1 (0.2)	0	1 (0.1)	0	0	0	1 (0.9)	2 (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	0	0	0	0	1 (0.9)	1 (<0.1)
膵腺癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
神経系障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脳損傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表9

[redacted]20[redacted] 14:27 [redacted]

UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-533 (CUTOFF [redacted]20[redacted])
R&D/21/0544 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 11

TABLE 14.3__2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All_UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
Any adverse event	85 (12.9)	47 (19.1)	132 (14.6)	2 (9.9)	0	11 (10.3)	12 (10.8)	155 (13.8)
心臓障害	5 (0.8)	0	5 (0.6)	0	0	0	0	5 (0.4)
不安定狭心症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
心房細動	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
心筋梗塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
心室性頻脈	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
胃腸障害	20 (3.0)	8 (3.2)	28 (3.1)	0	0	0	0	28 (2.5)
腹痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
裂肛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
潰瘍性大腸炎	9 (1.4)	6 (2.4)	15 (1.7)	0	0	0	0	15 (1.3)
下痢	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
胃食道逆流性疾患	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
イレウス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
鼠径ヘルニア	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
腸閉塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
大腸穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	3 (0.5)	0	3 (0.3)	0	0	0	0	3 (0.3)
悪心	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
嘔吐	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
一般・全身障害および投与部位の状態	5 (0.8)	0	5 (0.6)	0	0	0	0	5 (0.4)
胸痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
異形成	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
疲労	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
倦怠感	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
疼痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
感染症および寄生虫症	15 (2.3)	16 (6.5)	31 (3.4)	2 (9.9)	0	5 (4.7)	7 (6.3)	43 (3.8)
肛門膿瘍	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
虫垂炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
気管支炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
COVID-19	1 (0.2)	0	1 (0.1)	0	0	0	2 (1.8)	3 (0.3)
COVID-19肺炎	1 (0.2)	2 (0.8)	3 (0.3)	0	0	3 (2.8)	2 (1.8)	8 (0.7)
蜂巣炎	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
感染性胆嚢炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) 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	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
医療機器関連敗血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸菌感染	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸菌性敗血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
胃腸炎	1 (0.2)	3 (1.2)	4 (0.4)	1 (4.9)	0	0	0	4 (0.4)
消化管感染	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ヘリコバクター性胃炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
帯状疱疹	2 (0.3)	1 (0.4)	3 (0.3)	1 (4.9)	0	0	1 (0.9)	4 (0.4)
耳帯状疱疹	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
伝染性単核症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
精巣炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
毛巣嚢胞	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肺炎	4 (0.6)	0	4 (0.4)	0	0	0	0	4 (0.4)
細菌性肺炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ウイルス性肺炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腎盂腎炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
敗血症	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
傷害、中毒および処置合併症	9 (1.4)	1 (0.4)	10 (1.1)	0	0	1 (0.9)	0	11 (1.0)
挫傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腓骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
企図的過量投与	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
過量投与	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
処置後出血	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
術後イレウス	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
処置による腸管穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肋骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腱断裂	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脛骨骨折	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
子宮穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
代謝および栄養障害	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
低リン酸血症	0	2 (0.8)	2 (0.2)	0	0	0	0	2 (0.2)
筋骨格系および結合組織障害	7 (1.1)	4 (1.6)	11 (1.2)	0	0	0	1 (0.9)	12 (1.1)
背部痛	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
滑液包炎	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
椎間板障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
椎間板突出	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腰部脊柱管狭窄症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
骨壊死	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
四肢痛	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
横紋筋融解症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肩回旋筋腱板症候群	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
脊柱変形	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
変形性脊椎症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) 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）	2 (0.3)	3 (1.2)	5 (0.6)	0	0	2 (1.9)	2 (1.8)	9 (0.8)
結腸腺癌	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
膵腺癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
基底細胞癌	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
前立腺癌	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
子宮頚部扁平上皮癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
精巣（純粋）セミノーマ	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
精巣癌	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
甲状腺腺腫	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
子宮平滑筋腫	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
神経系障害	5 (0.8)	5 (2.0)	10 (1.1)	0	0	0	0	10 (0.9)
健忘	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
神経系障害 (Cont.)								
脳損傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
手根管症候群	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
構語障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頭痛	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
ラクナ梗塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
片頭痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
発作様現象	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
失神	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
精神障害	2 (0.3)	0	2 (0.2)	0	0	3 (2.8)	2 (1.8)	7 (0.6)
不安	0	0	0	0	0	1 (0.9)	1 (0.9)	2 (0.2)
うつ病	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	1 (0.9)	3 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
精神障害 (Cont.)								
自殺念慮	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
自殺企図	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
腎および尿路障害	6 (0.9)	5 (2.0)	11 (1.2)	0	0	0	0	11 (1.0)
膀胱タンポナーデ	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
尿路結石	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
腎結石症	3 (0.5)	2 (0.8)	5 (0.6)	0	0	0	0	5 (0.4)
腎仙痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
尿管閉塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
尿管結石症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
生殖系および乳房障害	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	0	3 (0.3)
子宮頚部障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)								
子宮頚部の炎症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
前立腺炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	5 (0.8)	0	5 (0.6)	0	0	0	0	5 (0.4)
喘息	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
口腔咽頭痛	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肺塞栓症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
肺腫瘤	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血管障害	3 (0.5)	1 (0.4)	4 (0.4)	0	0	0	0	4 (0.4)
深部静脈血栓症	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
静脈瘤	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
静脈血栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表10

[redacted]20[redacted] 14:27 [redacted]

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

TABLE 14.3__2.2.1

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All_UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
Any adverse event	30 (4.5)	26 (10.5)	56 (6.2)	2 (9.9)	0	6 (5.6)	3 (2.7)	65 (5.8)
血液およびリンパ系障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
リンパ球減少症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
胃腸障害	14 (2.1)	13 (5.3)	27 (3.0)	2 (9.9)	0	4 (3.8)	0	31 (2.8)
腹痛	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
潰瘍性大腸炎	12 (1.8)	9 (3.7)	21 (2.3)	2 (9.9)	0	2 (1.9)	0	23 (2.0)
結腸異形成	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
クローン病	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
悪心	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
膵炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.2.1

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
胃腸障害 (Cont.)								
直腸異形成	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
一般・全身障害および投与部位の状態	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
異形成	1 (0.2)	0	1 (0.1)	0	0	1 (0.9)	0	2 (0.2)
肝胆道系障害	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
硬化性胆管炎	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肝機能異常	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
感染症および寄生虫症	1 (0.2)	2 (0.8)	3 (0.3)	0	0	0	1 (0.9)	4 (0.4)
クロストリジウム・ディフィシレ感染	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
帯状疱疹	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
肺炎	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
結核	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.2.1

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	SA 1 Population Total (N=562) (PYs=906.8) Events (E/100 PYs)	SA 2 Population Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	SA UPA All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
傷害、中毒および処置合併症	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
処置による腸管穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
子宮穿孔	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
臨床検査	2 (0.3)	3 (1.2)	5 (0.6)	0	0	0	0	5 (0.4)
アラニンアミノトランスフェラーゼ増加	1 (0.2)	1 (0.4)	2 (0.2)	0	0	0	0	2 (0.2)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
血中クレアチンホスホキナーゼ増加	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
B型肝炎DNA測定陽性	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
代謝および栄養障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
低リン酸血症	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.2.1

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
筋骨格系および結合組織障害	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
横紋筋融解症	0	1 (0.4)	1 (0.1)	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）	2 (0.3)	2 (0.8)	4 (0.4)	0	0	1 (0.9)	2 (1.8)	7 (0.6)
結腸腺癌	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
膵腺癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
喉頭扁平上皮癌	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
前立腺癌	0	0	0	0	0	1 (0.9)	0	1 (<0.1)
子宮頚部扁平上皮癌	0	0	0	0	0	0	1 (0.9)	1 (<0.1)
精巣（純粋）セミノーマ	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
精巣癌	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
神経系障害	2 (0.3)	3 (1.2)	5 (0.6)	0	0	0	0	5 (0.4)
健忘	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.2.1

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=562) (PYs=660.4) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=222) (PYs=246.5) Events (E/100 PYs)	Total (N=562) (PYs=906.8) Events (E/100 PYs)	Placebo (N=36) (PYs=20.3) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.2) Events (E/100 PYs)	UPA 15 mg QD (N=136) (PYs=106.4) Events (E/100 PYs)	UPA 30 mg QD (N=178) (PYs=111.3) Events (E/100 PYs)	All UPA (N=877) (PYs=1126.7) Events (E/100 PYs)
神経系障害 (Cont.)								
脳損傷	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
頭痛	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
ラクナ梗塞	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
発作様現象	0	1 (0.4)	1 (0.1)	0	0	0	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
肺塞栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
皮膚および皮下組織障害	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
ざ瘡	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
血管障害	2 (0.3)	0	2 (0.2)	0	0	0	0	2 (0.2)
深部静脈血栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)
静脈血栓症	1 (0.2)	0	1 (0.1)	0	0	0	0	1 (<0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表11

[redacted]20[redacted] 09:26 [redacted]

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

TABLE 14.3__1.1.1_J

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All_UPA (N=112) n (%)
Subjects with:								
Any adverse event (AE)	42 (71.2)	10 (55.6)	46 (78.0)	5 (71.4)	0	12 (50.0)	17 (58.6)	75 (67.0)
Any AE with reasonable possibility of being related to study drug$	22 (37.3)	6 (33.3)	28 (47.5)	2 (28.6)	0	3 (12.5)	7 (24.1)	38 (33.9)
Any severe AE	3 (5.1)	1 (5.6)	4 (6.8)	2 (28.6)	0	0	2 (6.9)	6 (5.4)
Any serious AE	6 (10.2)	1 (5.6)	7 (11.9)	1 (14.3)	0	0	1 (3.4)	8 (7.1)
Any AE leading to discontinuation of study drug	2 (3.4)	2 (11.1)	4 (6.8)	1 (14.3)	0	0	0	4 (3.6)
Any AE leading to death	0	0	0	0	0	0	0	0
Deaths#	0	0	0	0	0	0	0	0
Occurring <= 30 days after last dose	0	0	0	0	0	0	0	0
Occurring > 30 days after last dose	0	0	0	0	0	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.
Includes non treatment emergent deaths.
$ As assessed by investigator.

Program Source Code: [redacted]

表12

[redacted]20[redacted] 09:26 [redacted]

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

TABLE 14.3__1.1.2_J

Overview of Treatment-Emergent Adverse Events and All Deaths per 100 Patient-Years (PYs)
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All_UPA (N=112) (PYs=153.4) Events (E/100 PYs)
Any treatment-emergent:								
Any adverse event (AE)	258 (269.6)	69 (367.0)	327 (285.6)	6 (176.5)	0	30 (144.2)	41 (226.5)	398 (259.5)
Any AE with reasonable possibility of being related to study drug$	62 (64.8)	15 (79.8)	77 (67.2)	3 (88.2)	0	9 (43.3)	9 (49.7)	95 (61.9)
Any severe AE	3 (3.1)	1 (5.3)	4 (3.5)	2 (58.8)	0	0	2 (11.0)	6 (3.9)
Any serious AE	14 (14.6)	3 (16.0)	17 (14.8)	1 (29.4)	0	0	1 (5.5)	18 (11.7)
Any AE leading to discontinuation of study drug	2 (2.1)	2 (10.6)	4 (3.5)	1 (29.4)	0	0	0	4 (2.6)
Any AE leading to death	0	0	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 = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.
Includes non treatment emergent deaths.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 14.3 1.1.2 J

Overview of Treatment-Emergent Adverse Events and All Deaths per 100 Patient-Years (PYs)
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
Deaths#	0	0	0	0	0	0	0	0
Occurring <= 30 days after last dose	0	0	0	0	0	0	0	0
Occurring > 30 days after last dose	0	0	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 = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.
Includes non treatment emergent deaths.
$ As assessed by investigator.

Program Source Code: [redacted]

表13

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

TABLE 14.3__1.2.1.1_J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All_UPA (N=112) n (%)
Any adverse event	42 (71.2)	10 (55.6)	46 (78.0)	5 (71.4)	0	12 (50.0)	17 (58.6)	75 (67.0)
血液およびリンパ系障害	6 (10.2)	0	6 (10.2)	0	0	3 (12.5)	2 (6.9)	11 (9.8)
貧血	1 (1.7)	0	1 (1.7)	0	0	1 (4.2)	0	2 (1.8)
鉄欠乏性貧血	1 (1.7)	0	1 (1.7)	0	0	1 (4.2)	0	2 (1.8)
白血球減少症	2 (3.4)	0	2 (3.4)	0	0	1 (4.2)	1 (3.4)	4 (3.6)
リンパ節症	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
リンパ球減少症	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
好中球減少症	3 (5.1)	0	3 (5.1)	0	0	0	2 (6.9)	5 (4.5)
心臓障害	1 (1.7)	0	1 (1.7)	0	0	0	2 (6.9)	3 (2.7)
上室性期外収縮	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
心室性期外収縮	0	0	0	0	0	0	2 (6.9)	2 (1.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
先天性、家族性および遺伝性障害	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
歯原性嚢胞	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
耳および迷路障害	0	1 (5.6)	1 (1.7)	0	0	1 (4.2)	2 (6.9)	4 (3.6)
メニエール病	0	0	0	0	0	0	1 (3.4)	1 (0.9)
耳鳴	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
回転性めまい	0	0	0	0	0	1 (4.2)	1 (3.4)	2 (1.8)
内分泌障害	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
副腎機能不全	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
甲状腺腫	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
眼障害	7 (11.9)	0	7 (11.9)	1 (14.3)	0	0	0	7 (6.3)
白内障	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
結膜嚢胞	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
結膜出血	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=59) n (%)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	SA 1 Population Total (N=59) n (%)	SA 2 Population Placebo (N=7) n (%)	SA 2 Population UPA 7.5 mg QD (N=0) n (%)	SA 2 Population UPA 15 mg QD (N=24) n (%)	SA 2 Population UPA 30 mg QD (N=29) n (%)	SA UPA All UPA (N=112) n (%)
眼障害 (Cont.)								
アレルギー性結膜炎	1 (1.7)	0	1 (1.7)	1 (14.3)	0	0	0	1 (0.9)
ドライアイ	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
眼充血	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
硝子体浮遊物	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
胃腸障害	18 (30.5)	5 (27.8)	23 (39.0)	1 (14.3)	0	3 (12.5)	2 (6.9)	28 (25.0)
腹部膨満	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
腹痛	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
下腹部痛	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
上腹部痛	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
口角口唇炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
アフタ性潰瘍	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
潰瘍性大腸炎	2 (3.4)	1 (5.6)	3 (5.1)	1 (14.3)	0	1 (4.2)	1 (3.4)	5 (4.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
胃腸障害 (Cont.)								
便秘	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
齲歯	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
消化不良	2 (3.4)	1 (5.6)	3 (5.1)	0	0	0	0	3 (2.7)
腸炎	1 (1.7)	0	1 (1.7)	0	0	0	1 (3.4)	2 (1.8)
胃ポリープ	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
胃炎	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
胃食道逆流性疾患	1 (1.7)	0	1 (1.7)	0	0	1 (4.2)	0	2 (1.8)
痔核	0	0	0	0	0	1 (4.2)	0	1 (0.9)
腸管ポリープ	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
大腸ポリープ	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
口腔扁平苔癬	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
直腸炎	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
胃腸障害 (Cont.)								
口内炎	3 (5.1)	1 (5.6)	4 (6.8)	0	0	0	0	4 (3.6)
歯痛	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
嘔吐	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
一般・全身障害および投与部位の状態	6 (10.2)	2 (11.1)	7 (11.9)	0	0	0	0	7 (6.3)
胸痛	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
末梢性浮腫	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
発熱	4 (6.8)	1 (5.6)	5 (8.5)	0	0	0	0	5 (4.5)
肝胆道系障害	5 (8.5)	1 (5.6)	6 (10.2)	0	0	0	1 (3.4)	7 (6.3)
肝機能異常	4 (6.8)	1 (5.6)	5 (8.5)	0	0	0	1 (3.4)	6 (5.4)
肝障害	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
免疫系障害	1 (1.7)	0	1 (1.7)	0	0	0	1 (3.4)	2 (1.8)
アナフィラキシー反応	0	0	0	0	0	0	1 (3.4)	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
免疫系障害 (Cont.)								
季節性アレルギー	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
感染症および寄生虫症	30 (50.8)	9 (50.0)	36 (61.0)	1 (14.3)	0	4 (16.7)	8 (27.6)	48 (42.9)
バルトリン腺炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
気管支炎	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
カンピロバクター胃腸炎	1 (1.7)	0	1 (1.7)	0	0	1 (4.2)	1 (3.4)	3 (2.7)
カンジダ感染	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
クロストリジウム・ディフィシレ感染	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
結膜炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
ウイルス性結膜炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
膀胱炎	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
感染性皮膚炎	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
爪の皮膚糸状菌症	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
感染症および寄生虫症 (Cont.)								
感染性腸炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
毛包炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
胃腸炎	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
ウイルス性胃腸炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
歯肉炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
ヘリコバクター感染	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
単純ヘルペス	1 (1.7)	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
帯状疱疹	7 (11.9)	0	7 (11.9)	1 (14.3)	0	0	2 (6.9)	9 (8.0)
麦粒腫	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
インフルエンザ	4 (6.8)	2 (11.1)	6 (10.2)	0	0	0	0	6 (5.4)
クレブシエラ感染	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
大腸感染	0	0	0	0	0	0	1 (3.4)	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
感染症および寄生虫症 (Cont.)								
潜伏結核	1 (1.7)	0	1 (1.7)	0	0	0	1 (3.4)	2 (1.8)
上咽頭炎	18 (30.5)	3 (16.7)	21 (35.6)	0	0	3 (12.5)	2 (6.9)	26 (23.2)
口腔ヘルペス	3 (5.1)	1 (5.6)	4 (6.8)	0	0	0	3 (10.3)	7 (6.3)
歯周炎	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
咽頭炎	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	1 (3.4)	3 (2.7)
肺炎	0	2 (11.1)	2 (3.4)	0	0	0	0	2 (1.8)
歯髄炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
腎盂腎炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
鼻炎	0	0	0	0	0	1 (4.2)	0	1 (0.9)
副鼻腔炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
皮膚感染	1 (1.7)	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
足部白癬	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
感染症および寄生虫症 (Cont.)								
上気道感染	2 (3.4)	1 (5.6)	3 (5.1)	0	0	0	0	3 (2.7)
水痘	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
傷害、中毒および処置合併症	4 (6.8)	2 (11.1)	6 (10.2)	0	0	1 (4.2)	1 (3.4)	8 (7.1)
動物咬傷	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
上顎炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
足骨折	0	1 (5.6)	1 (1.7)	0	0	0	1 (3.4)	2 (1.8)
過量投与	0	0	0	0	0	1 (4.2)	0	1 (0.9)
処置後出血	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
肋骨骨折	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
皮下血腫	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
脛骨骨折	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
臨床検査	11 (18.6)	3 (16.7)	14 (23.7)	0	0	1 (4.2)	3 (10.3)	18 (16.1)
アラニンアミノトランスフェラーゼ増加	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
アスパラギン酸アミノトランスフェラーゼ増加	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
血中クレアチンホスホキナーゼ増加	5 (8.5)	1 (5.6)	6 (10.2)	0	0	0	1 (3.4)	7 (6.3)
心電図異常	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
γ-グルタミルトランスフェラーゼ増加	1 (1.7)	1 (5.6)	2 (3.4)	0	0	1 (4.2)	0	3 (2.7)
高比重リポ蛋白増加	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
リンパ球数減少	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	1 (3.4)	3 (2.7)
好中球数減少	2 (3.4)	0	2 (3.4)	0	0	0	1 (3.4)	3 (2.7)
尿中白血球エステラーゼ陽性	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
白血球数減少	4 (6.8)	0	4 (6.8)	0	0	0	0	4 (3.6)
代謝および栄養障害	7 (11.9)	1 (5.6)	8 (13.6)	0	0	2 (8.3)	2 (6.9)	12 (10.7)
糖尿病	0	0	0	0	0	0	1 (3.4)	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
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The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
代謝および栄養障害 (Cont.)								
脂質異常症	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
高コレステロール血症	4 (6.8)	0	4 (6.8)	0	0	0	1 (3.4)	5 (4.5)
高脂血症	1 (1.7)	0	1 (1.7)	0	0	1 (4.2)	0	2 (1.8)
高尿酸血症	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
低蛋白血症	0	0	0	0	0	1 (4.2)	0	1 (0.9)
筋骨格系および結合組織障害	11 (18.6)	5 (27.8)	14 (23.7)	0	0	5 (20.8)	3 (10.3)	22 (19.6)
関節痛	2 (3.4)	1 (5.6)	3 (5.1)	0	0	1 (4.2)	1 (3.4)	5 (4.5)
関節炎	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
関節障害	0	0	0	0	0	1 (4.2)	0	1 (0.9)
背部痛	3 (5.1)	0	3 (5.1)	0	0	1 (4.2)	0	4 (3.6)
頚部脊柱管狭窄症	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
側腹部痛	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)

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The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
筋骨格系および結合組織障害 (Cont.)								
椎間板突出	3 (5.1)	1 (5.6)	4 (6.8)	0	0	0	1 (3.4)	5 (4.5)
腰部脊柱管狭窄症	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
筋痙縮	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
筋骨格系胸痛	0	0	0	0	0	1 (4.2)	0	1 (0.9)
筋骨格痛	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
筋肉痛	1 (1.7)	0	1 (1.7)	0	0	0	1 (3.4)	2 (1.8)
変形性関節症	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
骨端症	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
骨壊死	0	1 (5.6)	1 (1.7)	0	0	1 (4.2)	0	2 (1.8)
骨粗鬆症	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
四肢痛	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
関節周囲炎	0	0	0	0	0	1 (4.2)	0	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
筋骨格系および結合組織障害 (Cont.)								
横紋筋融解症	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
変形性脊椎症	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
弾発指	0	0	0	0	0	1 (4.2)	0	1 (0.9)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む)	4 (6.8)	0	4 (6.8)	0	0	0	1 (3.4)	5 (4.5)
大腸腺腫	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
線維腫	0	0	0	0	0	0	1 (3.4)	1 (0.9)
皮膚乳頭腫	2 (3.4)	0	2 (3.4)	0	0	0	1 (3.4)	3 (2.7)
神経系障害	7 (11.9)	2 (11.1)	9 (15.3)	0	0	0	0	9 (8.0)
浮動性めまい	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
異常感覚	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
頭痛	3 (5.1)	0	3 (5.1)	0	0	0	0	3 (2.7)
感覚鈍麻	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)

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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
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Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
神経系障害 (Cont.)								
片頭痛	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
後頭神経痛	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
失神	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
精神障害	2 (3.4)	2 (11.1)	4 (6.8)	0	0	0	0	4 (3.6)
不安	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
不眠症	1 (1.7)	2 (11.1)	3 (5.1)	0	0	0	0	3 (2.7)
腎および尿路障害	4 (6.8)	1 (5.6)	5 (8.5)	0	0	0	0	5 (4.5)
排尿困難	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
腎結石症	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
腎機能障害	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
尿管結石症	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)

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Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
生殖系および乳房障害	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
閉経期症状	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
呼吸器、胸郭および縦隔障害	3 (5.1)	2 (11.1)	4 (6.8)	0	0	1 (4.2)	1 (3.4)	6 (5.4)
喘息	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
咳嗽	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
発声障害	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
口腔咽頭不快感	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
口腔咽頭痛	0	0	0	0	0	1 (4.2)	1 (3.4)	2 (1.8)
アレルギー性鼻炎	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
上気道の炎症	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
皮膚および皮下組織障害	11 (18.6)	4 (22.2)	15 (25.4)	2 (28.6)	0	2 (8.3)	3 (10.3)	20 (17.9)
ざ瘡	3 (5.1)	1 (5.6)	4 (6.8)	0	0	0	0	4 (3.6)
皮膚嚢腫	0	0	0	0	0	0	1 (3.4)	1 (0.9)

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The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
皮膚および皮下組織障害 (Cont.)								
皮膚炎	0	0	0	1 (14.3)	0	0	0	0
ざ瘡様皮膚炎	0	0	0	0	0	1 (4.2)	0	1 (0.9)
接触皮膚炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
薬疹	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
湿疹	4 (6.8)	2 (11.1)	6 (10.2)	0	0	0	1 (3.4)	7 (6.3)
皮脂欠乏性湿疹	0	0	0	0	0	0	1 (3.4)	1 (0.9)
紅斑	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
汗疹	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
そう痒症	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
発疹	2 (3.4)	0	2 (3.4)	1 (14.3)	0	0	0	2 (1.8)
脂漏性皮膚炎	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
蕁麻疹	0	1 (5.6)	1 (1.7)	0	0	1 (4.2)	0	2 (1.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
血管障害	4 (6.8)	1 (5.6)	5 (8.5)	0	0	0	1 (3.4)	6 (5.4)
高血圧	4 (6.8)	1 (5.6)	5 (8.5)	0	0	0	0	5 (4.5)
静脈炎	0	0	0	0	0	0	1 (3.4)	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表14

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

TABLE 14.3__1.2.1.2_J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All_UPA (N=112) (PYs=153.4) Events (E/100 PYs)
Any adverse event	258 (269.6)	69 (367.0)	327 (285.6)	6 (176.5)	0	30 (144.2)	41 (226.5)	398 (259.5)
血液およびリンパ系障害	10 (10.4)	0	10 (8.7)	0	0	4 (19.2)	3 (16.6)	17 (11.1)
貧血	1 (1.0)	0	1 (0.9)	0	0	1 (4.8)	0	2 (1.3)
鉄欠乏性貧血	1 (1.0)	0	1 (0.9)	0	0	1 (4.8)	0	2 (1.3)
白血球減少症	2 (2.1)	0	2 (1.7)	0	0	2 (9.6)	1 (5.5)	5 (3.3)
リンパ節症	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
リンパ球減少症	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
好中球減少症	3 (3.1)	0	3 (2.6)	0	0	0	2 (11.0)	5 (3.3)
心臓障害	1 (1.0)	0	1 (0.9)	0	0	0	2 (11.0)	3 (2.0)
上室性期外収縮	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
心室性期外収縮	0	0	0	0	0	0	2 (11.0)	2 (1.3)

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
先天性、家族性および遺伝性障害	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
歯原性嚢胞	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
耳および迷路障害	0	1 (5.3)	1 (0.9)	0	0	1 (4.8)	2 (11.0)	4 (2.6)
メニエール病	0	0	0	0	0	0	1 (5.5)	1 (0.7)
耳鳴	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
回転性めまい	0	0	0	0	0	1 (4.8)	1 (5.5)	2 (1.3)
内分泌障害	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
副腎機能不全	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
甲状腺腫	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
眼障害	8 (8.4)	0	8 (7.0)	1 (29.4)	0	0	0	8 (5.2)
白内障	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
眼障害 (Cont.)								
結膜嚢胞	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
結膜出血	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
アレルギー性結膜炎	1 (1.0)	0	1 (0.9)	1 (29.4)	0	0	0	1 (0.7)
ドライアイ	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
眼充血	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
硝子体浮遊物	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
胃腸障害	32 (33.4)	10 (53.2)	42 (36.7)	1 (29.4)	0	3 (14.4)	2 (11.0)	47 (30.6)
腹部膨満	0	2 (10.6)	2 (1.7)	0	0	0	0	2 (1.3)
腹痛	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
下腹部痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
上腹部痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
胃腸障害 (Cont.)								
口角口唇炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
アフタ性潰瘍	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
潰瘍性大腸炎	2 (2.1)	1 (5.3)	3 (2.6)	1 (29.4)	0	1 (4.8)	1 (5.5)	5 (3.3)
便秘	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
齲歯	1 (1.0)	2 (10.6)	3 (2.6)	0	0	0	0	3 (2.0)
消化不良	4 (4.2)	1 (5.3)	5 (4.4)	0	0	0	0	5 (3.3)
腸炎	1 (1.0)	0	1 (0.9)	0	0	0	1 (5.5)	2 (1.3)
胃ポリープ	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
胃炎	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
胃食道逆流性疾患	1 (1.0)	0	1 (0.9)	0	0	1 (4.8)	0	2 (1.3)
痔核	0	0	0	0	0	1 (4.8)	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
胃腸障害 (Cont.)								
腸管ポリープ	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
大腸ポリープ	6 (6.3)	0	6 (5.2)	0	0	0	0	6 (3.9)
口腔扁平苔癬	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
直腸炎	0	2 (10.6)	2 (1.7)	0	0	0	0	2 (1.3)
口内炎	3 (3.1)	1 (5.3)	4 (3.5)	0	0	0	0	4 (2.6)
歯痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
嘔吐	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
一般・全身障害および投与部位の状態	6 (6.3)	2 (10.6)	8 (7.0)	0	0	0	0	8 (5.2)
胸痛	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
末梢性浮腫	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
発熱	4 (4.2)	1 (5.3)	5 (4.4)	0	0	0	0	5 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
肝胆道系障害	6 (6.3)	1 (5.3)	7 (6.1)	0	0	0	1 (5.5)	8 (5.2)
肝機能異常	5 (5.2)	1 (5.3)	6 (5.2)	0	0	0	1 (5.5)	7 (4.6)
肝障害	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
免疫系障害	1 (1.0)	0	1 (0.9)	0	0	0	1 (5.5)	2 (1.3)
アナフィラキシー反応	0	0	0	0	0	0	1 (5.5)	1 (0.7)
季節性アレルギー	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
感染症および寄生虫症	90 (94.0)	23 (122.3)	113 (98.7)	2 (58.8)	0	5 (24.0)	13 (71.8)	131 (85.4)
バルトリン腺炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
気管支炎	3 (3.1)	0	3 (2.6)	0	0	0	0	3 (2.0)
カンピロバクター胃腸炎	1 (1.0)	0	1 (0.9)	0	0	1 (4.8)	1 (5.5)	3 (2.0)
カンジダ感染	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) 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	1 (1.0)	5 (26.6)	6 (5.2)	0	0	0	0	6 (3.9)
結膜炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
ウイルス性結膜炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
膀胱炎	4 (4.2)	0	4 (3.5)	0	0	0	0	4 (2.6)
感染性皮膚炎	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
爪の皮膚糸状菌症	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
感染性腸炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
毛包炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
胃腸炎	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
ウイルス性胃腸炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
歯肉炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
ヘリコバクター感染	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
単純ヘルペス	2 (2.1)	1 (5.3)	3 (2.6)	0	0	0	0	3 (2.0)
帯状疱疹	8 (8.4)	0	8 (7.0)	2 (58.8)	0	0	2 (11.0)	10 (6.5)
麦粒腫	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
インフルエンザ	4 (4.2)	2 (10.6)	6 (5.2)	0	0	0	0	6 (3.9)
クレブシエラ感染	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
大腸感染	0	0	0	0	0	0	1 (5.5)	1 (0.7)
潜伏結核	1 (1.0)	0	1 (0.9)	0	0	0	1 (5.5)	2 (1.3)
上咽頭炎	27 (28.2)	4 (21.3)	31 (27.1)	0	0	3 (14.4)	2 (11.0)	36 (23.5)
口腔ヘルペス	14 (14.6)	1 (5.3)	15 (13.1)	0	0	0	5 (27.6)	20 (13.0)
歯周炎	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
咽頭炎	2 (2.1)	1 (5.3)	3 (2.6)	0	0	0	1 (5.5)	4 (2.6)
肺炎	0	2 (10.6)	2 (1.7)	0	0	0	0	2 (1.3)
歯髄炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
腎盂腎炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
鼻炎	0	0	0	0	0	1 (4.8)	0	1 (0.7)
副鼻腔炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
皮膚感染	2 (2.1)	1 (5.3)	3 (2.6)	0	0	0	0	3 (2.0)
足部白癬	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
上気道感染	3 (3.1)	1 (5.3)	4 (3.5)	0	0	0	0	4 (2.6)
水痘	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
傷害、中毒および処置合併症	6 (6.3)	2 (10.6)	8 (7.0)	0	0	1 (4.8)	1 (5.5)	10 (6.5)
動物咬傷	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
上顎炎	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
足骨折	0	1 (5.3)	1 (0.9)	0	0	0	1 (5.5)	2 (1.3)
過量投与	0	0	0	0	0	1 (4.8)	0	1 (0.7)
処置後出血	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
肋骨骨折	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
皮下血腫	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
脛骨骨折	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
臨床検査	21 (21.9)	3 (16.0)	24 (21.0)	0	0	2 (9.6)	3 (16.6)	29 (18.9)
アラニンアミノトランスフェラーゼ増加	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
アスパラギン酸アミノトランスフェラーゼ増加	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) 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	6 (6.3)	1 (5.3)	7 (6.1)	0	0	0	1 (5.5)	8 (5.2)
心電図異常	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
γ-グルタミルトランスフェラーゼ増加	1 (1.0)	1 (5.3)	2 (1.7)	0	0	2 (9.6)	0	4 (2.6)
高比重リポ蛋白増加	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
リンパ球数減少	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	1 (5.5)	3 (2.0)
好中球数減少	3 (3.1)	0	3 (2.6)	0	0	0	1 (5.5)	4 (2.6)
尿中白血球エステラーゼ陽性	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
白血球数減少	4 (4.2)	0	4 (3.5)	0	0	0	0	4 (2.6)
代謝および栄養障害	7 (7.3)	1 (5.3)	8 (7.0)	0	0	2 (9.6)	2 (11.0)	12 (7.8)
糖尿病	0	0	0	0	0	0	1 (5.5)	1 (0.7)
脂質異常症	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
高コレステロール血症	4 (4.2)	0	4 (3.5)	0	0	0	1 (5.5)	5 (3.3)
高脂血症	1 (1.0)	0	1 (0.9)	0	0	1 (4.8)	0	2 (1.3)
高尿酸血症	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
低蛋白血症	0	0	0	0	0	1 (4.8)	0	1 (0.7)
筋骨格系および結合組織障害	24 (25.1)	7 (37.2)	31 (27.1)	0	0	9 (43.3)	4 (22.1)	44 (28.7)
関節痛	2 (2.1)	1 (5.3)	3 (2.6)	0	0	1 (4.8)	2 (11.0)	6 (3.9)
関節炎	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
関節障害	0	0	0	0	0	1 (4.8)	0	1 (0.7)
背部痛	6 (6.3)	0	6 (5.2)	0	0	1 (4.8)	0	7 (4.6)
頚部脊柱管狭窄症	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
側腹部痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
椎間板突出	3 (3.1)	1 (5.3)	4 (3.5)	0	0	0	1 (5.5)	5 (3.3)
腰部脊柱管狭窄症	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
筋痙縮	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
筋骨格系胸痛	0	0	0	0	0	2 (9.6)	0	2 (1.3)
筋骨格痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
筋肉痛	1 (1.0)	0	1 (0.9)	0	0	0	1 (5.5)	2 (1.3)
変形性関節症	3 (3.1)	0	3 (2.6)	0	0	0	0	3 (2.0)
骨端症	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
骨壊死	0	1 (5.3)	1 (0.9)	0	0	1 (4.8)	0	2 (1.3)
骨粗鬆症	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
四肢痛	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) 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	0	0	2 (9.6)	0	2 (1.3)
横紋筋融解症	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
変形性脊椎症	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
弾発指	0	0	0	0	0	1 (4.8)	0	1 (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）	4 (4.2)	0	4 (3.5)	0	0	0	2 (11.0)	6 (3.9)
大腸腺腫	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
線維腫	0	0	0	0	0	0	1 (5.5)	1 (0.7)
皮膚乳頭腫	2 (2.1)	0	2 (1.7)	0	0	0	1 (5.5)	3 (2.0)
神経系障害	7 (7.3)	3 (16.0)	10 (8.7)	0	0	0	0	10 (6.5)
浮動性めまい	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
異常感覚	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
神経系障害 (Cont.)								
頭痛	3 (3.1)	0	3 (2.6)	0	0	0	0	3 (2.0)
感覚鈍麻	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
片頭痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
後頭神経痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
失神	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
精神障害	2 (2.1)	4 (21.3)	6 (5.2)	0	0	0	0	6 (3.9)
不安	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
不眠症	1 (1.0)	4 (21.3)	5 (4.4)	0	0	0	0	5 (3.3)
腎および尿路障害	5 (5.2)	2 (10.6)	7 (6.1)	0	0	0	0	7 (4.6)
排尿困難	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
腎結石症	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
腎および尿路障害 (Cont.)								
腎機能障害	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
尿管結石症	0	2 (10.6)	2 (1.7)	0	0	0	0	2 (1.3)
生殖系および乳房障害	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
閉経期症状	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
呼吸器、胸郭および縦隔障害	5 (5.2)	2 (10.6)	7 (6.1)	0	0	1 (4.8)	1 (5.5)	9 (5.9)
喘息	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
咳嗽	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
発声障害	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
口腔咽頭不快感	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
口腔咽頭痛	0	0	0	0	0	1 (4.8)	1 (5.5)	2 (1.3)
アレルギー性鼻炎	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
上気道の炎症	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
皮膚および皮下組織障害	15 (15.7)	6 (31.9)	21 (18.3)	2 (58.8)	0	2 (9.6)	3 (16.6)	26 (16.9)
ざ瘡	4 (4.2)	1 (5.3)	5 (4.4)	0	0	0	0	5 (3.3)
皮膚嚢腫	0	0	0	0	0	0	1 (5.5)	1 (0.7)
皮膚炎	0	0	0	1 (29.4)	0	0	0	0
ざ瘡様皮膚炎	0	0	0	0	0	1 (4.8)	0	1 (0.7)
接触皮膚炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
薬疹	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
湿疹	4 (4.2)	2 (10.6)	6 (5.2)	0	0	0	1 (5.5)	7 (4.6)
皮脂欠乏性湿疹	0	0	0	0	0	0	1 (5.5)	1 (0.7)
紅斑	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYs)
by System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
汗疹	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
そう痒症	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
発疹	2 (2.1)	0	2 (1.7)	1 (29.4)	0	0	0	2 (1.3)
脂漏性皮膚炎	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
蕁麻疹	0	1 (5.3)	1 (0.9)	0	0	1 (4.8)	0	2 (1.3)
血管障害	5 (5.2)	1 (5.3)	6 (5.2)	0	0	0	1 (5.5)	7 (4.6)
高血圧	5 (5.2)	1 (5.3)	6 (5.2)	0	0	0	0	6 (3.9)
静脈炎	0	0	0	0	0	0	1 (5.5)	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表15

[redacted]20[redacted] 09:26 [redacted]

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

TABLE 14.3__1.3.1.1.1_J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All_UPA (N=112) n (%)
Any adverse event	22 (37.3)	6 (33.3)	28 (47.5)	2 (28.6)	0	3 (12.5)	7 (24.1)	38 (33.9)
血液およびリンパ系障害	4 (6.8)	0	4 (6.8)	0	0	3 (12.5)	1 (3.4)	8 (7.1)
貧血	0	0	0	0	0	1 (4.2)	0	1 (0.9)
鉄欠乏性貧血	0	0	0	0	0	1 (4.2)	0	1 (0.9)
白血球減少症	2 (3.4)	0	2 (3.4)	0	0	1 (4.2)	1 (3.4)	4 (3.6)
リンパ球減少症	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
好中球減少症	3 (5.1)	0	3 (5.1)	0	0	0	1 (3.4)	4 (3.6)
耳および迷路障害	0	0	0	0	0	0	1 (3.4)	1 (0.9)
メニエール病	0	0	0	0	0	0	1 (3.4)	1 (0.9)
胃腸障害	3 (5.1)	1 (5.6)	4 (6.8)	1 (14.3)	0	0	0	4 (3.6)
口角口唇炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
アフタ性潰瘍	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
胃腸障害 (Cont.)								
潰瘍性大腸炎	0	0	0	1 (14.3)	0	0	0	0
胃炎	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
口内炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
一般・全身障害および投与部位の状態	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
発熱	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
感染症および寄生虫症	15 (25.4)	6 (33.3)	21 (35.6)	1 (14.3)	0	0	3 (10.3)	24 (21.4)
カンジダ感染	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
クロストリジウム・ディフィシレ感染	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
ウイルス性結膜炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
爪の皮膚糸状菌症	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
歯肉炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
帯状疱疹	7 (11.9)	0	7 (11.9)	1 (14.3)	0	0	2 (6.9)	9 (8.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
感染症および寄生虫症 (Cont.)								
インフルエンザ	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	0	2 (1.8)
潜伏結核	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
上咽頭炎	3 (5.1)	1 (5.6)	4 (6.8)	0	0	0	1 (3.4)	5 (4.5)
口腔ヘルペス	2 (3.4)	1 (5.6)	3 (5.1)	0	0	0	0	3 (2.7)
咽頭炎	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
肺炎	0	2 (11.1)	2 (3.4)	0	0	0	0	2 (1.8)
副鼻腔炎	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
皮膚感染	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
上気道感染	2 (3.4)	1 (5.6)	3 (5.1)	0	0	0	0	3 (2.7)
水痘	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
臨床検査	8 (13.6)	2 (11.1)	10 (16.9)	0	0	0	2 (6.9)	12 (10.7)
血中クレアチンホスホキナーゼ増加	3 (5.1)	1 (5.6)	4 (6.8)	0	0	0	0	4 (3.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
臨床検査 (Cont.)								
高比重リポ蛋白増加	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
リンパ球数減少	1 (1.7)	1 (5.6)	2 (3.4)	0	0	0	1 (3.4)	3 (2.7)
好中球数減少	2 (3.4)	0	2 (3.4)	0	0	0	1 (3.4)	3 (2.7)
尿中白血球エステラーゼ陽性	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
白血球数減少	4 (6.8)	0	4 (6.8)	0	0	0	0	4 (3.6)
代謝および栄養障害	4 (6.8)	0	4 (6.8)	0	0	1 (4.2)	0	5 (4.5)
脂質異常症	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
高コレステロール血症	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
低蛋白血症	0	0	0	0	0	1 (4.2)	0	1 (0.9)
筋骨格系および結合組織障害	0	0	0	0	0	1 (4.2)	0	1 (0.9)
関節障害	0	0	0	0	0	1 (4.2)	0	1 (0.9)
筋骨格系胸痛	0	0	0	0	0	1 (4.2)	0	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.1 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) n (%)	UPA 15 mg QD/ UPA 30 mg QD (N=18) n (%)	Total (N=59) n (%)	Placebo (N=7) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=24) n (%)	UPA 30 mg QD (N=29) n (%)	All UPA (N=112) n (%)
筋骨格系および結合組織障害 (Cont.)								
関節周囲炎	0	0	0	0	0	1 (4.2)	0	1 (0.9)
腎および尿路障害	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
腎機能障害	2 (3.4)	0	2 (3.4)	0	0	0	0	2 (1.8)
皮膚および皮下組織障害	1 (1.7)	2 (11.1)	3 (5.1)	0	0	0	1 (3.4)	4 (3.6)
ざ瘡	1 (1.7)	0	1 (1.7)	0	0	0	0	1 (0.9)
湿疹	0	0	0	0	0	0	1 (3.4)	1 (0.9)
そう痒症	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)
脂漏性皮膚炎	0	1 (5.6)	1 (1.7)	0	0	0	0	1 (0.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表16

[redacted]20[redacted] 09:26 [redacted]

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

TABLE 14.3__1.3.1.1.2_J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All_UPA (N=112) (PYs=153.4) Events (E/100 PYs)
Any adverse event	62 (64.8)	15 (79.8)	77 (67.2)	3 (88.2)	0	9 (43.3)	9 (49.7)	95 (61.9)
血液およびリンパ系障害	7 (7.3)	0	7 (6.1)	0	0	4 (19.2)	2 (11.0)	13 (8.5)
貧血	0	0	0	0	0	1 (4.8)	0	1 (0.7)
鉄欠乏性貧血	0	0	0	0	0	1 (4.8)	0	1 (0.7)
白血球減少症	2 (2.1)	0	2 (1.7)	0	0	2 (9.6)	1 (5.5)	5 (3.3)
リンパ球減少症	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
好中球減少症	3 (3.1)	0	3 (2.6)	0	0	0	1 (5.5)	4 (2.6)
耳および迷路障害	0	0	0	0	0	0	1 (5.5)	1 (0.7)
メニエール病	0	0	0	0	0	0	1 (5.5)	1 (0.7)
胃腸障害	3 (3.1)	1 (5.3)	4 (3.5)	1 (29.4)	0	0	0	4 (2.6)
口角口唇炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	SA 1 Population Total (N=59) (PYs=114.5) Events (E/100 PYs)	SA 2 Population Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	SA UPA All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
胃腸障害 (Cont.)								
アフタ性潰瘍	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
潰瘍性大腸炎	0	0	0	1 (29.4)	0	0	0	0
胃炎	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
口内炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
一般・全身障害および投与部位の状態	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
発熱	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
感染症および寄生虫症	30 (31.3)	9 (47.9)	39 (34.1)	2 (58.8)	0	0	3 (16.6)	42 (27.4)
カンジダ感染	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
クロストリジウム・ディフィシレ感染	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
ウイルス性結膜炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
爪の皮膚糸状菌症	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
歯肉炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
帯状疱疹	8 (8.4)	0	8 (7.0)	2 (58.8)	0	0	2 (11.0)	10 (6.5)
インフルエンザ	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	0	2 (1.3)
潜伏結核	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
上咽頭炎	3 (3.1)	1 (5.3)	4 (3.5)	0	0	0	1 (5.5)	5 (3.3)
口腔ヘルペス	7 (7.3)	1 (5.3)	8 (7.0)	0	0	0	0	8 (5.2)
咽頭炎	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
肺炎	0	2 (10.6)	2 (1.7)	0	0	0	0	2 (1.3)
副鼻腔炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
皮膚感染	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
上気道感染	3 (3.1)	1 (5.3)	4 (3.5)	0	0	0	0	4 (2.6)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
水痘	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
臨床検査	14 (14.6)	2 (10.6)	16 (14.0)	0	0	0	2 (11.0)	18 (11.7)
血中クレアチンホスホキナーゼ増加	4 (4.2)	1 (5.3)	5 (4.4)	0	0	0	0	5 (3.3)
高比重リポ蛋白増加	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
リンパ球数減少	1 (1.0)	1 (5.3)	2 (1.7)	0	0	0	1 (5.5)	3 (2.0)
好中球数減少	2 (2.1)	0	2 (1.7)	0	0	0	1 (5.5)	3 (2.0)
尿中白血球エステラーゼ陽性	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
白血球数減少	4 (4.2)	0	4 (3.5)	0	0	0	0	4 (2.6)
代謝および栄養障害	4 (4.2)	0	4 (3.5)	0	0	1 (4.8)	0	5 (3.3)
脂質異常症	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
高コレステロール血症	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)

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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
低蛋白血症	0	0	0	0	0	1 (4.8)	0	1 (0.7)
筋骨格系および結合組織障害	0	0	0	0	0	4 (19.2)	0	4 (2.6)
関節障害	0	0	0	0	0	1 (4.8)	0	1 (0.7)
筋骨格系胸痛	0	0	0	0	0	1 (4.8)	0	1 (0.7)
関節周囲炎	0	0	0	0	0	2 (9.6)	0	2 (1.3)
腎および尿路障害	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
腎機能障害	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
皮膚および皮下組織障害	1 (1.0)	2 (10.6)	3 (2.6)	0	0	0	1 (5.5)	4 (2.6)
ざ瘡	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
湿疹	0	0	0	0	0	0	1 (5.5)	1 (0.7)
そう痒症	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.2 J

Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
per 100 Patient-Years (PYs) by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	SA 1 Population UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	SA 1 Population UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	SA 1 Population Total (N=59) (PYs=114.5) Events (E/100 PYs)	SA 2 Population Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	SA 2 Population UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	SA 2 Population UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	SA 2 Population UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	SA UPA All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
脂漏性皮膚炎	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表17

[redacted]20[redacted] 09:26 [redacted]

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

TABLE 14.3 1.3.3 J

Treatment-Emergent Severe Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
Any adverse event	3 (3.1)	1 (5.3)	4 (3.5)	2 (58.8)	0	0	2 (11.0)	6 (3.9)
血液およびリンパ系障害	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
好中球減少症	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
胃腸障害	0	0	0	1 (29.4)	0	0	0	0
潰瘍性大腸炎	0	0	0	1 (29.4)	0	0	0	0
感染症および寄生虫症	1 (1.0)	0	1 (0.9)	1 (29.4)	0	0	1 (5.5)	2 (1.3)
帯状疱疹	1 (1.0)	0	1 (0.9)	1 (29.4)	0	0	1 (5.5)	2 (1.3)
臨床検査	1 (1.0)	0	1 (0.9)	0	0	0	1 (5.5)	2 (1.3)
好中球数減少	1 (1.0)	0	1 (0.9)	0	0	0	1 (5.5)	2 (1.3)
腎および尿路障害	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
尿管結石症	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表18

[redacted]20[redacted] 09:26 [redacted]

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

TABLE 14.3__2.3.1_J

Treatment-Emergent Adverse Events Leading to Death per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All_UPA (N=112) (PYs=153.4) Events (E/100 PYs)
Any adverse event	0	0	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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表19

[redacted]20[redacted] 09:26 [redacted]

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

TABLE 14.3__2.1.1_J

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All_UPA (N=112) (PYs=153.4) Events (E/100 PYs)
Any adverse event	14 (14.6)	3 (16.0)	17 (14.8)	1 (29.4)	0	0	1 (5.5)	18 (11.7)
胃腸障害	5 (5.2)	1 (5.3)	6 (5.2)	0	0	0	0	6 (3.9)
腹痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
潰瘍性大腸炎	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
胃食道逆流性疾患	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
大腸ポリープ	3 (3.1)	0	3 (2.6)	0	0	0	0	3 (2.0)
感染症および寄生虫症	3 (3.1)	0	3 (2.6)	1 (29.4)	0	0	1 (5.5)	4 (2.6)
帯状疱疹	2 (2.1)	0	2 (1.7)	1 (29.4)	0	0	1 (5.5)	3 (2.0)
腎盂腎炎	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
筋骨格系および結合組織障害	3 (3.1)	1 (5.3)	4 (3.5)	0	0	0	0	4 (2.6)
背部痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

TABLE 14.3 2.1.1 J

Treatment-Emergent Serious Adverse Events per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA_UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All UPA (N=112) (PYs=153.4) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
椎間板突出	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
腰部脊柱管狭窄症	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
骨壊死	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
神経系障害	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
頭痛	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
腎および尿路障害	2 (2.1)	1 (5.3)	3 (2.6)	0	0	0	0	3 (2.0)
腎結石症	2 (2.1)	0	2 (1.7)	0	0	0	0	2 (1.3)
尿管結石症	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

表20

[redacted]20[redacted] 09:26 [redacted]

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

TABLE 14.3__2.2.1_J

Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug per 100 Patient-Years (PYs)
by Primary MedDRA System Organ Class and Preferred Term
(SA1, SA2 and SA UPA Populations - Japan Analysis Set)

	SA 1 Population			SA 2 Population				SA UPA
MedDRA 23.0 System Organ Class Preferred Term	UPA 15 mg QD (N=59) (PYs=95.7) Events (E/100 PYs)	UPA 15 mg QD/ UPA 30 mg QD (N=18) (PYs=18.8) Events (E/100 PYs)	Total (N=59) (PYs=114.5) Events (E/100 PYs)	Placebo (N=7) (PYs=3.4) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=24) (PYs=20.8) Events (E/100 PYs)	UPA 30 mg QD (N=29) (PYs=18.1) Events (E/100 PYs)	All_UPA (N=112) (PYs=153.4) Events (E/100 PYs)
Any adverse event	2 (2.1)	2 (10.6)	4 (3.5)	1 (29.4)	0	0	0	4 (2.6)
胃腸障害	0	1 (5.3)	1 (0.9)	1 (29.4)	0	0	0	1 (0.7)
潰瘍性大腸炎	0	1 (5.3)	1 (0.9)	1 (29.4)	0	0	0	1 (0.7)
肝胆道系障害	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
肝機能異常	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
感染症および寄生虫症	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
肺炎	0	1 (5.3)	1 (0.9)	0	0	0	0	1 (0.7)
皮膚および皮下組織障害	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (0.7)
ざ瘡	1 (1.0)	0	1 (0.9)	0	0	0	0	1 (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/100PYs = Number of events per 100 patient-years.
The treatment-emergent adverse events (TEAEs) for SA1, SA2 and SA_UPA populations are defined as events that begin either on or after the first dose of study drug in the LTE study, and within 30 days after the last dose administration of the study drug.
The SA1 population includes all subjects who received at least one dose of study drug in Cohort 1. The UPA 15 mg QD group considers data during the UPA 15 mg QD treatment, the UPA 15 mg QD/UPA 30 mg QD considers data during the UPA 30 mg QD treatment after dose escalation, and the Total group considers data throughout the LTE treatment period.
The SA2 population includes all subjects who received at least one dose of study drug in Cohort 2.
The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

Program Source Code: [redacted]

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
前立腺癌	X	X		X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: ANXIETY	NOT REPORTED
OTHER: HEMORRHOIDS	20[redacted]
OTHER: LOW VITAMIN D	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	15	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 54	54
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 55	[redacted]20[redacted] / 418	364
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 419	[redacted]20[redacted] / 1110	692

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]
MERCAPTOPURINE	12.5 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: 8 WEEKLY	Y-M: 20[redacted]
INFLIXIMAB	500 mg/kg	OTHER: 8 WEEKLY	Y-M: 20[redacted]
MAGNESIUM	1 OTHER: TABLETS	QD	Y-M: 20[redacted]
VITAMIN D NOS	1000 IU	QD	Y-M: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MAGNESIUM	1 OTHER: TABLETS	QD	Y-M: 20[redacted]	ONGOING
VITAMIN D NOS	1000 IU	QD	Y-M: 20[redacted]	ONGOING
DOXYCYCLINE	50 mg	QD	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 668
ISOTRETINOIN	10 mg	QD	Y-M: 20[redacted] / 694	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC

Event Description	PROSTATE CANCER
Preferred term	前立腺癌
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1014 / 596
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 539): NPTST198-PSA: 6.3 [0.3 - 4.5] UG/L; [redacted]20[redacted] (RX DAY 547): NPTST198-PSA: 11.45 [0.3 - 4.5] UG/L; [redacted]20[redacted] (RX DAY 706): NPTST198-PSA: 5.43 [0.3 - 4.5] UG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 587): MRI PROSTATE: PI-RADS 5 LESION, PROSTATE BASE TRANSITION ZONE ON THE RIGHT, WITH LIKELY MICROSCOPIC EXTRACAPSULAR EXTENSION; PET CT: THE 18F-DCFPYL PET DEMONSTRATES A FOCUS OF INTENSELY AVID TRACER UPTAKE IN THE RIGHT ANTERIOR ASPECT OF THE PROSTATIC BASE EXTENDING INTO THE MID TO INVOLVING THE TRANSITION ZONE. THIS IS MOST SUSPICI OUS FOR A PRIMARY TUMOUR. THE REMAINDER OF THE GLAND HAS HETEROGENEOUS MILDLY

TO MODERATELY INCREASED ACTIVITY SUGGESTING INFLAMMATORY CHANGE. NO EVIDENCE FOR TRACER AVID LOCAL REGIONAL OR DISTANT MET ASTATIC DISEASE.; [redacted]20[redacted] (RX DAY 596): PROSTATE BIOPSY: TRANSPERINEAL PROSTATE CORE BIOPSIES. PROSTATE ADENOCARCINOMA, INVOLVING TWO SITES (3 CORES), GLEASON SCORE 3+3=6 (GRADE GROUP 1).

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FAMILY HISTORY - BROTHER ALSO HAD RADICAL PROSTATECTOMY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオーストラリアの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，前立腺癌の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 15 年間），潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与1014日後＊，被験者は前立腺癌を発現した。

本事象により，治験薬の投与は完全に中止された。

治験責任医師によると，投与の約32ヵ月後＊からの PSA 上昇（11.34 ug/L）の病歴が本事象と関連のある危険因子であった。

The patient's past medications include:

MEZAVANT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

6 MERCAPTOPURINE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Prostate cancer (10060862) (Prostate cancer (10060862)) [v.24.0] [10060862]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of PROSTATE CANCER

- Investigator: Family history - Brother also had radical prostatectomy

- AbbVie: Approximately 12.1 percent of men will be diagnosed with prostate cancer at some point during their lifetime. The highest incidence is in the age group greater than 50 years and older. Additional risk factors include age and family history.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **MRI PROSTATE:** PI-RADS 5 lesion, prostate base transition zone on the right, with likely microscopic extra capsular extension

[redacted] **PET CT:** The 18F-DCFPyl PET demonstrates a focus of intensely avid tracer uptake in the right anterior aspect of the prostatic base extending into the mid to involving the transition zone. This is most suspicious for a primary tumour. The remainder of the gland has heterogeneous mildly to moderately increased activity suggesting inflammatory change. No evidence for tracer avid local regional or distant metastatic disease.

[redacted] **20[redacted] PROSTATE BIOPSY:** Transperineal prostate core biopsies. Prostate adenocarcinoma, involving two sites (3 cores), Gleason score 3+3=6 (Grade Group 1).

[redacted] **20[redacted] PSA:** 6.3 ug/L (normal 0.30 to 4.5)

[redacted] **20[redacted] PSA:** 11.45 ug/L (normal 0.3 to 4.5)

[redacted] **20[redacted] PSA:** 5.43 ug/L (normal 0.3 to 4.5)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
滑液包炎	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	4[redacted]	MALE	WHITE

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: KIDNEY STONES (SELF-RESOLVED)	20[redacted]

Prior Procedures	Procedure Year
SURGERY: INGUINAL HERNIA REPAIR	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 60	[redacted]20[redacted] / 424	365
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 424		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2 g	OTHER: DAILY	Y: 20[redacted]
MESALAZINE	4.8 g	OTHER: DAILY	Y: 20[redacted]
BUDESONIDE	1.2 g	OTHER: DAILY	Y: 20[redacted]
BUDESONIDE	2016 mg	QD	Y: 20[redacted]
PREDNISOLONE	5 mg	OTHER: DAILY	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CEFALEXIN	500 mg	QID	Y-M: 20[redacted] / 392	Y-M: 20[redacted] / 392
FLUCLOXACILLIN	2 g	OTHER: 6/24	Y-M: 20[redacted] / 392	Y-M: 20[redacted] / 396
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 395
OXYCODONE	2.5 mg	PRN	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 393
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 395
LORATADINE	10 mg	PRN	Y-M: 20[redacted] / 394	Y-M: 20[redacted] / 394
FLUCLOXACILLIN	1 g	TID	Y-M: 20[redacted] / 396	Y-M: 20[redacted] / 413
MESALAZINE	4.8 g	OTHER: DAILY	Y: 20[redacted]	Not reported

Event #1: Serious Adverse Event

Event Description	BURSITIS RIGHT ELBOW
Preferred term	滑液包炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 752 / 329
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 392): Lymphocytes/Leukocytes: 25 [45 - 75] %; Monocytes/Leukocytes: 0 [2 - 8] %; NPTST150-LEUCOCYTES: 11400 [0 - 203] U/L; Neutrophils/Leukocytes: 75 [55 - 70] %

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	PT LIFTS WEIGHTS AND HAS HAD PREVIOUS TENNIS ELBOW
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオーストラリアの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右肘の滑液包炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，腎結石，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与752日後＊，被験者は右肘の滑液包炎を発現した。

投与813日後＊　の朝，被験者は肘に痛みを感じ始めた。午後からは，被験者は肘周辺の腫脹に気づき始めた。投与814日後＊　，被験者は紅斑を発現した。被験者は医師の診察を受け，実際に熱は出ておらず，セファレキシンを投与された。被験者は自宅で 2 回分を既に服用していた。医師は関節穿刺を行い，数ミリリットルの透明な黄色の液体を吸引した。午後 6 時頃，被験者の体温は摂氏 37.8°C 及び 38°C を記録し，ふらつきを感じた。医師は，被験者に救急科を受診するよう助言した。投与815日後＊　，被験者は入院した。肘部位への直接の損傷はなく，他の感染性の症状もなく，他の関節にも痛みはなかった。肘に氷を当てたところ，痛みが悪化した。被験者は肘に体重をかけることはできるが，痛みを感じていた。フルクロキサシリンの静脈内投与が開始された。投与816日後＊　，超音波検査が実施された。投与819日後＊　，被験者は，フルクロキサシリンを経口投与され，退院した。

治験責任医師によると，被験者はテニス肘の病歴があった。

投与された薬剤は，エノキサパリン，セファレキシン，フルクロキサシリン，paracetamol，オキシコドン及びロラタジンであった。

The patient's past medications include:

SALOFALK for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

BUDENOFALK for ULCERATIVE COLITIS (20[redacted] - [redacted] [redacted] 20[redacted])

CORTIMENT for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

PREDNISOLONE for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Elbow bursitis (10073532) (Bursitis (10006811)) [v.23.0] [10073532]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of BURSITIS RIGHT ELBOW

- Investigator: PT LIFTS WEIGHTS AND HAS HAD PREVIOUS TENNIS ELBOW

- AbbVie: Risk factors include frequent exercise involving the elbow as well as prior history of tennis elbow as noted by PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] 20[redacted] **RIGHT ELBOW ASPIRATE LEUKOCYTES:** 11400 U/L (normal 0 to 203)

[redacted] [redacted] 20[redacted] **RIGHT ELBOW ASPIRATE LYMPHOCYTES:** 25 % (normal 45 to 75)

[redacted] [redacted] 20[redacted] **RIGHT ELBOW ASPIRATE MONOCYTES:** 0 % (normal 2 to 8)

[redacted] [redacted] 20[redacted] **RIGHT ELBOW ASPIRATE NEUTROPHILS:** 75 % (normal 55 to 70)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血				X
ニューモシスチス・イロベチイ感染				X
肺炎	X			X
肺腫瘤	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	MALE	WHITE

Medical History	Onset Year
ASTHMA	20[redacted]
LEFT SIDED UC	20[redacted]
PNEUMONIA	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 60		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BECLOMETASONE;FORMOTEROL	1 DF	BID	Y-M: 20[redacted]
LECITHIN	1 DF	TID	Y-M: 20[redacted] / -337
MESALAZINE	1 DF	QD	Y-M: 20[redacted] / -306
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -306
INFLIXIMAB	10 g	OTHER: EVERY 8 WEKS	Y-M: 20[redacted] / -241
TIOTROPIUM	18 OTHER: MCG	QD	Y-M: 20[redacted] / -155
MAGNESIUM CARBONATE;MAGNESIUM OXIDE	1 DF	OTHER: TWICE PER WEEK	Y-M: 20[redacted] / -60

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BECLOMETASONE;FORMOTEROL	1 DF	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 39
LECITHIN	1 DF	TID	Y-M: 20[redacted] / -337	Y-M: 20[redacted] / 179
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -306	Y-M: 20[redacted] / 140
TIOTROPIUM	18 OTHER: MCG	QD	Y-M: 20[redacted] / -155	Y-M: 20[redacted] / 39
MAGNESIUM CARBONATE;MAGNESIUM OXIDE	1 DF	OTHER: TWICE PER WEEK	Y-M: 20[redacted] / -60	Y-M: 20[redacted] / 26
BECLOMETASONE;FORMOTEROL	2 DF	BID	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 144
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 42
TIOTROPIUM	5 OTHER: MCG	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 144
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 49
AZITHROMYCIN	1.5 g	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 48
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 50
DEXIBUPROFEN	400 mg	TID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 87
AZELASTINE;FLUTICASONE	1 OTHER: PUFF	BID	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 112
PROBIOTICS [UMBRELLA TERM]	1 DF	BID	Y-M: 20[redacted] / 137	Y-M: 20[redacted] / 303
SULFAMETROLE;TRIMETHOPRIM	1 DF	TID	Y-M: 20[redacted] / 137	Y-M: 20[redacted] / 303
TIOTROPIUM	2.5 OTHER: MCG	QD	Y-M: 20[redacted] / 145	Y-M: 20[redacted] / 180
LECITHIN	1 DF	BID	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 348

PROBIOTICS [UMBRELLA TERM]	1 DF	PRN	Y-M: 20[redacted] / 304	ONGOING
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 330
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 362	Y-M: 20[redacted] / 362
LACTOBACILLUS ACIDOPHILUS	2 DF	TID	Y-M: 20[redacted] / 605	Y-M: 20[redacted] / 607
SACCHAROMYCES BOULARDII	2 DF	TID	Y-M: 20[redacted] / 605	Y-M: 20[redacted] / 607
BECLOMETASONE;FORMOTEROL	100/6 ug	BID	Y-M: 20[redacted] / 709	Y-M: 20[redacted] / 809
FENOTEROL;IPRATROPIUM	1 DF	PRN	Y-M: 20[redacted] / 709	ONGOING
INFLUENZA VACCINE	1 DF	OTHER: ONCE	Y-M: 20[redacted] / 729	Y-M: 20[redacted] / 729
BECLOMETASONE;FORMOTEROL	200/12 ug	BID	Y-M: 20[redacted] / 810	ONGOING
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / 810	Y-M: 20[redacted] / 911
OTHER VIRAL VACCINES	0.3 mL	OTHER: ONCE	Y-M: 20[redacted] / 1162	Y-M: 20[redacted] / 1162
OTHER VIRAL VACCINES	0.3 mL	OTHER: ONCE	Y-M: 20[redacted] / 1183	Y-M: 20[redacted] / 1183

Event #1: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 81 / 22
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	142 / 83
Duration of AE	62 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 98 / 39
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
[redacted]20[redacted] (RX DAY 41): BLOOD NPTST030-ANTIGEN OF ASPERGILLUS SPP.: Negative; BLOOD NPTST031-ANTIGEN OF CRYPTOCOCCUS NEOFORM: Negative; SPUTUM NPTST038-BACTERIAL AND FUNGAL CULTURE: Negative; URINE NPTST218-S. PNEUMONIAE AND L. PNEUMOPHIL: Negative; [redacted]20[redacted] (RX DAY 42): BLOOD NPTST086-CULTURE: Negative	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 40): THORAX CT: PNEUMONIA IN RIGHT UPPER LOBE; [redacted]20[redacted] (RX DAY 41): CHEST X RAY: CONSOLIDATION IN RIGHT UPPER PART OF THE LUNG; [redacted]20[redacted] (RX DAY 42): BRONCHOSCOPY: REDENING OF MUCOSA; [redacted]20[redacted] (RX DAY 46): CHEST X RAY: COMPARED TO CHEST X RAY OF [redacted]-[redacted]-20[redacted] CONSOLIDATION ALMOST COMPLETELY GONE	
AE Stopped Initial Rx Day / Rx Day	107 / 48
Duration of AE	10 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PNEUMONIA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zoster

Event Description	PRESENCE IF PNEUMOCYSTIS JIROVECII IN LUNG
Preferred term	ニューモシスチス・イロベチイ感染
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 102 / 43
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	

AE Stopped Initial Rx Day / Rx Day	362 / 303
Duration of AE	261 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Serious Adverse Event

Event Description	ENLARGEMENT OF PULMONARY NODULE IN RIGHT LUNG FROM 3 TO 4 MM
Preferred term	肺腫瘤
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 135 / 76
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 124): OTHER BRONCHOALVEOLAR LAVAGE NPTST086-CULTURE: Positive-MORAXELLA CATARRHALIS 10E4 CBU/ML

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 124): BRONCHOSCOPY WITH BIOPSY: IN BIOPSY SIGNS OF PNEUMONIA WITHOUT ANY CAUSATIVE ORGANISM

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオーストリアの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，肺炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，喘息，肺炎，非喫煙者及び非飲酒者であった。

Event 2 の臨床経過：

投与98日後＊，被験者は肺炎を発現した。投与107日後＊，肺炎は消失した。

投与98日後＊ ，被験者は発熱及び咳嗽があり，入院した。投与99日後＊ ，胸部 CT 検査で右肺の上葉に肺炎を認めた。被験者は抗生物質で治療された。投与109日後＊ ，被験者は退院した。

投与された薬剤は pantoloc，アベロックス，セフトリアキソン，zithromax 及び lovenox であった。

The patient's past medications include:

SALOFALK KLYSMEN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK SUPP for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IFX for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.20.1] [10035664]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of PNEUMONIA

- Investigator: Pneumonia.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANTIGEN OF ASPERGILLUS SPP.:** Negative.

[redacted] **20[redacted] ANTIGEN OF CRYPTOCOCCUS NEOFORMANS:** Negative.

[redacted] **20[redacted] BLOOD CULTURE:** Negative.

[redacted] **20[redacted] BRONCHOSCOPY:** Reddening of mucosa.

[redacted] **20[redacted] CHEST X RAY:** Consolidation in right upper part of the lung.

[redacted] **20[redacted] CHEST X RAY:** Compared to chest x ray of [redacted] 20[redacted] consolidation almost completely gone.

[redacted] **20[redacted] CT OF THORAX:** Pneumonia in right upper lobe

[redacted] **20[redacted] SPUTUM-BACTERIAL AND FUNGAL CULTURE:** Negative.

[redacted] **20[redacted] URINE- S. PNEUMONIAE AND L. PNEUMOPHILA:** Negative.
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオーストリアの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，右肺の肺結節の腫大（3 mm から 4 mm）の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 4 の臨床経過：

投与135日後＊，被験者は右肺の肺結節の腫大（3 mm から 4 mm）を発現した。

被験者は，臨床的な徴候及び症状はなかった。投与182日後＊　，被験者は小さな肺結節があるため，入院した。投与183日後＊　，被験者は気管支鏡検査及び生検を受け，肺炎が発見されたが，結節の組織検査及び組織培養では原因不明であった。同日，被験者は退院した。

Causality for UPADACITINIB (Open Label)

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1) Lung nodule (10049498) (Pulmonary mass (10056342)) [v.24.0] [10049498]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of ENLARGEMENT OF PULMONARY NODULE IN RIGHT LUNG FROM 3 TO 4 MM

- Investigator: Unknown

- AbbVie: Event is more likely related to prior pneumonia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BRONCHOALVEOLAR CULTURE: Positive:** Moraxella catarrhalis; 10E4 CBU/ml

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	3[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: ALLERGY OF HOUSE DUST AND CAT HAIR	20[redacted]
OTHER: BROKEN ARM	20[redacted]
OTHER: EXANTHEMA WHOLE BODY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: ADENECTOMY	19[redacted]
SURGERY: TONSILLECTOMY	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 56		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	225 mg	QD	Y-M: 20[redacted]
GOLIMUMAB	50 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	100 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -358
SULFAMETROLE;TRIMETHOPRIM	400 mg	QD	Y-M: 20[redacted] / -280
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted] / -150

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PREDNISOLONE	50 mg	QD	Y-M: 20[redacted] / 242	Y-M: 20[redacted] / 242
ELECTROLYTES NOS	500 mL	QD	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 243
ELECTROLYTES NOS	500 mL	BID	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 244
ELECTROLYTES NOS	500 mL	QD	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 245

Event #1: Serious Adverse Event

Event Description	WORSENING OF COLITIS ULCEROSA
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 298 / 243
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 243): Alkaline Phosphatase: 69 [30 - 120] U/L; Bilirubin: 14.880384 [0 - 20.524668] UMOL/L; Calcium: 2.4 [2.2 - 2.6] MMOL/L; Creatinine: 89.287293 [61.882282 - 106.083912] UMOL/L; NPTST059-CALPROTECTIN: 1000 [0 - 50] ?G/G; NPTST085-CRP: 0.84 [0 - 0.5] MG/DL; NPTST147-LDH: 217 [0 - 248] U/L; Potassium: 3.85 [3.6 - 4.8] MMOL/L; Sodium: 143 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 244): NPTST059-CALPROTECTIN: >1000 [0 - 50] ?G/G

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 244): ENDOSCOPY: MAYO SCORE 1 TO 3

AE Stopped Initial Rx Day / Rx Day	301 / 246
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUSPECTED FLARE OF STUDY DISEASE OR DUE TO INFECTION, FURTHER INVESTIGATIONS HAVE TO BE DONE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオーストリアの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

Event 1 の臨床経過：

投与298日後＊，被験者は潰瘍性大腸炎の悪化を発現した。投与301日後＊　，潰瘍性大腸炎の悪化は消失した。

投与298日後＊，被験者は治療のために入院した。被験者は 1 日に 8–10 回の排便と共に血便を経験した。被験者は prednisolon を 1 日 5 mg から 1 日 50 mg に増量し，治療を受けた。入院中に合併症は報告されず，手術も行われなかった。投与301日後＊，被験者は退院した。

投与された薬剤は，elomel 及び prednisolon であった。

The patient's past medications include:

SIMPONI for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.1] [10009901]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of WORSENING OF COLITIS ULCEROSA

- Investigator: Suspected flare of study disease or due to infection, further investigations have to be done.

- AbbVie: Event is more likely related to flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 69 U/L (normal 30 to 120)

[redacted] **20[redacted] BILIRUBIN TEST:** 0.87 mg/dL (normal 0 to 1.20)

[redacted] **20[redacted] CALCIUM:** 2.40 MCMOL/L (normal 2.20 to 2.60)

[redacted] **20[redacted] CREATININE:** 1.01 mg/dL (normal 0.7 to 1.2)

[redacted] **20[redacted] CRP:** 0.84 mg/dL (normal 0 to 0.50)

[redacted] **20[redacted] ENDOSCOPY:** Mayo score 1-3

[redacted] **20[redacted] LDH:** 217 U/L (normal 0 to 248)

[redacted] **20[redacted] POTASSIUM:** 3.85 MMOL/L (normal 3.60 to 4.80)

[redacted] **20[redacted] SODIUM:** 143 MMOL/L (normal 135 to 145)

[redacted] **20[redacted] STOOL CALPROTECTIN:** 1000 ug/dL (normal 0 to 50)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
胸痛	X			
帯状疱疹				X
腱断裂	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
COGNITIVE OR PSYCHIATRIC DISORDER: INSOMNIA	20[redacted]
HEARING DISORDER: TINNITUS	NOT REPORTED
HYPOTHYROIDISM	20[redacted]
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.14 PACK	8	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 60		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CALCIUM CARBONATE;ERGOCALCIFEROL	500 mg	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	OTHER: 3 TIMES WEEKLY	Y-M: 20[redacted]
MESALAZINE	3000 mg	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	3000 mg	QD	Y-M: 20[redacted]
MESALAZINE	4 g	OTHER: 2 TIMES PER WEEK	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
CEFUROXIME	500 mg	BID	Y-M: 20[redacted]
COLECALCIFEROL-CHOLESTERIN	30 gtt	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
MOXIFLOXACIN	400 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
LEVOTHYROXINE	88 ug	QD	Y-M: 20[redacted] / -184
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -16
TRIAZOLAM	0,25 mg	OTHER: AS NEEDED	Y: 20[redacted]
METAMIZOLE	30 mg	OTHER: AS NEEDED	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CALCIUM CARBONATE;ERGOCALCIFEROL	500 mg	QD	Y-M: 20[redacted]	Not reported
MESALAZINE	3000 mg	QD	Y-M: 20[redacted]	Not reported
COLECALCIFEROL-CHOLESTERIN	30 gtt	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 600
LEVOTHYROXINE	88 ug	QD	Y-M: 20[redacted] / -184	Not reported
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -16	Y-M: 20[redacted] / 509
PRAMIPEXOLE	0.18 mg	PRN	Y-M: 20[redacted] / 250	Not reported
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 510	ONGOING

AMLODIPINE	5 mg	OTHER: AS NEEDED	Y-M: 20[redacted] / 794	Y-M: 20[redacted] / 876
CANDESARTAN	8 mg	BID	Y-M: 20[redacted] / 794	Not reported
AMLODIPINE;CANDESARTAN	8/5 mg	OTHER: ONCE A DAY	Y-M: 20[redacted] / 846	Not reported
CARBOMER;HYALURONIC ACID;XANTHAN GUM	3 OTHER: TABLETTS	TID	Y-M: 20[redacted] / 877	Y-M: 20[redacted] / 936
MOMETASONE	1 OTHER: HUB	BID	Y-M: 20[redacted] / 877	Y-M: 20[redacted] / 936
COLECALCIFEROL-CHOLESTERIN	30 gtt	QD	Y-M: 20[redacted] / 1090	Not reported
TRIAMCINOLONE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 1091	ONGOING
MAGNESIUM	NA mg	OTHER: ONE CAPSULE TWICE A DAY	Y-M: 20[redacted] / 1093	Y-M: 20[redacted] / 1114
LIDOCAINE	5 mL	OTHER: ONCE	Y-M: 20[redacted] / 1170	Y-M: 20[redacted] / 1170
TRIAMCINOLONE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 1170	Y-M: 20[redacted] / 1170
METAMIZOLE	500 mg	QD	Y-M: 20[redacted] / 1265	Y-M: 20[redacted] / 1266
METAMIZOLE	500 MG mg	OTHER: 3X2	Y-M: 20[redacted] / 1267	Y-M: 20[redacted] / 1301
TRAMADOL	15 GTT gtt	OTHER: UP TO MAX. 3X DAILY	Y-M: 20[redacted] / 1267	Not reported
TRAMADOL	2X 100 MG mg	OTHER: AS LONG AS SEVERE PAIN	Y-M: 20[redacted] / 1267	Not reported
OTHER VIRAL VACCINES	0.3 mL	QD	Y-M: 20[redacted] / 1295	Y-M: 20[redacted] / 1295
OTHER VIRAL VACCINES	0.3 mL	QD	Y-M: 20[redacted] / 1317	Y-M: 20[redacted] / 1317
TRIAZOLAM	0,25 mg	OTHER: AS NEEDED	Y: 20[redacted]	ONGOING
METAMIZOLE	30 mg	OTHER: AS NEEDED	Y: 20[redacted]	ONGOING

Event #1: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 280 / 221
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	479 / 420
Duration of AE	200 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	CHEST PAIN
Preferred term	胸痛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 923 / 864
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 794): NPTST252-TROPONIN-I HS (ABBOTT): 3 [0 - 26] NG/L; [redacted]20[redacted] (RX DAY 864): NPTST049-BRAIN NATRIURETIC PEPTIDE: 26 [0 - 120] PG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 865): CT CORONAR ANGIO: SLIGHT CALCIFICATIONS IN CORONARY ARTERY, NO SIGNIFICANT STENOSIS; ECHOCARDIOGRAPHY: NO CLINICALLY SIGNIFICANT FINDINGS; LONG-TERM BLOOD PRESSURE MEASUREMENT: SYSTOLIC BLOOD PRESSURE INCREASED DURING THE DAY

AE Stopped Initial Rx Day / Rx Day	1240 / 1181
Duration of AE	318 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CHEST PAIN WITH MUSCULAR SKELETAL ORIGIN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	PARTIAL TENDON RUPTURE RIGHT SHOULDER
Preferred term	腱断裂
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1087 / 1028
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 1265): DIAGNOSTIC ARTHROSCOPY: POST-OPERATIVE COURSE WITHOUT COMPLICATIONS, PATIENT COULD BE DISCHARGED IN GOOD GENERAL CONDITION.	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RUPTURE OF THE SHOULDER
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオーストリアの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，胸痛の事象を発現した。関連する病歴は，元喫煙者（1 日 0.14 箱を 8 年間），甲状腺機能低下症，潰瘍性大腸炎，認知障害又は精神障害（不眠症）及び非飲酒者であった。

Event 2 の臨床経過：

投与923日後＊，被験者は胸痛を発現した。投与の約41ヵ月後＊，胸痛は消失した。

投与923日後＊　，被験者は胸痛があり，入院した。被験者は，この数ヶ月間続く，運動と無関係に発現する左胸部の刺すような痛みを繰り返し経験していた。被験者は動脈性高血圧で，高血圧のエピソードを繰り返しており，カンデサルタンを増量した。被験者の血圧は上昇したままであった。24 時間血圧測定検査の結果，日中に特に血圧値が上昇することが判明した。被験者はさらにアムロジピンを投与された。冠動脈疾患イベントを除外するために冠血管造影 CT 検査を受けたところ，軽度の硬化が認められたが，著しい狭窄は認められなかった。所見及び痛みの種類から，心疾患の可能性は極めて低いと判断された。投与925日後＊　，被験者は退院した。

The patient's past medications include:

SALOFALK for ULCERATIVE COLITIS ([redacted])

SALOFALK KLYSMEN for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

Causality for UPADACINIB (Open Label)

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1)　Chest pain (10008479)　(Chest pain (10008479))　[v.24.0]　[10008479]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of CHEST PAIN

- Investigator: Chest pain with muscular skeletal origin

- AbbVie: Event is common in the general population. The mean annual prevalence of non-cardiac chest pain in 6 population-based studies was approximately 25%.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** Systolic blood pressure increased during the day

[redacted] **20[redacted] BNP:** 26 PG/ML (normal 0 to 120)

[redacted] **20[redacted] CHEST X-RAY:** Normal.

[redacted] **20[redacted] CHOLESTEROL TOTAL:** 233 mg/dL (normal 100 to 200)

[redacted] **20[redacted] CT CORONARY ANGIOGRAPHY:** Slight calcifications in coronary artery. No significant stenosis

[redacted] **20[redacted] DOPPLER ULTRASOUND:** Color Doppler: Mild aortic insufficiency. Left ventricle function sustained with mild septal left ventricular hypertrophy, no evidence of regional wall movement disorders. Mild aortic insufficiency. No increase of pressure in the pulmonary circulation. Diastolic function normal for patient's age.

[redacted] **20[redacted] ECG:** Findings: Ventricular rate: 53 BPM, P-R interval: 160 ms, QRS duration: 82 ms, QT/QTc: 402/377 ms, Sinus bradycardia, Left axis deviation

[redacted] **20[redacted] ECHOCARDIOGRAM:** Ultrasound examination visibility: satisfactory from apical and parasternal, examination in sinus rhythm. Left ventricular EDD: 41mm, Right ventricular EDD: 28mm, Left atrium: 32mm, right atrium: 33mm. The left ventricular is of normal size with low basal septal hypertrophy. Right ventricle normal size, normal function. Atria not enlarged. No pericardial effusion. HEART VALVES: Aortic valve: tricuspid, delicate. Mitral valve: inconspicuous in ultrasound examination. Tricuspid valve: inconspicuous

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Normal

[redacted] **20[redacted] HDL:** 44.0 mg/dL (normal 40 to 100)

[redacted] **20[redacted] LDL:** 130.4 mg/dL (normal <160)

[redacted] **20[redacted] POTASSIUM:** 4.0 MMOL/L (normal 3.2 to 5.2)

[redacted] **20[redacted] SODIUM:** 138 MMOL/L (normal 135 to 150)

[redacted] **20[redacted] TRIGLYCERIDES:** 293 mg/dL (normal 25 to 180)

[redacted] 20[redacted] **TROPONIN 1 HS:** 3 NG/L (normal 0 to 26)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオーストリアの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，右肩部の部分的な腱断裂の事象を発現した。関連する病歴は，元喫煙者（1 日 0.14 箱を 8 年間），潰瘍性大腸炎及び非飲酒者であった。

Event 3 の臨床経過：
投与1087日後＊，被験者は右肩部の部分的な腱断裂を発現した。

投与1323日後＊　，被験者は，右肩部の部分的な腱断裂の外科的修復のために予定された手術のため，入院した。手術では，合併症は認められなかった。投与1326日後＊　，被験者は良好な全身状態で退院した。

投与された薬剤は，xyloneural 及び volon a であった。

The patient's past medications include:

SALOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALOFALK KLYSMEN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLON HNP for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

APREDNISOLON for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLON NYC for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AVELOX for PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1)　Tendon rupture (10043248)　(Tendon rupture (10043248))　[v.24.0]　[10043248]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

Event of PARTIAL TENDON RUPTURE RIGHT SHOULDER

- Investigator: Rupture of the shoulder

- AbbVie: Rotator cuff injuries are common in the general population with age being the single most important risk factor for rotator cuff tears with a prevalence of 10.7% in subjects whose age was in the 50's.

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Herpes zoster: One dermatone.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血				X
裂肛	X			
胃腸炎	X			X
伝染性単核症	X			X
腎仙痛	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: ARTRALGIA	20[redacted]
OTHER: BACK PAIN	20[redacted]
OTHER: CRAMPS CALF	20[redacted]
OTHER: CUSHINGOID FACE	20[redacted]
OTHER: FATIGUE	20[redacted]
OTHER: FEMOROACETABULAR (TYPE PINCER) IMPINGEMENT SYNDROME	20[redacted]
OTHER: MUSCULAR ATROPHY	20[redacted]
OTHER: PRECORDIALGY	20[redacted]
OTHER: PYROSIS AND RETROSTERNAL BURNING	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 50	50
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 51	[redacted]20[redacted] / 98	48
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 98		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2 g	BID	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
BECLOMETASONE	5 mg	BID	Y-M: 20[redacted]
MESALAZINE	1 OTHER: SUPPO	QD	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY WEEK	Y-M: 20[redacted]
MESALAZINE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted]
BLINDED THERAPY	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
ETROLIZUMAB	105 mg	OTHER: Q4W	Y-M: 20[redacted]
USTEKINUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -228
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / -210
BECLOMETASONE	5 mg	BID	Y-M: 20[redacted] / -174

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	2 g	BID	Y-M: 20[redacted]	Not reported

CODEINE;PARACETAMOL	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 27
GLYCERYL TRINITRATE	1 OTHER: FNIGERTIP	QD	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 90
SODIUM CHLORIDE	10 mL	BID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 27
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 28
ALIZAPRIDE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
ELECTROLYTES NOS	1000 mL	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 29
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 39	Y-M: 20[redacted] / 65
IRON	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 53
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / 170	Not reported
CHLORHEXIDINE;LIDOCAINE	1 DF	OTHER: 6 TIMES / DAY	Y-M: 20[redacted] / 284	Y-M: 20[redacted] / 288
PELARGONIUM SIDOIDES	20 mg	TID	Y-M: 20[redacted] / 284	Y-M: 20[redacted] / 288
SODIUM CHLORIDE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / 286	Y-M: 20[redacted] / 287
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 287	Y-M: 20[redacted] / 287
PARACETAMOL	1 g	TID	Y-M: 20[redacted] / 287	Y-M: 20[redacted] / 287
ALIZAPRIDE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 288	Y-M: 20[redacted] / 288
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 288	Y-M: 20[redacted] / 330
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 921	Not reported
IRON	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 1101	Y-M: 20[redacted] / 1101
HAMAMELIS VIRGINIANA;ICHTHAMMOL;TITANIC HYDROXIDE;TITANIUM DIOXIDE;ZINC	1 DF	PRN	Y-M: 20[redacted] / 1120	Y-M: 20[redacted] / 1214
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 1121	Y-M: 20[redacted] / 1133
METHYLPREDNISOLONE	12 mg	QD	Y-M: 20[redacted] / 1134	Y-M: 20[redacted] / 1165
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 1166	Y-M: 20[redacted] / 1184
METHYLPREDNISOLONE	4 mg	OTHER: EOD	Y-M: 20[redacted] / 1185	Y-M: 20[redacted] / 1199
METHYLPREDNISOLONE	8 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / 1186	Y-M: 20[redacted] / 1199
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / 1200	Y-M: 20[redacted] / 1252

METHYLPREDNISOLONE	2 mg	QD	Y-M: 20[redacted] / 1253	Y-M: 20[redacted] / 1316
AMOXICILLIN	500 mg	TID	Y-M: 20[redacted] / 1261	Y-M: 20[redacted] / 1264
ALIZAPRIDE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 1264	Y-M: 20[redacted] / 1264
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	OTHER: 1X / 12HOURS	Y-M: 20[redacted] / 1264	Y-M: 20[redacted] / 1267
IBUPROFEN	600 mg	OTHER: ONCE	Y-M: 20[redacted] / 1264	Y-M: 20[redacted] / 1264
METHYLPREDNISOLONE	125 mg	OTHER: ONCE	Y-M: 20[redacted] / 1264	Y-M: 20[redacted] / 1264
PARACETAMOL	1 g	OTHER: ONCE	Y-M: 20[redacted] / 1264	Y-M: 20[redacted] / 1264
SODIUM CHLORIDE;TRAMADOL	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 1264	Y-M: 20[redacted] / 1264
AMOXICILLIN	1000 mg	BID	Y-M: 20[redacted] / 1265	Y-M: 20[redacted] / 1265
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 1265	Y-M: 20[redacted] / 1268
TRAMADOL	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 1265	Y-M: 20[redacted] / 1265
MAGALDRATE	800 mg	OTHER: ONCE	Y-M: 20[redacted] / 1266	Y-M: 20[redacted] / 1266
PARACETAMOL	1 g	OTHER: ONCE	Y-M: 20[redacted] / 1266	Y-M: 20[redacted] / 1266
SERTRALINE	50 mg	QD	Y-M: 20[redacted] / 1333	Y-M: 20[redacted] / 1334

Event #1: Serious Adverse Event

Event Description	RENAL COLIC
Preferred term	腎仙痛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 124 / 27
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 27): NPTST101-ERYTHROCYTES: 290 [0 - 25] /UL; [redacted]20[redacted] (RX DAY 28): NPTST166-MRSA: NEGATIVE [NOT REPORTED - NOT REPORTED] NA

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 27): CT ABDOMEN: NO ARGUMENTS FOR UROLITHIASIS, LOW ACCENTUATION OF THE PYELOCALICIAL SYSTEM AND OF THE RIGHT URETER TO DISTAL COMPARED WITH CONTRALATERAL: STONE PASSAGE?; [redacted]20[redacted] (RX DAY 28): RX THORAX: NO FINDINGS

AE Stopped Initial Rx Day / Rx Day	126 / 29
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NO CLEAR CAUSE OF EVENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 150 / 53
Age at AE Onset	2[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	183 / 86
Duration of AE	34 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Serious Adverse Event

Event Description	PERIANAL FISSURE
Preferred term	裂肛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 188 / 91
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 91): INTERNAL LATERAL SFINCTEROTOMY: NO COMPLICATIONS AFTER SURGERY WERE DETECTED. THE PATIENT LEFT THE HOSPITAL IN GOOD CONDITION.; PATHOLOGY REPORT ANAL MUCOSA: BENIGN DISCRETE TRAUMATIZED ANAL POLYP. NO EVIDENCE FOR KOILOCYTOTIC ATYPIA, DYSPLASIA OR MALIGNANCY

AE Stopped Initial Rx Day / Rx Day	189 / 92
Duration of AE	2 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COLITIS ULCEROSA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #4: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	GASTROENTERITIS
Preferred term	胃腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 383 / 286
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 286): NPTST085-CRP: 97 [0 - 7] MG/L; [redacted]20[redacted] (RX DAY 287): NPTST085-CRP: 73 [0 - 7] MG/L; NPTST166-MRSA: NEGATIVE [NOT REPORTED - NOT REPORTED] NA

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 287): ULTRASOUND ABDOMEN: NORMAL, VIRAL GASTROENTERITIS

AE Stopped Initial Rx Day / Rx Day	385 / 288
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	VIRAL INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #5: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1186 / 1089
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #6: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	INFECTIOUS MONONUCLEOSIS
Preferred term	伝染性単核症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1355 / 1258
Age at AE Onset	2[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 1264): NPTST085-CRP: 18.7 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 1266): Leukocytes: 11.2 [4.2 - 9.8] 10^9/L; NPTST085-CRP: 7.4 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 1267): Leukocytes: 7.33 [4.2 - 9.8] 10^9/L; NPTST085-CRP: 4.1 [0 - 5] MG/L	
Microbiology	
[redacted]20[redacted] (RX DAY 1261): OTHER NASAL SWAB NPTST081-COVID 19 TEST: Negative; [redacted]20[redacted] (RX DAY 1264): BLOOD NPTST097-EPSTEIN BARR IGG: Negative; BLOOD NPTST098-EPSTEIN BARR IGM: Positive-STRONG POSITIVE TEST; BLOOD NPTST163-MONONUCLEOSE QUICKTEST: Positive-POSITIVE TEST ==> VIRAL CAUSE OF TONSILLITIS	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED

Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腎仙痛の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

Event 1 の臨床経過：

投与124日後＊，被験者は腎仙痛を発現した。

投与124日後＊　，被験者は入院した。被験者は，投与123日後＊　から右側腹部及び恥骨上の部分へ放散する右季肋部付近の激しい腹痛を呈していた。また，被験者は排尿時にも痛みを経験していた。投与124日後＊　，被験者は血尿が出たが，発熱はなかった。徴候及び症状には，激しい腹痛，悪心及び血尿が含まれた。臨床経過には，腎臓結石の通過によると思われる右側腹部及び右季肋部の激しい痛みが含まれた。腹部 CT 検査では，結石は確認されなかった。尿検査では，顕微鏡的血尿が認められた。投与126日後＊，被験者は退院した。

投与された薬剤は，paracetamol fresenius，mini-plasco 塩化ナトリウム 0.9%，dafalgan forte，sterofundin b，litican 及び tradonal odis であった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS (Started [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COLITOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Renal colic (10038419) (Renal colic (10038419)) [v.20.0] [10038419]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: NotApplicable

Alternative Etiology for ABT-494 (Open Label)

Event of RENAL COLIC

- Investigator: Not reported.

- AbbVie: No plausible mechanism to implicate study drug

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN:** No arguments for urolithiasis, low accentuation of the pyelocalicial sytem and of the right ureter to distal compared with contralateral: stone passage?

[redacted] **20[redacted] MRSA NASAL SWAB:** negative

[redacted] **20[redacted] RX THORAX:** no findings

[redacted] **20[redacted] URINE ERYTHROCYTES:** 290 uL (normal 0 to 25)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，肛門周囲の裂傷の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 3 の臨床経過：

投与188日後＊　，被験者は肛門周囲の裂傷を発現した。投与189日後＊　，肛門周囲の裂傷は消失した。

本事象発現前に，投与98日後＊　から 投与187日後＊ まで，被験者は肛門周囲の裂傷（非重篤）を経験し，悪化し続けていた。そのため，手術が推奨された。

投与188日後＊　，被験者は手術のため入院した。被験者は疼痛を経験していた。同日，内側側面の括約筋切開術が行われた。手術中，肛門鏡検査が行われ，肛門ポリープも切除された。手術後，スポンゴスタンが所定の位置に装着された。手術中又は手術後に，合併症は確認されなかった。投与189日後＊，被験者は良好な状態で退院した。

The patient's past medications include:

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], Stopped [redacted] 20[redacted])

DAFALGAN CODEINE for PERIANAL FISSURE ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1)　Anal fissure (10002153)　(Anal fissure (10002153))　[v.20.1]　[10002153]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of PERIANAL FISSURE

- Investigator: Colitis ulcerosa.

- AbbVie: Event more likely a complication of underlying ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **PATHOLOGY:** BENIGN DISCRETE TRAUMATIZED ANAL POLYP. NO EVIDENCE FOR KOILOCYTOTIC ATYPIA, DYSPLASIA OR MALIGNANCY
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，胃腸炎の事象を発現した。関連する病歴は，広範囲な潰瘍性大腸炎（全大腸炎型），結腸内視鏡検査，非喫煙者及び非飲酒者であった。

Event 4 の臨床経過：

投与383日後＊，被験者は胃腸炎を発現した。投与385日後＊，胃腸炎は消失した。

投与383日後＊，被験者は腹痛，下痢，嘔吐及び発熱感があり，救急科を受診し，入院した。被験者は，1 週間前からこれらの症状を患っていた。一般開業医により，ウイルス症候群の疑いで支持療法が既に開始されていた。被験者は排便時に多少の出血があった。一般開業医での 2 日前の血液検査では，CRP が 60 mg/dL であった。身体検査では，腹部及び右窩を押すと痛みがあった。胃腸炎が疑われた。CRP の上昇（97 mg/dL）が認められた。被験者は発熱がなかった。支持療法の方針が継続され，炎症性パラメータのフォローアップが行われた。投与384日後＊，腹部超音波検査が実施された。投与385日後＊，被験者は退院した。治験責任医師によると，被験者には本事象に関連する危険因子はなかった。

投与された薬剤は，paracetamol，塩化ナトリウム，alizapride 及び stereofundin・ブドウ糖合剤であった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS (Started [redacted] 20[redacted], Stopped 201[redacted]

COLITOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], Stopped [redacted] 20[redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ETROLIZUMAB OR PLACEBO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

STELARA OR PLACEBO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Gastroenteritis (10017888) (Gastroenteritis (10017888)) [v.21.0] [10017888]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of GASTROENTERITIS

- Investigator: VIRAL INFECTION

- AbbVie: EVENT IS COMMON IN THE GENERALPOPULATION. ADDITIONAL RISK FACTOR INCLUDES PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 97 mg/dL (normal 0.0 to 7.0)

[redacted] **20[redacted] CRP:** 73 mg/dL (normal 0.0 to 7.0)

[redacted] **20[redacted] ULTRASOUND ABDOMEN:** Normal, viral gastroenteritis
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブを投与され，伝染性単核症の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 6 の臨床経過：

投与1355日後＊，被験者は伝染性単核症を発現した。

投与1355日後＊，被験者は発熱，咽頭痛，脱力感及び頭痛を経験していた。 投与1358日後＊，一般開業医を受診し，COVID-19 検査を受けたが結果は陰性であった。アモキシシリンで治療されたが，改善しなかった。その後も咽頭痛が続き，飲食も困難であった。

投与1361日後＊，咽頭痛，白い点が散らばった扁桃腺の大きな腫脹，左右対称の腫脹，口蓋垂の偏りなし，膿瘍の徴候なし，頭痛，熱っぽさ，脱力感，会話や飲食が困難，といった症状があり，救急治療室を受診した。単核症の迅速診断テストの結果は陽性であった。投与1363日後＊，エプスタイン・バーウイルスによる扁桃腺炎の経過は，臨床的に良好であった。被験者は全身倦怠感があり，飲食が困難であったが，大幅な回復が認められた。投与1365日後＊，被験者は退院した。

投与された薬剤は，paracetamol，トラマドール，methylprednisolon，litican，riopan，オーグメンチン，イブプロフェン，sterofundin・ブドウ糖合剤及びアモキシシリンであった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

COLITOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

CLAVERSAL for ULCERATIVE COLITIS ([redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted])

COLITOFALK ENEMA ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Infectious mononucleosis (10021914) (Infectious mononucleosis (10021914)) [v.23.1] [10021914]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of INFECTIOUS MONONUCLEOSIS

- Investigator: Not applicable.

- AbbVie: Event is common in the general population. Worldwide seropositive prevalence is estimated to be 90 to 95 percent. Primary Epstein-Barr virus (EBV) infection during childhood is usually subclinical, whereas infection of adolescents or adults results in infectious mononucleosis (IM) in 30 to 70% of cases and can prove severe.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **COVID 19 TEST:** Negative

[redacted] **CRP:** 18.7 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 7.4 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 4.1 MG/L (normal 0 to 5)

[redacted] **20[redacted] EPSTEIN BARR IGG:** Negative

[redacted] **20[redacted] EPSTEIN BARR IGM:** STRONG POSITIVE TEST

[redacted] **20[redacted] MONONUCLEOSE QUICKTEST:** POSITIVE TEST VIRAL CAUSE OF TONSILLITIS

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.20 X10**3/MCL (normal 4.2 to 9.8)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.33 X10**3/MCL (normal 4.2 to 9.8)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ヘリコバクター性胃炎	X			X
帯状疱疹				X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: ALLERGY IMURAN	20[redacted]
DRUG ALLERGIES/REACTIONS: REMICADE ALLERGIC REACTION	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ANXIETY DISORDER	NOT REPORTED
OTHER: ARTHRALGIA	NOT REPORTED
OTHER: CHRONIC SINUSITIS	20[redacted]
OTHER: CRAMPS	NOT REPORTED
OTHER: FIBROMYALGIA	20[redacted]
OTHER: HARD STOOL	20[redacted]
OTHER: RESECTION ENDO-ANAL POLYP (APO: TROMBOSED HEMORRHOID)	20[redacted]

Prior Procedures	Procedure Year
SAE SUPPLEMENTAL PROCEDURE: ABDOMINAL ULTRASOUND	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: CT ABDOMEN	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: RX ABDOMEN	20[redacted]
SURGERY: CESARIAN SECTION	19[redacted]
SURGERY: FISTULA RESECTION	20[redacted]
SURGERY: HAEMORRHOIDECETOMY	20[redacted]
SURGERY: SINUS SURGERY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	25	20[redacted]

CIGARS	NEVER
PIPES	NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 50	50
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 51	[redacted]20[redacted] / 91	41
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 93		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	250 mg	BID	Y-M: 20[redacted]
MESALAZINE	1 DF	QD	Y-M: 20[redacted]
MESALAZINE	500 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted]
BUDESONIDE	2 mg	OTHER: 2 TIMES A WEEK	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	325 mg	OTHER: WEEK 0 AND WEEK 2	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY WEEK	Y-M: 20[redacted]
BECLOMETASONE	5 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]
MESALAZINE	500 mg	QD	Y-M: 20[redacted]
BECLOMETASONE	3 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -337
BUDESONIDE	2 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -337
VEDOLIZUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted] / -317

BECLOMETASONE	5 mg	BID	Y-M: 20[redacted] / -323
METHYLPREDNISOLONE	8 mg	OTHER: EVERY 2 DAYS	Y-M: 20[redacted] / -242
MAGNESIUM SULFATE	450 mg	QD	Y-M: 20[redacted] / -202
INFLIXIMAB	375 mg	OTHER: ONCE	Y-M: 20[redacted] / -170
ANTIDEPRESSANTS IN COMBINATION WITH PSYCHOLEPTICS	1 DF	QD	Y-M: 20[redacted] / -172
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -92
CYSTEINE;DL-METHIONINE;HESPERIDIN;MINERALS NOS;PHOSPHORUS;VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -63
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -78
ENOXAPARIN	100 mg	QD	Y-M: 20[redacted] / -1
MOMETASONE	1 DF	BID	Y-M: 20[redacted] / -19
AMOXICILLIN;CLAVULANIC ACID	1 OTHER: TABLET	TID	Y-M: 20[redacted] / -3
DIHYDROCODEINE	10 mg	TID	Y-M: 20[redacted] / -3
ETHINYLESTRADIOL;LEVONORGESTREL	1 OTHER: TABLET	QD	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
MAGNESIUM SULFATE	450 mg	QD	Y-M: 20[redacted] / -202	Not reported
ANTIDEPRESSANTS IN COMBINATION WITH PSYCHOLEPTICS	1 DF	QD	Y-M: 20[redacted] / -172	Not reported
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -92	Not reported
CYSTEINE;DL-METHIONINE;HESPERIDIN;MINERALS NOS;PHOSPHORUS;VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -63	Not reported
MACROGOL 4000	1 OTHER: SACHET	PRN	Y-M: 20[redacted] / 63	Not reported
PARAFFIN, LIQUID	1 OTHER: TEASPOON	PRN	Y-M: 20[redacted] / 225	Not reported
MOMETASONE	1 OTHER: PUFF	PRN	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 894
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 489
ALIZAPRIDE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 490
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 491
HYOSCINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 490

PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 491
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 491
ENOXAPARIN	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 491	Y-M: 20[redacted] / 491
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 491	Y-M: 20[redacted] / 924
BISMUTH;METRONIDAZOLE;TETRACYCLINE	3 OTHER: TABLETS	QID	Y-M: 20[redacted] / 496	Y-M: 20[redacted] / 505
DYDROGESTERONE;ESTRADIOL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 712	Y-M: 20[redacted] / 1016
HERBAL POLLEN NOS;TOCOPHEROL	1 DF	BID	Y-M: 20[redacted] / 712	Not reported
ACICLOVIR	800 mg	OTHER: 5/DAY	Y-M: 20[redacted] / 830	Y-M: 20[redacted] / 837
FURAZOLIDONE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 830	Y-M: 20[redacted] / 837
AMOXICILLIN;CLAVULANIC ACID	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 833	Y-M: 20[redacted] / 836
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 833	Y-M: 20[redacted] / 840
ETHINYLESTRADIOL;LEVONORGESTREL	1 OTHER: TABLET	QD	Y: 20[redacted]	Y-M: 20[redacted] / 681

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	GASTRITIS WITH POSITIVE HELICOBACTER PYLORI
Preferred term	ヘリコバクター性胃炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 581 / 489
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 490): GASTROSCOPY: EROSIVE ANTRUM GASTRITIS AND REFLUX OESOPHAGITIS GRADE A; [redacted]20[redacted] (RX DAY 491): ABDOMINAL ULTRASOUND: NORMAL	
AE Stopped Initial Rx Day / Rx Day	597 / 505
Duration of AE	17 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NONE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 922 / 830
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	954 / 862
Duration of AE	33 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，ヘリコバクター・ピロリ陽性の胃炎の事象を発現した。関連する病歴は，瘻孔の切除，元喫煙者（1 日 1 箱を 25 年間），肛門内ポリープの切除（血栓性外痔核），痔瘻切除術，潰瘍性大腸炎（左側），硬便，不安障害及び現飲酒者（1 日 2 杯未満）であった。

この被験者は，先行の M14-234 試験では，被験者番号 [redacted] であり，20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで盲検化された治験薬を投与された。

Event 1 の臨床経過：

投与581日後＊，被験者はヘリコバクター・ピロリ陽性の胃炎を発現した。投与597日後＊，ヘリコバクター・ピロリ陽性の胃炎は消失した。

投与581日後＊　の夕方，被験者は咽頭まで至る心窩部仙痛，食道の焼けるような痛み，悪心を経験したが，嘔吐はなかった。投与582日後＊　，被験者は入院した。生化学検査では詳細は不明であり，胃内視鏡検査では，前庭部のびらん性胃炎及びグレード A の逆流性食道炎が指摘された。ヘリコバクター・ピロリの生検が行われた。超音波検査での差異は，目視では確認できなかった。不特定の鎮痛薬及び pantomed の投与が開始された。投与583日後＊ ，被験者は退院を許可された。投与587日後＊ ，免疫組織化学染色でヘリコバクター・ピロリの複数のコロニーが確認された。不特定の薬物治療が開始された。

投与された薬剤は，pantomed，tryplera，alizapride，paracetamol 及びブスコパンであった。

The patient's past medications include:

COLITOFALK SUPPO for ULCERATIVE COLITIS ([redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted])

CIPROXINE for ULCERATIVE COLITIS ([redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted])

MEDROL for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

REMSIMA for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　Helicobacter pylori gastritis (10051790)　(Helicobacter gastritis (10054272))　[v.22.1]　[10051790]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of GASTRITIS WITH POSITIVE HELICOBACTER PYLORI

- Investigator: None

- AbbVie: Event more likely related to Helicobacter pylori which is prevalent in the general population.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** normal

Unknown date BLOOD URINE: not reported

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** No inflammation seen (normal mucosa)

[redacted] **20[redacted] GASTROSCOPY:** Erosive antrum gastritis and reflux oesophagitis grade A.

[redacted] **20[redacted] IMMUNOHISTOCHEMICAL STAINING:** multiple colonies of Helicobacter pylori

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Herpes zoster: One dermatone.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肺炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
EYE DISEASE/DISORDER: KERATOCONJUNCTIVITIS SICCA	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ALLERGIC RHINITIS (HAY FEVER)	20[redacted]
OTHER: BACK PAIN	20[redacted]
OTHER: ERYTHEMA NODOSUM	20[redacted]
OTHER: HEAD ACHE	20[redacted]
OTHER: HYPERVENTILATION	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: PSORIASIS	20[redacted]
OTHER: PSYCHOLOGICAL SUPPORT NEEDED	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 60	60
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 74		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	TID	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: ONCE	Y-M: 20[redacted]
METHYLPREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BECLOMETASONE	2.5 mg	OTHER: EOD	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: DOSE UNIT	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	OTHER: EOD	Y-M: 20[redacted]
MESALAZINE	500 mg	QD	Y-M: 20[redacted]
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	10 mg/kg	OTHER: Q4W	Y-M: 20[redacted]
HYDROCORTISONE	1 DF	QD	Y-M: 20[redacted]
MESALAZINE	1 DF	QD	Y-M: 20[redacted]
BECLOMETASONE	1 DF	NOT REPORTED	Y-M: 20[redacted]
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted]
BECLOMETASONE	3 mg	NOT REPORTED	Y-M: 20[redacted]
BECLOMETASONE	5 mg	NOT REPORTED	Y-M: 20[redacted]
BECLOMETASONE	5 mg	BID	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
MESALAZINE	500 mg	OTHER: 4 TIMES 2 PER DAY	Y-M: 20[redacted]
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted]
METHOTREXATE	12 mg	1 time per week	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
MESALAZINE	3 g	QD	Y-M: 20[redacted]

MESALAZINE	500 mg	OTHER: 3 TIMES 2 PER DAY	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: Q4W	Y-M: 20[redacted]
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / -357
MESALAZINE	3 g	QD	Y-M: 20[redacted] / -357
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -357
METHYLPREDNISOLONE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / -357
BUDESONIDE	3 mg	QD	Y-M: 20[redacted] / -262
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted] / -214
ADALIMUMAB	40 mg	OTHER: Q2W	Y-M: 20[redacted] / -175
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted] / -129
ETHINYLESTRADIOL;LEVONORGESTREL	1 OTHER: TABLET	QD	Y: 20[redacted]
MESALAZINE	1 DF	QD	Y: 20[redacted]
FLUCONAZOLE	200 mg	OTHER: 1/MONTH	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
MESALAZINE	3 g	QD	Y-M: 20[redacted] / -357	ONGOING
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted] / -214	Y-M: 20[redacted] / 707
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 63	ONGOING
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 614	Y-M: 20[redacted] / 617
AMOXICILLIN	1 g	TID	Y-M: 20[redacted] / 616	Y-M: 20[redacted] / 617
AMOXICILLIN;CLAVULANIC ACID	1 g	OTHER: 4 X PER DAY	Y-M: 20[redacted] / 617	Y-M: 20[redacted] / 621
AZITHROMYCIN	250 mg	BID	Y-M: 20[redacted] / 617	Y-M: 20[redacted] / 621
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 618	Y-M: 20[redacted] / 620
AMOXICILLIN;CLAVULANIC ACID	875/125 mg	TID	Y-M: 20[redacted] / 621	Y-M: 20[redacted] / 625
AZITHROMYCIN	250 mg	QD	Y-M: 20[redacted] / 621	Y-M: 20[redacted] / 621
ETHINYLESTRADIOL;LEVONORGESTREL	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 690 / 617
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 617): NPTST085-CRP: 198 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (RX DAY 620): NPTST085-CRP: 140.1 [NOT REPORTED - 5] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 617): RX THORAX: PNEUMONIA

AE Stopped Initial Rx Day / Rx Day	694 / 621
Duration of AE	5 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，肺炎の事象を発現した。関連する病歴は，過換気，アレルギー性鼻炎，花粉症，乾癬，潰瘍性大腸炎（左側），非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与690日後＊，被験者は肺炎を発現した。投与694日後＊，肺炎は消失した。

投与690日後＊，被験者は発熱，咳嗽及び嗄声があり，救急治療室を受診し，入院した。胸部 X 線検査を行い，肺炎と診断された。抗生物質の静脈内投与による治療を開始した。被験者は具合が良くなり，投与694日後＊に退院した。

投与された薬剤は，paracetamol fresensius，オーグメンチン，azithromycine，clamoxyl，duovent 及び dafalgan であった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS ([redacted])

CLAVERSAL ENEMA for ULCERATIVE COLITIS ([redacted])

MEDROL for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted])

COLOFOAM for ULCERATIVE COLITIS ([redacted])

BECLOMETHASONE DIPROPIONATE SUPPOSITORY for ULCERATIVE COLITIS ([redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted])

COLITOFALK GRANULATE for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

SOLU-MEDROL for ULCERATIVE COLITIS ([redacted])

BUDENOFALK for ULCERATIVE COLITIS ([redacted])

HUMIRA VIAL for ULCERATIVE COLITIS ([redacted])

ALPHARIX TETRA for FLU VACCINE ([redacted])

Causality for UPADACITINIB (Open Label)

＊新薬承認情報提供時に置き換え

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.22.1] [10035664]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

Event of PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 198 MG/L (normal <5)

[redacted] **20[redacted] CRP:** 140.1 MG/L (normal <5)

[redacted] **20[redacted] WEIGHT: 7[redacted]** KG

[redacted] **20[redacted] XRAY:** pneumonia

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	5[redacted]	MALE	WHITE

Medical History	Onset Year
DEPRESSION: DEPRESSIVE FEELINGS	20[redacted]
HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA	NOT REPORTED
HYPOTHYROIDISM	20[redacted]
LEFT SIDED UC	19[redacted]
OTHER: ANXIETY DISORDER	NOT REPORTED
OTHER: BACK PAIN(INTERMITTENT)	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 84	28

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 91	[redacted]20[redacted] / 100	10

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BECLOMETASONE	5 mg	OTHER: QW	Y-M: 19[redacted]
INFLIXIMAB	10 mg/kg	OTHER: 1/4WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: QW	Y-M: 20[redacted]
MESALAZINE	1.5 g	BID	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: 1/8WEEKS	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: 1/4WEEKS	Y-M: 20[redacted]
LEVOTHYROXINE	25 ug	QD	Y-M: 20[redacted]
CLORAZEPIC ACID	10 mg	BID	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: 1/8WEEKS	Y-M: 20[redacted] / -327
BECLOMETASONE	5 mg	BID	Y-M: 20[redacted] / -279
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -279
VEDOLIZUMAB	300 mg	OTHER: 1/4WEEKS	Y-M: 20[redacted] / -241
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / -5
LOPERAMIDE	2 mg	PRN	Y: 19[redacted]
MESALAZINE	4 g	QD	Y: 19[redacted]
AZATHIOPRINE	200 mg	QD	Y: 20[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y: 20[redacted]
FENOFIBRATE	267 mg	QD	Y: 20[redacted]
PANTOPRAZOLE	20 mg	QD	Y: 20[redacted]
PAROXETINE	30 mg	BID	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
OLANZAPINE	12.5 mg	QD	Not reported	ONGOING
MESALAZINE	1.5 g	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 39
LEVOTHYROXINE	25 ug	QD	Y-M: 20[redacted]	ONGOING
CLORAZEPIC ACID	10 mg	BID	Y-M: 20[redacted]	ONGOING
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / -5	Y-M: 20[redacted] / 11
BECLOMETASONE	5 mg	BID	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 25
ASCORBIC ACID;CALCIUM CARBONATE;COLECALCIFEROL; ERGOCALCIFEROL	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 38

METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 38
METHYLPREDNISOLONE	28 mg	QD	Y-M: 20[redacted] / 39	Y-M: 20[redacted] / 40
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 40	ONGOING
HYDROCORTISONE	50 mg	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 40
LEVOBUPIVACAINE	250 mg	PRN	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 40
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 43
PIPERACILLIN;TAZOBACTAM	4 g	QID	Y-M: 20[redacted] / 40	ONGOING
SUFENTANIL	200 mL	PRN	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 40
HYDROCORTISONE	50 mg	BID	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 41
MORPHINE	7 mg	PRN	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 42
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 42
HYDROCORTISONE	25 mg	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
LORAZEPAM	1 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 43
METHYLPREDNISOLONE	28 mg	QD	Y-M: 20[redacted] / 43	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 43	ONGOING
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 43	ONGOING
TRAMADOL	100 mg	BID	Y-M: 20[redacted] / 43	ONGOING
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 43	ONGOING
LOPERAMIDE	2 mg	PRN	Y: 19[redacted]	Y-M: 20[redacted] / 39
FENOFIBRATE	267 mg	QD	Y: 20[redacted]	ONGOING
PANTOPRAZOLE	20 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 40
PAROXETINE	30 mg	BID	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	WORSENING UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 128 / 38 (28 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 38): Hemoglobin: 141 [140 - 180] G/L; NPTST054-C REACTIVE PROTEIN: 6.0 [NOT REPORTED - 5] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 40): TOTAL COLECTOMY: TOTAL COLECTOMY WITH ILEOSTOMY

AE Stopped Initial Rx Day / Rx Day ONGOING

Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNDERLYING DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，及び潰瘍性大腸炎での入院であった。

Event 1 の臨床経過：

投与128日後＊，被験者は潰瘍性大腸炎の悪化を発現した。

投与100日後＊，有効性が認められないため，治験薬の投与は中止された。投与128日後＊，被験者は血性下痢があり，入院した。入院中，血性下痢が続いた。投与130日後＊，被験者は回腸瘻造設を伴う結腸全摘術を受けた。投与140日後＊，被験者は退院した。

治験責任医師によると，被験者の本事象に関連する危険因子には，潰瘍性大腸炎の病歴が含まれた。被験者は投与の約11年7ヵ月前＊に潰瘍性大腸炎の悪化があり，入院していた。

投与された薬剤は，chirocaine，オンダンセトロン，クレキサン，モルヒネ，ピペラシリン・タゾバクタム合剤，contramal，tradonal，dafalgan，paracetamol，temesta，ソル・コーテフ及び sufentanil であった。

The patient's past medications include:

BECLOMETHASONE DIPROPIONATE for ULCERATIVE COLITIS ([redacted] 19[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.20.1] [10009901]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of WORSENING UC

- Investigator: Underlying disease.

- AbbVie: Event is clearly consistent with progression or worsening of the underlying disease and is considered expected for this study.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] **20[redacted] C REACTIVE PROTEIN:** 6.0 MG/L (normal <5.0)

[redacted] [redacted] **20[redacted] HEMOGLOBIN:** 14.1 G/DL (normal 14.0 to 18.0)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	5[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
EYE DISEASE/DISORDER: BILATERAL SEROSA CENTRALIS	20[redacted]
EYE DISEASE/DISORDER: BLEPHARITIS	20[redacted]
EYE DISEASE/DISORDER: GLAUCOMA	NOT REPORTED
HEPATITIS: AZATHIOPRINE INDUCED HEPATITIS	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ARTHRALGIA KNEES	20[redacted]
OTHER: FOLIC ACID DEPLETION	20[redacted]
OTHER: INTERMITTENT ARTHRALGIA	20[redacted]
OTHER: TIREDNESS	NOT REPORTED
OTHER: TRIGEMINAL NEURALGIA	19[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.15 PACK	24	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted] / 1	[redacted] / 53	53
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 54	[redacted] / 430	377

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
PARACETAMOL	1 g	PRN	Y-M: [redacted]
INFLIXIMAB	5 mg/kg	OTHER: 1/8WEEKS	Y-M: [redacted]
BUDESONIDE	3 mg	NOT REPORTED	Y-M: [redacted]
INFLIXIMAB	5 mg/kg	OTHER: 1/4WEEKS	Y-M: [redacted]
GOLIMUMAB	50 mg	OTHER: 1/4WEEKS	Y-M: [redacted]
MESALAZINE	2 g	BID	Y-M: [redacted]
MESALAZINE	4 g	QD	Y-M: [redacted]
BLINDED THERAPY	105 mg	OTHER: 1/4WEEKS	Y-M: [redacted]
ETROLIZUMAB	105 mg	OTHER: 1/4WEEKS	Y-M: [redacted]
BECLOMETASONE	5 mg	OTHER: QOD	Y-M: [redacted]
BLINDED THERAPY	NOT REPORTED	NOT REPORTED	Y-M: [redacted] / -335
INVESTIGATIONAL DRUG	600 mg	NOT REPORTED	Y-M: [redacted] / -245
INVESTIGATIONAL DRUG	200 mg	NOT REPORTED	Y-M: [redacted] / -155
PANTOPRAZOLE	20 mg	QD	Y-M: [redacted] / -129
ISONIAZID	300 mg	QD	Y-M: [redacted] / -67
PYRIDOXINE	250 mg	Every week	Y-M: [redacted] / -67
TRAMADOL	50 mg	PRN	Y-M: [redacted] / -12
SODIUM CHLORIDE;WATER	100 mL	PRN	Y-M: [redacted] / -13
ACETYLSALICYLIC ACID	80 mg	QD	Y-M: [redacted] / -7
LEVOFLOXACIN	500 mg	QD	Y-M: [redacted] / -8
AZATHIOPRINE	150 mg	QD	Y: [redacted]
MESALAZINE	NOT REPORTED	QD	Y: [redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	1 g	PRN	Y-M: [redacted]	ONGOING

MESALAZINE	2 g	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 401
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -129	Y-M: 20[redacted] / 402
SODIUM CHLORIDE;WATER	100 mL	PRN	Y-M: 20[redacted] / -13	ONGOING
ACETYLSALICYLIC ACID	80 mg	QD	Y-M: 20[redacted] / -7	ONGOING
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 107	ONGOING
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / 382	Y-M: 20[redacted] / 401
IRON	1 g	QD	Y-M: 20[redacted] / 382	Y-M: 20[redacted] / 382
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 399	ONGOING
ALPRAZOLAM	0.5 mg	QD	Y-M: 20[redacted] / 400	Y-M: 20[redacted] / 402
ACETYLSALICYLIC ACID	500 mg	QD	Y-M: 20[redacted] / 401	Y-M: 20[redacted] / 401
PIPERACILLIN;TAZOBACTAM	4 g	BID	Y-M: 20[redacted] / 401	ONGOING
SODIUM PHOSPHATE	133 mL	QD	Y-M: 20[redacted] / 401	Y-M: 20[redacted] / 401
LEVOBUPIVACAINE	250 mg	QD	Y-M: 20[redacted] / 402	Y-M: 20[redacted] / 403
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 402	Y-M: 20[redacted] / 406
SUFENTANIL	10 ug	PRN	Y-M: 20[redacted] / 402	Y-M: 20[redacted] / 403
HYDROCORTISONE	50 mg	BID	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 403
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 408
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 404
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 404	ONGOING
MORPHINE	5 mg	PRN	Y-M: 20[redacted] / 404	Y-M: 20[redacted] / 405
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 405	Y-M: 20[redacted] / 405
TRAMADOL	50 mg	QD	Y-M: 20[redacted] / 405	Y-M: 20[redacted] / 405
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;GLYCINE MAX;OLEA EUROPAEA	2 ug/m2	PRN	Y-M: 20[redacted] / 406	ONGOING
LOPERAMIDE	2 mg	TID	Y-M: 20[redacted] / 406	Y-M: 20[redacted] / 406
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 406	Y-M: 20[redacted] / 406
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 407	ONGOING
TRAMADOL	100 mg	BID	Y-M: 20[redacted] / 407	Y-M: 20[redacted] / 407
DOMPERIDONE	10 mg	TID	Y-M: 20[redacted] / 409	Y-M: 20[redacted] / 409

Event #1: AE Leading to Discontinuation of Study Drug

Event Description	WORSENING ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 429 / 376
Age at AE Onset	5[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	452 / 399 (22 DAYS AFTER LAST TREATMENT)
Duration of AE	24 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	WORSENING UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 452 / 399 (22 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 402): LAPAROSCOPIC TOTAL COLECTOMY WITH ILEOSTOMA: SURGERY WITHOUT COMPLICATIONS

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNDERLYING DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.15 箱を 24 年間）及び禁酒であった。

Event 2 の臨床経過：

投与452日後＊，被験者は潰瘍性大腸炎の悪化を発現した。

投与429日後＊ から 投与452日後＊ に，被験者は潰瘍性大腸炎の悪化（非重篤）を経験した。

投与452日後＊ ，被験者は潰瘍性大腸炎の症状の悪化により予定された手術のため，入院した。被験者は血性下痢，腹部仙痛及び断続的な発熱を経験した。投与455日後＊ ，被験者は回腸瘻造設を伴う腹腔鏡下での結腸全摘術を受け，合併症は認められなかった。

投与された薬剤は，pantomed，sufentanil，オンダンセトロン，ソル・コーテフ，paracetamol，tpn periolimel，imodium 及び motilium であった。

The patient's past medications include:

5-ASA for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

IMURAN for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BUDENOFALK for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

SIMPONI for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

COLITOFALK for ULCERATIVE COLITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted])

ANTI IL-23 for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.1] [10009901]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of WORSENING UC

- Investigator: UNDERLYING DISEASE

- AbbVie: EVENT IS MORE LIKELY RELATED TO RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
AMENORRHEA	20[redacted]
ANAL HEMORROIDS	20[redacted]
ANAL PAIN INTERMITTENT	20[redacted]
ARTHRALGIA INTERMITTENT	20[redacted]
CHONDROSIS L4-L5	20[redacted]
DEPRESSIVE FEELINGS INTERMITTENT	20[redacted]
DISCUS BULGING L4-L5	20[redacted]
DISCUSHERNIA L5S1	20[redacted]
EPIGASTRIC PAIN INTERMITTENT	20[redacted]
FATIGUE INTERMITTENT	20[redacted]
HEADACHE INTERMITTENT	20[redacted]
IRON DEFICIENCY INTERMITTENT	20[redacted]
LEFT SIDED UC	19[redacted]
LUMBO-ISCHIALGIA LEFT	20[redacted]
MYALGIA	20[redacted]
POLYCYSTIC OVARY SYNDROME	20[redacted]
PSORIASIFORM RASH DUE TO REMICADE	20[redacted]
SEBORREIC ECZEMA	20[redacted]
STRESS	20[redacted]
URINARY TRACT INFECTION INTERMITTENT	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: SURGERY FOR DISCUSHERNIA	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	12	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 54	[redacted]20[redacted] / 195	142
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 195	[redacted]20[redacted] / 224	30

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
BECLOMETASONE	3 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	160 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	80 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	5 mg/kg	OTHER: WK 0, WK 2 AND WEK 6	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	10 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
MESALAZINE	500 mg	QD	Y-M: 20[redacted]-[redacted]

BECLOMETASONE	5 mg	OTHER: EOD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
BECLOMETASONE	3 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted]
BECLOMETASONE	3 mg	OTHER: EOD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 6 WEEKS AND AFTERWARDS EVERY 4 WEEKS	Y-M: 20[redacted] / -324
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / -280
BECLOMETASONE	10 mg	QD	Y-M: 20[redacted] / -299
CODEINE;PARACETAMOL	530 mg	PRN	Y-M: 20[redacted] / -244
BECLOMETASONE	3 mg	QD	Y-M: 20[redacted] / -251
BALLOTA NIGRA;CRATAEGUS LAEVIGATA;PASSIFLORA INCARNATA	1 OTHER: TABLET	BID	Y-M: 20[redacted] / -172
ORIGANUM VULGARE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -172
LOPERAMIDE	4 mg	QD	Y-M: 20[redacted] / -19
BUDESONIDE	3 mg	QD	Y: 19[redacted]
SULFASALAZINE	1 g	BID	Y: 19[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CODEINE;PARACETAMOL	530 mg	PRN	Y-M: 20[redacted] / -244	ONGOING
BALLOTA NIGRA;CRATAEGUS LAEVIGATA;PASSIFLORA INCARNATA	1 OTHER: TABLET	BID	Y-M: 20[redacted] / -172	ONGOING
ORIGANUM VULGARE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -172	Y-M: 20[redacted] / 4
LOPERAMIDE	4 mg	QD	Y-M: 20[redacted] / -19	ONGOING
PNEUMOCOCCAL VACCINE	0.5 mL	OTHER: ONC	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
ESTRADIOL;NOMEGESTROL	UNKNOWN mg	QD	Y-M: 20[redacted] / 17	ONGOING
DILTIAZEM	UNKNOWN OTHER: UNKNOWN	BID	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 66
ALIZAPRIDE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 31
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 34
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 34
PARACETAMOL	1 g	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 34
TRAMADOL	50 mg	TID	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 34

CALCIUM CARBONATE;COLECALCIFEROL	1000 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 66
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 48
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 66
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 66
TRAMADOL	40 mg	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 66
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 28

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	WORSENING ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 225 / 31 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 31): SIGMOIDOSCOPY: MAYO 3 COLITIS

AE Stopped Initial Rx Day / Rx Day	228 / 34 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	LACK OF RESPONSE TO STUDY DRUG
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，多嚢胞性卵巣症候群，断続的な心窩部痛，断続的な鉄欠乏，ストレス，元喫煙者（1 日 0.5 箱を 12 年間），断続的な肛門痛，肛門の痔核及び禁酒であった。

Event 1 の臨床経過：

投与225日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与228日後＊　，潰瘍性大腸炎の悪化は消失した。

投与225日後＊　，全身状態の悪化を伴う潰瘍性大腸炎の悪化があり，入院した。症状には，触診時の左側腹部窩及び恥骨上の部位の痛みが含まれた。投与228日後＊　，被験者は退院した。

投与された薬剤は，litican 及びソル・メドロールであった。

The patient's past medications include:

ENTOCORT for ULCERATIVE COLITIS (19[redacted] - 20[redacted], 19[redacted] - 20[redacted])

MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted], [redacted] 20[redacted] - 20[redacted], [redacted] 20[redacted] - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BECLOMETHASONE DIPROPRIONATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

A.D.P. BIOTICS (ORAGANO EXTRACT) for SUPPLEMENT ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.22.1]　[10009901]

C**ausality as per reporter (Drug/Vaccine):** No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of WORSENING ULCERATIVE COLITIS

- Investigator: LACK OF RESPONSE TO STUDY DRUG

- AbbVie: Event is more likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] SIGMOIDOSCOPY:** MAYO 3 COLITIS

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
尿路結石	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	3[redacted]	MALE	WHITE

Medical History	Onset Year
ACNE	20[redacted]
HEMORRHOIDS	20[redacted]
LEFT SIDED UC	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0 PACK	13	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS2 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 113	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 114	[redacted]20[redacted] / 144	31

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 144

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	40 mg	OTHER: EVERY WEEK	Y-M: 20[redacted]-[redacted]
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted]-[redacted]
CALCIUM CARBONATE;COLECALCIFEROL	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	10 mg/kg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]-[redacted]
METHOTREXATE	5 mg/kg	1 time per week	Y-M: 20[redacted]-[redacted]
BECLOMETASONE	NOT REPORTED	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / -326
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted] / -326
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted]-[redacted] / -332
BUDESONIDE	NOT REPORTED	OTHER: UKNOWN	Y: 20[redacted]
BUDESONIDE	NOT REPORTED	OTHER: UNKNOWN	Y: 20[redacted]
MESALAZINE	2 g	BID	Y: 20[redacted]
MESALAZINE	NOT REPORTED	OTHER: UNKNOWN	Y: 20[redacted]
MESALAZINE	4 g	QD	Y: 20[redacted] / -2

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BECLOMETASONE	NOT REPORTED	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / -326	Not reported
PARACETAMOL	UNK mg	PRN	Y-M: 20[redacted]-[redacted] / 224	Y-M: 20[redacted]-[redacted] / 232
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]-[redacted] / 224	Y-M: 20[redacted]-[redacted] / 232
TRAMADOL	50 mg	BID	Y-M: 20[redacted]-[redacted] / 230	Y-M: 20[redacted]-[redacted] / 232
BUDESONIDE	NOT REPORTED	OTHER: UKNOWN	Y: 20[redacted]	Not reported
BUDESONIDE	NOT REPORTED	OTHER: UNKNOWN	Y: 20[redacted]	Not reported
MESALAZINE	2 g	BID	Y: 20[redacted]	Y: 20[redacted] / 364
MESALAZINE	NOT REPORTED	OTHER: UNKNOWN	Y: 20[redacted]	Not reported
MESALAZINE	4 g	QD	Y: 20[redacted] / -2	Not reported

Event #1: Serious Adverse Event

Event Description	UROLITHIASIS
Preferred term	尿路結石
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 367 / 224
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 229): Erythrocytes: POSITIVE [0 - 6] /?L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 230): CT ABDOMEN LOW DOSE: REGRESSION OF UROLITHIASIS, MILD HYDRONEFROSIS, SOME LITHIASIS FRAGMENTS IN BLADDER; [redacted]20[redacted] (RX DAY 231): ECHO ABDOMEN: SUSPECION OF SOME UROLITHIASIS FRAGMENTS AT THE VESICOURETERAL JUNCTION

AE Stopped Initial Rx Day / Rx Day	374 / 231
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INSUFFICIENT FLUID INTAKE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はベルギーの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，尿路結石症の事象を発現した。関連する病歴は，元喫煙者（13 年間）及び潰瘍性大腸炎であった。

Event 1 の臨床経過：

投与367日後＊　，被験者は尿路結石症を発現した。投与374日後＊　，尿路結石症は消失した。

本事象発現前の 投与304日後＊，被験者は顕微鏡的血尿（非重篤）を経験した
。

投与372日後＊　，被験者は入院した。被験者は同日，既知の尿路結石症に対して，体外衝撃波結石破砕術（ESWL）を受けた。数時間後に右側腹部に仙痛が生じ，救急科を受診した。被験者は全血球計算，CRP，肝機能検査，腎機能検査，生化学検査及びアルブミン検査を受けた（検査結果は提供されなかった）。投与374日後＊，被験者は退院した。

投与された薬剤は，contramal retard，tradonal 及び paracetamol であった。

The patient's past medications include:

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

LEDERTREXAAT for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

CLIPPER for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

TRAMADOL for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　Urolithiasis (10046707)　(Calculus urinary (10007027))　[v.23.0]　[10046707]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of UROLITHIASIS

- Investigator: Insufficient fluid intake

- AbbVie: Renal stone is a relatively common problem with an estimated 16 percent of men will be diagnosed with a kidney stone by age of 70 years. Additional risk factor is "insufficient fluid intake" as noted by PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN LOW DOSE:** Regression of urolithiasis, mild hydronefrosis, some lithiasis fragments in bladder

[redacted] **20[redacted] ECHO ABDOMEN:** Suspicion of some urolithiasis fragments at the vesicoureteral junction

[redacted] **20[redacted] URINE RED BLOOD CELLS:** positive (0-6)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19 肺炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	6[redacted]	MALE	WHITE

Medical History	Onset Year
HERNIA	20[redacted]
LEFT FOOT TRAUMA	20[redacted]
LEFT HAND TRAUMA	20[redacted]
LEFT SIDED UC	20[redacted]
LOWER LIMB PAIN	20[redacted]
PTERYGIUM	20[redacted]
TUBERCULOSIS	20[redacted]
ULCERATIVE COLITIS	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: LEFT FOOT ORTHOPEDIC SURGERY	20[redacted]
PRIOR PROCEDURES: LEFT HAND ORTHOPEDIC SURGERY	20[redacted]
PRIOR PROCEDURES: LEFT INGUINAL HERNIORRHAPHY	20[redacted]
PRIOR PROCEDURES: PTERYGIUM EXERESIS	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	More than 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 81	81
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 82	[redacted]20[redacted] / 278	197
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 282		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	2 g	QD	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
METRONIDAZOLE	400 mg	TID	Y-M: 20[redacted] / -57
PREDNISONE	20 mg	BID	Y-M: 20[redacted] / -57
MESALAZINE	1 g	QD	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LOSARTAN	50 mg	QD	Y-M: 20[redacted] / 35	ONGOING
METAMIZOLE	1 g	BID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 111
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 114
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 115
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 111	Y-M: 20[redacted] / 122
CODEINE;PARACETAMOL	250 mg	TID	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 119
METAMIZOLE	1 g	QD	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 112
METAMIZOLE	1 g	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 114
PIPERACILLIN;TAZOBACTAM	4 g	QID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 123
DEXAMETHASONE	6 mg	QD	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 122
COLCHICINE	0,5 mg	TID	Y-M: 20[redacted] / 118	Y-M: 20[redacted] / 122
RIVAROXABAN	10 mg	QD	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 153

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	COVID-19 PNEUMONIA INFECTION
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted] / 385 / 104
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted] (RX DAY 111): Leukocytes: 13.5 [3.79 - 10.33] 10^9/L; NPTST058-C-REACTIVE PROTEIN: 42.10 [0 - 1] MG/DL; [redacted] (RX DAY 116): Leukocytes: 9.7 [3.79 - 10.33] 10^9/L; NPTST055-C- REACTIVE PROTEIN: 26.00 [0 - 1] MG/DL; [redacted] (RX DAY 119): Leukocytes: 9.1 [3.79 - 10.33] 10^9/L; NPTST055-C- REACTIVE PROTEIN: 7.50 [0 - 1] MG/DL; [redacted] (RX DAY 123): Leukocytes: 11.3 [3.79 - 10.33] 10^9/L; NPTST055-C-REACTIVE PROTEIN: 1.00 [0 - 1] MG/DL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted] (RX DAY 116): CT-SCAN: COMPATIBLE OPACITIES WITH THE HYPOTHESIS OF MODERATE VIRAL PNEUMONIA OF COVID-19 AND RIGHT INFERIOR BACTERIAL OU FUNGAL PNEUMONIA ASSOCIATED. CARDIOMEGALIA AND INFLAMMATORY MEDIASTINAL LYMPHADENOPATHY .

AE Stopped Initial Rx Day / Rx Day	421 / 140
Duration of AE	37 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はブラジルの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，COVID-19 肺炎の感染症の事象を発現した。関連する病歴は，潰瘍性大腸炎，結核，非喫煙者及び元飲酒者（1 日 4 杯以上）であった。

Event 1 の臨床経過：

投与385日後＊ ，被験者はCOVID-19肺炎の感染症を発現した。投与421日後＊ ，COVID-19肺炎の感染症は消失した。

本事象発現前の 投与288日後＊から 投与315日後＊ ，被験者はCOVID-19 感染症（非重篤）を経験していた。

投与392日後＊ ，被験者は全身状態の悪化，分泌物を含む咳嗽，呼吸困難，悪寒，及び聞き取れる程度の喘鳴があり，入院した。被験者の血球数及び C-反応性タンパク質の検査値が細菌感染を示唆する数値であったため，当初は細菌性肺炎の治療を受けた。アジスロマイシン及びセフトリアキソンによる治療が開始された。投与393日後＊ ，ウイルス学的にCOVID-19 が確認されたが，同日に行った別の COVID-19 の検査の結果は陰性であった。被験者が COVID-19 に再感染したかは，確認できなかった。胸部 CT スキャン検査では，COVID-19 感染及び細菌性肺炎が確認された。抗生物質による治療は，病院の COVID-19 治療の実施要項にあるデキサメタゾン及びコルヒチンに加えて，タゾシンに変更され実施された。投与404日後＊ ，被験者は退院した。最終的な診断は，COVID-19 肺炎の感染症及び原因不明の同時感染であった。

投与された薬剤は，エノキサパリン，dipirone，アジスロマイシン，セフトリアキソン，タゾシン，paco，デキサメタゾン，colchicina 及びリバーロキサバンであった。

The patient's past medications include:

SULFASALAZINE for ULCERATIVE COLITIS ([redacted])

MESALAZINE for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

METRONIDAZOLE for WORSENING OF ULCERATIVE COLITIS ([redacted])

PREDNISONE for WORSENING OF ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.24.0] [10084380]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, outcome unknown

Alternative Etiology for UPADACITINIB (Open Label)

Event of COVID-19 PNEUMONIA INFECTION

- Investigator: Not applicable.

- AbbVie: Event is more likely related to the COVID-19 pandemic outbreak.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 31.4 kg/m2

[redacted] **20[redacted] CHEST X-RAY (WEEK 0):** Normal

[redacted] **20[redacted] CHEST X-RAY:** Normal

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Positive

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Positive

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Negative

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Positive

[redacted] **20[redacted] SARS-COV-2 TEST:** Nasopharyngeal Swab: Negative

[redacted] **20[redacted] CT SCAN:** Compatible opacities with the hypothesis of moderate viral pneumonia of Covid-19 and right inferior bacterial or fungal pneumonia associated. Cardiomegalia and inflammatory mediastinal lymphadenopathy.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
静脈血栓症	X	X		X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
POST MENOPAUSAL	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS2 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 117	61
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 118	[redacted]20[redacted] / 201	84

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 209	[redacted]20[redacted] / 236	28

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EACH 8 WEEKS	Y-M: 20[redacted]
ETROLIZUMAB	105 mg	OTHER: EACH 4 WEEKS	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -18
PREGABALIN	75 mg	QD	Y-M: 20[redacted] / -22
ASCORBIC ACID	500 mg	QD	Y: 20[redacted]
CRATAEGUS SPP.	1 OTHER: CAPSULE	QD	Y: 20[redacted]
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	5000 ug	OTHER: EACH 3 MONTHS	Y: 20[redacted]
FOLIC ACID	5 mg	QD	Y: 20[redacted]
VITAMIN D NOS	1000 IU	QD	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -18	Not reported
PREGABALIN	75 mg	QD	Y-M: 20[redacted] / -22	Not reported
ENOXAPARIN	60 mg	BID	Y-M: 20[redacted] / 18	Y-M: 20[redacted] / 21
RIVAROXABAN	15 mg	BID	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 34
ASCORBIC ACID	500 mg	QD	Y: 20[redacted]	Not reported
CRATAEGUS SPP.	1 OTHER: CAPSULE	QD	Y: 20[redacted]	Not reported
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	5000 ug	OTHER: EACH 3 MONTHS	Y: 20[redacted]	Not reported
FOLIC ACID	5 mg	QD	Y: 20[redacted]	Not reported
VITAMIN D NOS	1000 IU	QD	Y: 20[redacted]	Not reported

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	ACUTE VENOUS THROMBOSIS
Preferred term	静脈血栓症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 226 / 18
Age at AE Onset	6[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 20): NPTST193-PROTHROMBIN ACTIVITY TIME: 12.6 [11 - 15] SEC; Platelets: 238 [140 - 440] 10^9/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	229 / 21
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はブラジルの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，急性静脈血栓症の事象を発現した。関連する病歴は，閉経後，広範囲な潰瘍性大腸炎（全大腸炎型），貧血，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与226日後＊，被験者は急性静脈血栓症を発現した。投与229日後＊，急性静脈血栓症は消失した。

本事象発現前の 投与の約5ヵ月後＊に，被験者は潰瘍性大腸炎の悪化（非重篤）と診断され，発現時に継続していた。

投与226日後＊，被験者は左下腿の疼痛及び重度の浮腫があり，救急治療室を受診した。超音波検査で，左総大腿静脈及び左大腿深静脈の急性血栓症と診断された。投与226日後＊，被験者は入院した。被験者は，血栓症に対して，圧迫包帯，体位の調節，内服薬及び皮下注射薬で治療された。投与229日後＊，被験者はイグザレルトを投与され，退院した。

治験責任医師によると，本事象に関連する危険因子は，被験者の年齢が 40 歳以上であること，及び炎症性腸疾患であった。

本事象により，被験者の治験は中止された。

投与された薬剤は，エノキサパリン，イグザレルト及びプレガバリンであった。

The patient's past medications include:

MESALAZINE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Venous thrombosis (10047249) (Venous thrombosis (10047249)) [v.23.1] [10047249]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of ACUTE VENOUS THROMBOSIS

- Investigator: Not applicable

- AbbVie: Risk factors include concurrent worsening of ulcerative colitis (Chronic inflammatory diseases have been associated with activation of coagulation and an increased risk of venous thromboembolic events (VTEs), in particular during active disease. This has been shown for inflammatory bowel disease) and advanced age (Per the AHA -American Heart Associaton - patients older than 40 years are at higher risk, and that risk doubles with each subsequent decade.)

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] DOPPLER ULTRASOUND LEFT LOWER EXTREMITY:** Acute thrombosis of the left femoral common, femoral and deep femoral veins

[redacted] **20[redacted] PLATELET COUNT:** 238 X10**3/MM**3 (normal 140 to 440)

[redacted] **20[redacted] PT:** 12.6 SEC (normal 11 to 15)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ヘモグロビン減少				X
肺塞栓症	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
ALLERGY TO IMMURAN	20[redacted]
HEAVY MENSES	20[redacted]
LEFT SIDED UC	20[redacted]
NAUSEA	20[redacted]
PULMONARY EMBOLI	20[redacted]
SICKLE CELL ANEMIA	19[redacted]
VOMITTING	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted] / 1	[redacted] / 59	59
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 60	[redacted] / 101	42
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 102		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 g	QD	Y-M: [redacted] / -219
PREDNISONE	10 mg	QD	Y-M: [redacted] / -14
INFLIXIMAB	5 mg	OTHER: MONTHLY	Y: [redacted]
ADALIMUMAB	40 mg	QD	Y: [redacted]
VEDOLIZUMAB	300 mg	OTHER: Q 8 WEEKS	Y: [redacted]
PREDNISONE	5 mg	QD	Y: [redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PREDNISONE	10 mg	QD	Y-M: [redacted] / -14	Y-M: [redacted] / 169
CALCIUM	500 mg	BID	Y-M: [redacted] / 7	ONGOING
IRON	200 mg	OTHER: ONCE	Y-M: [redacted] / 7	Y-M: [redacted] / 7
PANTOPRAZOLE	40 mg	QD	Y-M: [redacted] / 7	ONGOING
RIVAROXABAN	15 mg	BID	Y-M: [redacted] / 7	ONGOING
VITAMIN D NOS	1000 IU	QD	Y-M: [redacted] / 7	ONGOING
PREDNISONE	7.5 mg	QD	Y-M: [redacted] / 170	Y-M: [redacted] / 201
PREDNISONE	5 mg	QD	Y-M: [redacted] / 202	Y-M: [redacted] / 230
PREDNISONE	2.5 mg	QD	Y-M: [redacted] / 231	Y-M: [redacted] / 306

Event #1: Serious Adverse Event, Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	PULMONARY EMBOLUS
Preferred term	肺塞栓症
AE Onset Date / Initial Rx Day / Rx Day	[redacted] / 102 / 1
Age at AE Onset	[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 2): NPTST048-BLOOD GASES: PH 7.46 PCO2 35 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 1): CT SCAN: RIGHT PULMONARY INFARCT SUSPECTED; [redacted]20[redacted] (RX DAY 3): ECHOCARDIOGRAM: NO ABNORMALITIES; [redacted]20[redacted] (RX DAY 5): CXR: OPACITY RLL

AE Stopped Initial Rx Day / Rx Day	108 / 7
Duration of AE	7 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	WORSENING OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: Event of Interest - Anemia

Event Description	LOW HEMAGLOBIN
Preferred term	ヘモグロビン減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 188 / 87
Age at AE Onset	2[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ラクナ梗塞	X	X		X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	4[redacted]	MALE	WHITE

Medical History	Onset Year
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: SHOULDER SURGERY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-675 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 119	63
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 120	[redacted]20[redacted] / 168	49
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 225	57

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	5 mg	QD	Y-M: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 30	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 49

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated MACE *

Event Description	ACUTE LACUNAR INFARCT RIGHT THALAMUS
Preferred term	ラクナ梗塞
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 197 / 29
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 29): CAROTID DUPLEX EXAM: NORMAL; [redacted]20[redacted] (RX DAY 30): MRI HEAD: ACUTE LACUNAR INFARCT RIGHT THALMUS

AE Stopped Initial Rx Day / Rx Day	199 / 31
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INVESTIGATIONS ONGOING
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はカナダの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，右視床部の急性期ラクナ梗塞の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与197日後＊　，被験者は右視床部の急性期ラクナ梗塞を発現した。投与199日後＊　，右視床部の急性期ラクナ梗塞は消失した。

投与197日後＊　，被験者は全身の脱力感，左側（顔及び腕）の動作及び/又は感覚の喪失，失語症，並びに浮動性及び回転性めまいがあり，入院した。被験者は，これらの症状はあるものの，重大な障害は認められず，通常の業務及び活動が全て可能であった。投与199日後＊　，被験者は退院した。

投与された薬剤は，プラビックス及びアセチルサリチル酸腸溶錠であった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1)　Lacunar infarction (10051078)　(Lacunar infarction (10051078))　[v.23.1]　[10051078]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of ACUTE LACUNAR INFARCT RIGHT THALAMUS

- Investigator: Investigations ongoing

- AbbVie: The prevalence of ischemic stroke is double in Ulcerative colitis patients 20-60 years of age. (Horta,E., et.al., Prevalence of Ischemic Stroke in Cohort of Ulcerative Colitis Patients, Neurology, [redacted],20[redacted]; 88). Additional risk factor includes obesity (BMI is 30 at time of event and 29.8 at screening in M14-675).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 29.9 kg/m2

[redacted] **20[redacted] CAROTID DOPPLER:** Normal

[redacted] **20[redacted] HEAD MRI:** Acute lacunar infarct right thalamus

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
深部静脈血栓症				X
処置による腸管穿孔	X	X		
子宮穿孔	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: IRON DEFICIENT ANEMIA	20[redacted]
CLOTTING/BLEEDING PROBLEMS: DVT	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: BILATERAL HIP PAIN	20[redacted]
OTHER: MENOPAUSE	20[redacted]
OTHER: OSTEOPENIA	20[redacted]
OTHER: RT SHOULDER PAIN	20[redacted]
OTHER: SALMONELLA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: ROTATOR CUFF REPAIR	20[redacted]
SURGERY: TUBALIGATION	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	2 - 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted] / 1	[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 57	[redacted] / 478	422

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1000 mg	QD	Y-M: [redacted]
HYDROCORTISONE	1 OTHER: DOSE	QD	Y-M: [redacted]
MESALAZINE	4 g	QD	Y-M: [redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: [redacted]
MESALAZINE	4000 mg	QD	Y-M: [redacted]
METRONIDAZOLE	500 mg	BID	Y-M: [redacted]
ADALIMUMAB	80 mg	OTHER: Q 2 WEEKS	Y-M: [redacted]
AZATHIOPRINE	50 mg	BID	Y-M: [redacted]
PREDNISONE	2.5 mg	QD	Y-M: [redacted]
PREDNISONE	2.5 mg	QD	Y-M: [redacted]
VEDOLIZUMAB	300 mg	OTHER: Q 8 WEEKS	Y-M: [redacted]
PREDNISONE	2.5 mg	QD	Y-M: [redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: [redacted]
METRONIDAZOLE	500 mg	BID	Y-M: [redacted]
INFLIXIMAB	400 mg	OTHER: Q 4 WEEKS	Y-M: [redacted]
PREDNISONE	2.5 mg	QD	Y-M: [redacted]
PREDNISONE	5 mg	QD	Y-M: [redacted]
BUDESONIDE	9 mg	QD	Y-M: [redacted] / -258
PANTOPRAZOLE	40 mg	QD	Y-M: [redacted] / -166
PREDNISONE	10 mg	QD	Y-M: [redacted] / -166
CALCIUM	500 mg	QD	Y: [redacted]
VITAMIN D NOS	2000 IU	QD	Y: [redacted]
VITAMINS NOS	1 OTHER: TAB	QD	Y: [redacted]
RISEDRONIC ACID	35 mg	OTHER: WEEKLY	Y: [redacted]
ASCORBIC ACID	1000 mg	QD	Y: [redacted]
IRON	11 mg	QD	Y: [redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -166	ONGOING
PARACETAMOL	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / 158	ONGOING
CODEINE;PARACETAMOL	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / 178	ONGOING
DIMENHYDRINATE	50 mg	PRN	Y-M: 20[redacted] / 424	Y-M: 20[redacted] / 425
MORPHINE	10 mg	PRN	Y-M: 20[redacted] / 424	Y-M: 20[redacted] / 425
PIPERACILLIN;TAZOBACTAM	3.75 g	QID	Y-M: 20[redacted] / 424	Y-M: 20[redacted] / 434
TRANEXAMIC ACID	1000 mg	QD	Y-M: 20[redacted] / 424	Y-M: 20[redacted] / 425
FLUCONAZOLE	400 mg	QD	Y-M: 20[redacted] / 425	Y-M: 20[redacted] / 433
HEPARIN	5000 ug	QD	Y-M: 20[redacted] / 425	Y-M: 20[redacted] / 432
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 425	Y-M: 20[redacted] / 432
ONDANSETRON	8 mg	PRN	Y-M: 20[redacted] / 425	Y-M: 20[redacted] / 435
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 432
HYDROMORPHONE	0.25 mg	PRN	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 435
MAGNESIUM SULFATE	4 g	QD	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 432
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 431
POTASSIUM	40 mEq	BID	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 436
TINZAPARIN	4500 ug	QD	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 436
DICLOFENAC	2.32 %	BID	Y-M: 20[redacted] / 427	Y-M: 20[redacted] / 436
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 432	Y-M: 20[redacted] / 436
AMOXICILLIN;CLAVULANIC ACID	AMOXICILLIN: 875 POTASSIUM: 125 mg	BID	Y-M: 20[redacted] / 434	Y-M: 20[redacted] / 436
MACROGOL	17 g	QD	Y-M: 20[redacted] / 434	Y-M: 20[redacted] / 435
CALCIUM	500 mg	QD	Y: 20[redacted]	ONGOING
VITAMIN D NOS	2000 IU	QD	Y: 20[redacted]	ONGOING
VITAMINS NOS	1 OTHER: TAB	QD	Y: 20[redacted]	ONGOING
RISEDRONIC ACID	35 mg	OTHER: WEEKLY	Y: 20[redacted]	ONGOING
ASCORBIC ACID	1000 mg	QD	Y: 20[redacted]	ONGOING
IRON	11 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	PROCEDURAL SMALL BOWEL PERFORATION
Preferred term	処置による腸管穿孔
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 479 / 423 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 424): Creatinine: 108 [40 - 100] UMOL/L; NPTST143-LACTATE: 3.6 [0.5 - 2.2] MMOL/L; NPTST256-UREA: 9.3 [2.5 - 8] MMOL/L; [redacted]20[redacted] (RX DAY 425): Albumin: 22 [35 - 50] G/L; Aspartate Aminotransferase: 69 [0 - 40] U/L; NPTST139-INR: 1.6 [0.8 - 1.2] RATIO; NPTST155-MAGNESIUM: 0.59 [0.7 - 1] MMOL/L; NPTST188-PO4: 0.56 [0.8 - 1.45] MMOL/L; NPTST241-TOTAL CO2: 20 [23 - 31] MMOL/L; [redacted]20[redacted] (RX DAY 426): Chloride: 109 [96 - 107] MMOL/L; NPTST190-POTASSIUM - WBK (WHOLE BODY): 2.9 [3.3 - 4.8] MMOL/L; [redacted]20[redacted] (RX DAY 427): Hemoglobin: 95 [120 - 160] G/L; [redacted]20[redacted] (RX DAY 429): Calcium: 1.99 [2.1 - 2.6] MMOL/L; [redacted]20[redacted] (RX DAY 432): Leukocytes: 14 [4 - 11] 10^9/L; [redacted]20[redacted] (RX DAY 436): Platelets: 591 [140 - 450] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 423): OTHER UTERUS/ENDOMETRIAL POLYP BIOPSY NPTST026-ANATOMICAL PATHOLOGY: Negative-COMPATIBLE WITH ATROPHIC ENDOMETRIUM, NO DEFINITE POLYP OR MALIGNANCY IS IDENTIFIED; [redacted]20[redacted] (RX DAY 425): OTHER SMALL BOWEL EXCISION NPTST239-SURGICAL PATHOLOGY REPORT: Positive-PORTION OF SMALL BOWEL WITH TRANSMURAL ACUTE INFLAMMATORY CHANGES, COMPATIBLE WITH SITE OF SMALL BOWEL PERFORATION INJURY; [redacted]20[redacted] (RX DAY 432): OTHER PELVIC FLUID NPTST109-FLUID CULTURE: Negative-NO GROWTH AEROBICALLY OR ANAEROBICALLY AFTER 72HRS.; [redacted]20[redacted] (RX DAY 433): OTHER ABSCESS PELVIC FLUID NPTST109-FLUID CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 424): ABDOMEN 2 OR MORE PROJECTIONS: PNUEMOPERITONEUM IS IDENTIFIED, MAY RELATE TO POSSIBLE UTERINE PERFORMATION; CT ABDOMEN AND PELVIS ENHANCED: SMALL VOLUMES OF INRAPERITONEAL FREE AIR AND FREE FLUIDWITH A HYPOATTENUATING TRACK THROUGH THE ANTERIOR WALL OF THE UTERUS LIKELY REPRESENTS A UTERINE WALL PERFORATION IN THE CONTEXT OF THE RECENT D &C. ADJACENT BOWEL INJURY IS NOT DEFINITELY IDENTIFIED, BUT CANNOT BE RULED OUT; X-RAY CHEST ERECT PA: PNEUMOPERITONEUM UNDER RIGHT HEMIDIAPHRAGM IS IDENTIFIED, SOME MINOR LEFT BASAL ATELACTASIS IS SEEN; [redacted]20[redacted] (RX DAY 425): CT ABDOMEN AND PELVIS ENHANCED: LARGE VOLUME OF FREE INTRAPERITONEAL FLUID WITH MILD PNUEMOPERITONEUM IN KEEPING WITH KNOWN UTERINE PERFORATION. WORSENING LARGE COMPLEX FLUID COLLECTIONS IN THE PELVIS SUSPICIOUS FOR BOWEL PERFORATI ON (TOO EARLY FOR ABSCESS). INTERVAL DEVELOPMENT OF SMALL RIGHT AND TRACE LEFT PLEURAL EFFUSIONS WITH MODERATE BIBASILAR ATELECTASIS. MILDLY DILATED SMALL BOWEL LOOPS WITH NO TRANSITION POINT FAVOUR ED TO REPRESENT ILEUS.; LAPAROTOMY TO REPAIR SMALL BOWEL PERFORATION: SMALL BOWEL REPAIRED; X-RAY CHEST ERECT AP: SIGNIFICANT DECREASE IN LUNG VOLUME (COMPARED TO PREVIOUS EXAM ON [redacted] [redacted] 20[redacted]). LED TO EXTENSIVE BIBASAL ATELECTASIS. TRACE PLEURAL EFFUSIONS ARE FELT LIKELY TO BE PRESENT. NEUMOPERITONEUM IDENTIFIED ON THE PREVIOUS DAY'S STUDY IS NO LONGER VISIBLE. A NUMBER OF GAS-FILLED LOOPS OF BOWEL ARE NOTED WHICH MAY INDICATE THE PRESENCE OF ADYNAMIC ILEUS.; X-RAY CHEST SUPINE AP: SOME IMPROVEMENT IN THE BIBASAL ATELACTASIS BUT PATCHY ATELECTASIS PERSISTS. SMALL BILATERAL EFFUSIONS. ENDOTRACHEAL TUBE JUST INTO THE RIGHT MAINSTEM BRONCHUS. THIS SHOULD BE PULLED BACK APPROX. 2.5 - 3 CM.; [redacted]20[redacted] (RX DAY 426): X-RAY CHEST SUPINE AP:

INTERVAL REPOSITIONING OF THE ENDOTRACHEAL TUBE WITH THE TIP NOW LOCATED APPORX. 2 CM ABOVE THE CARINA. OTHERWISE NO SIGNIFICANT INTERVAL CHANGE. PERSISTENT BIBASILAR ATELECTASIS; [redacted]20[redacted] (RX DAY 427): X-RAY CHEST ERECT AP: ENDOTRACHEAL TUBE HAS BEEN REMOVED WITH CONCOMITANT INCREASING BIBASAL ATELECTASIS. ESOPHAGOENTERIC TUBE REMAINS IN SITU. NO ADDITIONAL INTERVAL CHANGE SINCE THE EXAMINATION OF PREVIOUS DAY, ALLOWING FOR DIFFERENCES IN TECHNIQUE.; [redacted]20[redacted] (RX DAY 429): X-RAY ABDOMEN, 2 OR MORE PROJECTIONS: ONGOING SMALL BILATERAL PLEURAL EFFUSIONS, RIGHT GREATER THAN LEFT. MULTIPLE GASEOUS DISTENDED SMALL BOWEL LOOPS WHICH MEASURE AT THE UPPER LIMITS OF NORMAL. FINDINGS RAISE CONCERN FOR A DEVELOPING/PA RTIAL SMALL BOWEL OBSTRUCTION. THE COLON APPEARS RELATIVELY COLLAPSED AND THEREFORE LIEUS IS THOUGHT LESS LIKELY DESPITE THE PATIENT'S STATUS POST OP.; X-RAY CHEST ERECT PA: ONGOING SMALL BILATERAL PLEURAL EFFUSIONS, RIGHT GREATER THAN LEFT. MULTIPLE GASEOUS DISTENDED SMALL BOWEL LOOPS WHICH MEASURE AT THE UPPER LIMITS OF NORMAL IN CALIBER WITH MULTIPLE AIR-FLUID LEVELS, AND FINDINGS RAISE CONCERN FOR A DEVELOPING/PARTIAL SMALL BOWEL OBSTRUCTION. THE COLON APPEARS RELATIVELY OLLAPSED, AND THEREFORE, ILEUS IS THOUGHT LESS LIKELY DESPITE THE PATIENT'S STATUS POST OP.; [redacted]20[redacted] (RX DAY 432): CT ABDOMEN AND PELIVS, ENHANCED: SMALL PERIPHERALLY ENHANCING FLUID COLLECTION WITH THE LEFT LOWER QUADRANT. THERE IS MURAL THICKENING OF THE RECTOSIGMOID COLON AS WELL AS THE DESCENDING COLON EXTENDING TO THE SPLENIC FLEXURE POSSIBL Y SECONDARY TO PT'S KNOWN ULCERATIVE COLITIS. MILD RECTAL WALL MURAL THICKENING IS NOTED LIKELY SECONDARY TO THE ADJACENT ABSCESS WITHIN THE PELVIS. EVIDENCE OF A SUSPECTED LOW-GRADE/PARTIAL SMALL BO WEL OBSTRUCTION WITH A TRANSITION POINT WITHIN THE PROXIMAL ILEUM WITHIN THE RIGHT LOWER QUADRANT. SMALL R SIDED PLEURAL EFFUSION.; US ABSCESS ASPIRATION/DRAINAGE: U/S GUIDED ASPIRATION OF COMPLEX FLUID COLLECTION WITHIN THE ANTERIOR PELVIS YEILDING 15 CC OF CLOUDY YELLOW FLUID. POST PROCEDURE IMAGES SHOW THAT NEARLY ALL OF THE LIQUIFIED FLUID HAS RESOLVED. U/S GUIDED DIAGNOSTIC AND THERAPEUTIC ASPIRATION OF A SMALL FLUID COLLECTION WITHIN THE RIGHT UPPER QUADRANT.; [redacted]20[redacted] (RX DAY 433): CT ABSCESS ASPIRATION OR DRAINAGE: SUCCESSFUL PLACEMENT OF A LOCKING LOOP PIGTAIL DRAIN WITHIN A PELVIC ABSCESS

AE Stopped Initial Rx Day / Rx Day	481 / 425 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PT HAD A SCHEDULED DILATION AND CURETTAGE PROCEDURE TO REMOVE AN ENDOMETRIAL POLYP ON [redacted] WHICH RESULTED IN A BOWEL PERFORATION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	PROCEDURAL UTERINE PERFORATION
Preferred term	子宮穿孔
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 479 / 423 (1 DAY AFTER LAST TREATMENT)

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 424): Creatinine: 108 [40 - 100] UMOL/L; Creatinine: 108 [40 - 100] UMOL/L; NPTST143-LACTATE: 3.6 [0.5 - 2.2] MMOL/L; NPTST143-LACTATE: 3.6 [0.5 - 2.2] MMOL/L; NPTST256-UREA: 9.3 [2.5 - 8] MMOL/L; NPTST256-UREA: 9.3 [2.5 - 8] MMOL/L; [redacted]20[redacted] (RX DAY 425): Albumin: 22 [35 - 50] G/L; Albumin: 22 [35 - 50] G/L; Aspartate Aminotransferase: 69 [0 - 40] U/L; Aspartate Aminotransferase: 69 [0 - 40] U/L; NPTST139-INR: 1.6 [0.8 - 1.2] RATIO; NPTST139-INR: 1.6 [0.8 - 1.2] RATIO; NPTST155-MAGNESIUM: 0.59 [0.7 - 1] MMOL/L; NPTST155-MAGNESIUM: 0.59 [0.7 - 1] MMOL/L; NPTST188-PO4: 0.56 [0.8 - 1.45] MMOL/L; NPTST188-PO4: 0.56 [0.8 - 1.45] MMOL/L; NPTST241-TOTAL CO2: 20 [23 - 31] MMOL/L; NPTST241-TOTAL CO2: 20 [23 - 31] MMOL/L; [redacted]20[redacted] (RX DAY 426): Chloride: 109 [96 - 107] MMOL/L; Chloride: 109 [96 - 107] MMOL/L; NPTST190-POTASSIUM - WBK (WHOLE BODY): 2.9 [3.3 - 4.8] MMOL/L; NPTST190-POTASSIUM - WBK (WHOLE BODY): 2.9 [3.3 - 4.8] MMOL/L; [redacted]20[redacted] (RX DAY 427): Hemoglobin: 95 [120 - 160] G/L; Hemoglobin: 95 [120 - 160] G/L; [redacted]20[redacted] (RX DAY 429): Calcium: 1.99 [2.1 - 2.6] MMOL/L; Calcium: 1.99 [2.1 - 2.6] MMOL/L; [redacted]20[redacted] (RX DAY 432): Leukocytes: 14 [4 - 11] 10^9/L; Leukocytes: 14 [4 - 11] 10^9/L; [redacted]20[redacted] (RX DAY 436): Platelets: 591 [140 - 450] 10^9/L; Platelets: 591 [140 - 450] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 423): OTHER UTERUS/ENDOMETRIAL POLYP BIOPSY NPTST026-ANATOMICAL PATHOLOGY: Negative-COMPATIBLE WITH ATROPHIC ENDOMETRIUM, NO DEFINITE POLYP OR MALIGNANCY IS IDENTIFIED; [redacted]20[redacted] (RX DAY 425): OTHER SMALL BOWEL EXCISION NPTST239-SURGICAL PATHOLOGY REPORT: Positive-PORTION OF SMALL BOWEL WITH TRANSMURAL ACUTE INFLAMMATORY CHANGES, COMPATIBLE WITH SITE OF SMALL BOWEL PERFORATION INJURY; [redacted]20[redacted] (RX DAY 432): OTHER PELVIC FLUID NPTST109-FLUID CULTURE: Negative-NO GROWTH AEROBICALLY OR ANAEROBICALLY AFTER 72HRS.; [redacted]20[redacted] (RX DAY 433): OTHER ABSCESS PELVIC FLUID NPTST109-FLUID CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 424): ABDOMEN 2 OR MORE PROJECTIONS: PNUEMOPERITONEUM IS IDENTIFIED, MAY RELATE TO POSSIBLE UTERINE PERFORMATION; CT ABDOMEN AND PELVIS ENHANCED: SMALL VOLUMES OF INRAPERITONEAL FREE AIR AND FREE FLUIDWITH A HYPOATTENUATING TRACK THROUGH THE ANTERIOR WALL OF THE UTERUS LIKELY REPRESENTS A UTERINE WALL PERFORATION IN THE CONTEXT OF THE RECENT D &C. ADJACENT BOWEL INJURY IS NOT DEFINITELY IDENTIFIED, BUT CANNOT BE RULED OUT; X-RAY CHEST ERECT PA: PNEUMOPERITONEUM UNDER RIGHT HEMIDIAPHRAGM IS IDENTIFIED, SOME MINOR LEFT BASAL ATELACTASIS IS SEEN; [redacted]20[redacted] (RX DAY 425): CT ABDOMEN AND PELVIS ENHANCED: LARGE VOLUME OF FREE INTRAPERITONEAL FLUID WITH MILD PNUEMOPERITONEUM IN KEEPING WITH KNOWN UTERINE PERFORATION. WORSENING LARGE COMPLEX FLUID COLLECTIONS IN THE PELVIS SUSPICIOUS FOR BOWEL PERFORATI ON (TOO EARLY FOR ABSCESS). INTERVAL DEVELOPMENT OF SMALL RIGHT AND TRACE LEFT PLEURAL EFFUSIONS WITH MODERATE BIBASILAR ATELECTASIS. MILDLY DILATED SMALL BOWEL LOOPS WITH NO TRANSITION POINT FAVOUR ED TO REPRESENT ILEUS.; LAPAROTOMY TO REPAIR SMALL BOWEL PERFORATION: SMALL BOWEL REPAIRED; X-RAY CHEST ERECT AP: SIGNIFICANT DECREASE IN LUNG VOLUME (COMPARED TO PREVIOUS EXAM ON [redacted] 20[redacted]). LED TO EXTENSIVE BIBASAL ATELECTASIS. TRACE PLEURAL EFFUSIONS ARE FELT LIKELY TO BE PRESENT. NEUMOPERITONEUM IDENTIFIED ON THE PREVIOUS DAY'S STUDY IS NO LONGER VISIBLE. A NUMBER OF GAS-FILLED LOOPS OF BOWEL ARE NOTED WHICH MAY INDICATE THE PRESENCE OF ADYNAMIC ILEUS.; X-RAY CHEST SUPINE AP: SOME IMPROVEMENT IN THE BIBASAL ATELACTASIS BUT PATCHY ATELECTASIS PERSISTS. SMALL BILATERAL EFFUSIONS. ENDOTRACHEAL TUBE JUST INTO THE RIGHT MAINSTEM BRONCHUS. THIS SHOULD BE PULLED BACK APPROX. 2.5 - 3 CM.; [redacted]20[redacted] (RX DAY 426): X-RAY CHEST SUPINE AP: INTERVAL REPOSITIONING OF THE ENDOTRACHEAL TUBE WITH THE TIP NOW LOCATED APPORX. 2 CM ABOVE THE CARINA. OTHERWISE NO SIGNIFICANT INTERVAL CHANGE. PERSISTENT BIBASILAR

ATELECTASIS; [redacted]20[redacted] (RX DAY 427): X-RAY CHEST ERECT AP: ENDOTRACHEAL TUBE HAS BEEN REMOVED WITH CONCOMITANT INCREASING BIBASAL ATELECTASIS. ESOPHAGOENTERIC TUBE REMAINS IN SITU. NO ADDITIONAL INTERVAL CHANGE SINCE THE EXAMINATION OF PREVIOUS DAY, ALLOWING FOR DIFFERENCES IN TECHNIQUE.; [redacted]20[redacted] (RX DAY 429): X-RAY ABDOMEN, 2 OR MORE PROJECTIONS: ONGOING SMALL BILATERAL PLEURAL EFFUSIONS, RIGHT GREATER THAN LEFT. MULTIPLE GASEOUS DISTENDED SMALL BOWEL LOOPS WHICH MEASURE AT THE UPPER LIMITS OF NORMAL. FINDINGS RAISE CONCERN FOR A DEVELOPING/PA RTIAL SMALL BOWEL OBSTRUCTION. THE COLON APPEARS RELATIVELY COLLAPSED AND THEREFORE LIEUS IS THOUGHT LESS LIKELY DESPITE THE PATIENT'S STATUS POST OP.; X-RAY CHEST ERECT PA: ONGOING SMALL BILATERAL PLEURAL EFFUSIONS, RIGHT GREATER THAN LEFT. MULTIPLE GASEOUS DISTENDED SMALL BOWEL LOOPS WHICH MEASURE AT THE UPPER LIMITS OF NORMAL IN CALIBER WITH MULTIPLE AIR-FLUID LEVELS, AND FINDINGS RAISE CONCERN FOR A DEVELOPING/PARTIAL SMALL BOWEL OBSTRUCTION. THE COLON APPEARS RELATIVELY OLLAPSED, AND THEREFORE, ILEUS IS THOUGHT LESS LIKELY DESPITE THE PATIENT'S STATUS POST OP.; [redacted]20[redacted] (RX DAY 432): CT ABDOMEN AND PELIVS, ENHANCED: SMALL PERIPHERALLY ENHANCING FLUID COLLECTION WITH THE LEFT LOWER QUADRANT. THERE IS MURAL THICKENING OF THE RECTOSIGMOID COLON AS WELL AS THE DESCENDING COLON EXTENDING TO THE SPLENIC FLEXURE POSSIBL Y SECONDARY TO PT'S KNOWN ULCERATIVE COLITIS. MILD RECTAL WALL MURAL THICKENING IS NOTED LIKELY SECONDARY TO THE ADJACENT ABSCESS WITHIN THE PELVIS. EVIDENCE OF A SUSPECTED LOW-GRADE/PARTIAL SMALL BO WEL OBSTRUCTION WITH A TRANSITION POINT WITHIN THE PROXIMAL ILEUM WITHIN THE RIGHT LOWER QUADRANT. SMALL R SIDED PLEURAL EFFUSION.; US ABSCESS ASPIRATION/DRAINAGE: U/S GUIDED ASPIRATION OF COMPLEX FLUID COLLECTION WITHIN THE ANTERIOR PELVIS YEILDING 15 CC OF CLOUDY YELLOW FLUID. POST PROCEDURE IMAGES SHOW THAT NEARLY ALL OF THE LIQUIFIED FLUID HAS RESOLVED. U/S GUIDED DIAGNOSTIC AND THERAPEUTIC ASPIRATION OF A SMALL FLUID COLLECTION WITHIN THE RIGHT UPPER QUADRANT.; [redacted]20[redacted] (RX DAY 433): CT ABSCESS ASPIRATION OR DRAINAGE: SUCCESSFUL PLACEMENT OF A LOCKING LOOP PIGTAIL DRAIN WITHIN A PELVIC ABSCESS

AE Stopped Initial Rx Day / Rx Day	481 / 425 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PT HAD A SCHEDULED DILATION AND CURETTAGE PROCEDURE TO REMOVE AN ENDOMETRIAL POLYP ON [redacted] WHICH RESULTED IN AN UTERINE PERFORATION.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Event #3: Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	RIGHT ARM DEEP VEIN THROMBOSIS AT PICC LINE INSERTION SITE
Preferred term	深部静脈血栓症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 495 / 439 (17 DAYS AFTER LAST TREATMENT)

Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はカナダの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，処置による子宮穿孔，及び処置による小腸穿孔の事象を発現した。関連する病歴は，卵管結紮，閉経，潰瘍性大腸炎（左側），非喫煙者及び中程度の現飲酒者であった。

Event 1 及び 2 の臨床経過：

投与479日後＊，被験者は処置による子宮穿孔，及び処置による小腸穿孔を発現した。投与481日後＊，処置による子宮穿孔，及び処置による小腸穿孔は消失した。

投与381日後＊　，被験者は子宮内膜ポリープ（非重篤）と診断され，投与479日後＊　　に頸管拡張及び掻爬術により，ポリープが切除された。ポリープ切除後の 投与480日後＊ ，被験者は腹痛の増強，悪寒，悪心及び嘔吐があり，救急治療室を受診した。受診当初は無熱であったが，その後発熱した。投与480日後＊　，被験者は入院した。CT スキャン検査で，腹腔内の遊離ガス及び液体が確認された（子宮穿孔の可能性あり）。投与481日後＊　　，被験者は開腹手術

を受け，洗浄，創傷郭清及び小腸の修復が行われ，成功した。投与488日後＊　の再 CT スキャン検査では，術後の膿瘍と考えうる液体が骨盤の深部に貯留していた。投与489日後＊　，被験者は CT ガイド下での膿瘍ドレナージ及び経皮的ドレーン挿入を受けた。投与492日後＊　，ドレーンが抜去され，同日，被験者は退院した。

治験薬の投与は完全に中止され，最終投与日は 投与478日後＊であった。

投与された薬剤は，ラシックス，maxeran，pantoloc 及びピペラシリンであった。

The patient's past medications include:

SALOFALK SUPPOSITORY for ULCERATIVE COLITIS ([redacted])

CORTIFOAM for ULCERATIVE COLITIS ([redacted])

SALOFALK ENEMA for ULCERATIVE COLITIS ([redacted])

CIPROFLOXACIN for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1)　Uterine perforation (10046810)　(Uterine perforation (10046810))　[v.21.1]　[10046810]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Procedural intestinal perforation (10074065) (Procedural intestinal perforation (10074065)) [v.21.1] [10074065]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Open Label)

Event of PROCEDURAL UTERINE PERFORATION

- Investigator: Patient had a scheduled dilation and curettage procedure to remove an endometrial polyp on [redacted] which resulted in a uterine perforation.

- AbbVie: Event is more likely a complication of dilation and curettage procedure, as reported by the investigator.

Event of PROCEDURAL SMALL BOWEL PERFORATION

- Investigator: Patient had a scheduled dilation and curettage procedure to remove an endometrial polyp on [redacted] which resulted in a bowel perforation.

- AbbVie: Event is more likely a complication of dilation and curettage procedure, as reported by the investigator.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMEN 2 OR MORE PROJECTIONS:** PNUEMOPERITONEUM IS IDENTIFIED, MAY RELATE TO POSSIBLE UTERINE PERFORMATION

[redacted] **20[redacted] ABSCESS PELVIC FLUID CULTURE:** negative

[redacted] **20[redacted] ALBUMIN:** 22 G/L (normal 35 to 50)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 69 U/L (normal 0 to 40)

[redacted] **20[redacted] CALCIUM:** 1.99 MMOL/L (normal 2.10 to 2.60)

[redacted] **20[redacted] CHLORIDE:** 109 MMOL/L (normal 96 to 107)

[redacted] **20[redacted] CREATININE:** 108 MCMOL/L (normal 40 to 100)

[redacted] **20[redacted] CT ABDOMEN AND PELVIS ENHANCED:** SMALL VOLUMES OF INRAPERITONEAL FREE AIR AND FREE FLUIDWITH A HYPOATTENUATING TRACK THROUGH THE ANTERIOR WALL OF THE UTERUS LIKELY REPRESENTS A UTERINE WALL PERFORATION IN THE CONTEXT OF THE RECENT D &C. ADJACENT BOWEL INJURY IS NOT DEFINITELY IDENTIFIED, BUT CANNOT BE RULED OUT

[redacted] **20[redacted] CT ABDOMEN AND PELVIS ENHANCED:** LARGE VOLUME OF FREE INTRAPERITONEAL FLUID WITH MILD PNUEMOPERITONEUM IN KEEPING WITH KNOWN UTERINE PERFORATION. WORSENING LARGE COMPLEX FLUID COLLECTIONS IN THE PELVIS SUSPICIOUS FOR BOWEL PERFORATION (TOO EARLY FOR ABSCESS). INTERVAL DEVELOPMENT OF SMALL RIGHT AND TRACE LEFT PLEURAL EFFUSIONS WITH MODERATE BIBASILAR ATELECTASIS. MILDLY DILATED SMALL BOWEL LOOPS WITH NO TRANSITION POINT FAVOURED TO REPRESENT ILEUS.

[redacted] **20[redacted] CT ABDOMEN AND PELVIS ENHANCED:** SMALL PERIPHERALLY ENHANCING FLUID COLLECTION WITH THE LEFT LOWER QUADRANT. THERE IS MURAL THICKENING OF THE RECTOSIGMOID COLON AS WELL AS THE DESCENDING COLON EXTENDING TO THE SPLENIC FLEXURE POSSIBLY SECONDARY TO PT'S KNOWN ULCERATIVE COLITIS. MILD RECTAL WALL MURAL THICKENING IS NOTED LIKELY SECONDARY TO THE ADJACENT ABSCESS WITHIN THE PELVIS. EVIDENCE OF A SUSPECTED LOW-GRADE/PARTIAL SMALL BOWEL OBSTRUCTION WITH A TRANSITION POINT WITHIN THE PROXIMAL ILEUM WITHIN THE RIGHT LOWER QUADRANT. SMALL R SIDED PLEURAL EFFUSION.

[redacted] **20[redacted] CT ABSCESS ASPIRATION OR DRAINAGE:** SUCCESSFUL PLACEMENT OF A LOCKING LOOP PIGTAIL DRAIN WITHIN A PELVIC ABSCESS

[redacted] **20[redacted] HGB:** 95 G/L (normal 120 to 160)

[redacted] **20[redacted] INR:** 1.6 NO UNIT (normal 0.8 to 1.2)

[redacted] **20[redacted] LACTATE:** 3.6 MMOL/L (normal 0.5 to 2.2)

[redacted] **20[redacted] MAGNESIUM:** 0.59 MMOL/L (normal 0.70 to 1.00)

[redacted] **20[redacted] PELVIC FLUID CULTURE:** NO GROWTH AEROBICALLY OR ANAEROBICALLY AFTER 72HRS.

[redacted] **20[redacted] PLATELET COUNT:** 591 X10**9/L (normal 140 to 450)

[redacted] **20[redacted] PO4:** 0.56 MMOL/L (normal 0.80 to 1.45)

[redacted] **20[redacted] POTASSIUM - WBK (WHOLE BODY)):** 2.9 MMOL/L (normal 3.3 to 4.8)

[redacted] **20[redacted] SMALL BOWEL EXCISION SURGICAL PATHOLOGY REPORT:** Positive, portion of small bowel with transmural acute inflammatory changes, compatible with site of small bowel perforation injury.

[redacted] **20[redacted] PATHOLOGY:** SMALL BOWEL: PORTION OF SMALL BOWEL WITH TRANSMURAL ACUTE INFLAMMATORY CHANGES, COMPATIBLE WITH SITE OF SMALL BOWEL PERFORATION INJURY

[redacted] **20[redacted] TEMPERATURE:** 39.2 Degrees C

[redacted] **20[redacted] TOTAL CO2:** 20 MMOL/L (normal 23 to 31)

[redacted] **20[redacted] UREA:** 9.3 MMOL/L (normal 2.5 to 8.0)

[redacted] **20[redacted] US ABSCESS ASPIRATION/DRAINAGE:** U/S GUIDED ASPIRATION OF COMPLEX FLUID COLLECTION WITHIN THE ANTERIOR PELVIS YEILDING 15 CC OF CLOUDY YELLOW FLUID. POST PROCEDURE IMAGES SHOW THAT NEARLY ALL OF THE LIQUIFIED FLUID HAS RESOLVED. U/S GUIDED DIAGNOSTIC AND THERAPEUTIC ASPIRATION OF A SMALL FLUID COLLECTION WITHIN THE RIGHT UPPER QUADRANT.

[redacted] **20[redacted] UTERINE ENDOMETRIAL POLYP BIOPSY:** Negative, compatible with atrophic endometrium, no definite polyp or malignancy is identified.

[redacted] **20[redacted] WBC:** 14.0 X10**9/L (normal 4.0 to 11.0)

[redacted] **20[redacted] X-RAY CHEST ERECT AP:** SIGNIFICANT DECREASE IN LUNG VOLUME (COMPARED TO PREVIOUS EXAM ON [redacted] 20[redacted]). LED TO EXTENSIVE BIBASAL ATELECTASIS. TRACE PLEURAL EFFUSIONS ARE FELT LIKELY TO BE PRESENT. {NEUMOPERITONEUM IDENTIFIED ON THE PREVIOUS DAY'S STUDY IS NO LONGER VISIBLE. A NUMBER OF GAS-FILLED LOOPS OF BOWEL ARE NOTED WHICH MAY INDICATE THE PRESENCE OF ADYNAMIC ILEUS.

[redacted] **20[redacted] X-RAY CHEST ERECT AP:** ENDOTRACHEAL TUBE HAS BEEN REMOVED WITH CONCOMITANT INCREASING BIBASAL ATELECTASIS. ESOPHAGOENTERIC TUBE REMAINS IN SITU. NO ADDITIONAL INTERVAL CHANGE SINCE THE EXAMINATION OF PREVIOUS DAY, ALLOWING FOR DIFFERENCES IN TECHNIQUE.

[redacted] **20[redacted] X-RAY CHEST ERECT PA:** PNEUMOPERITONEUM UNDER RIGHT HEMIDIAPHRAGM IS IDENTIFIED, SOME MINOR LEFT BASAL ATELACTASIS IS SEEN

[redacted] **20[redacted] X-RAY CHEST ERECT PA:** ONGOING SMALL BILATERAL PLEURAL EFFUSIONS, RIGHT GREATER THAN LEFT. MULTIPLE GASEOUS DISTENDED SMALL BOWEL LOOPS WHICH MEASURE AT THE UPPER LIMITS OF NORMAL IN CALIBER WITH MULTIPLE AIR-

FLUID LEVELS, AND FINDINGS RAISE CONCERN FOR A DEVELOPING/PARTIAL SMALL BOWEL OBSTRUCTION. THE COLON APPEARS RELATIVELY OLLAPSED, AND THEREFORE, ILEUS IS THOUGHT LESS LIKELY DESPITE THE PATIENT'S STATUS POST OP.

[redacted] **20[redacted] X-RAY CHEST SUPINE AP:** SOME IMPROVEMENT IN THE BIBASAL ATELACTASIS BUT PATCHY ATELECTASIS PERSISTS. SMALL BILATERAL EFFUSIONS. ENDOTRACHEAL TUBE JUST INTO THE RIGHT MAINSTEM BRONCHUS. THIS SHOULD BE PULLED BACK APPROX. 2.5 - 3 CM.

[redacted] **20[redacted] X-RAY CHEST SUPINE AP:** INTERVAL REPOSITIONING OF THE ENDOTRACHEAL TUBE WITH THE TIP NOW LOCATED APPORX. 2 CM ABOVE THE CARINA. OTHERWISE NO SIGNIFICANT INTERVAL CHANGE. PERSISTENT BIBASILAR ATELECTASIS

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
子宮平滑筋腫	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: ANEMIA	20[redacted]
ASTHMA: EXERCISE INDUCED ASTHMA	20[redacted]
DEPRESSION: DEPRESSION	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: 10MM CYST ON KIDNEY	20[redacted]
OTHER: ALLERGY DUST MITES	20[redacted]
OTHER: ALLERGY LINALOOL OIL	20[redacted]
OTHER: BLOOD TRANSFUSION	20[redacted]
OTHER: C-DIFF POSITIVE	20[redacted]
OTHER: ENVIROMENTAL ALLERGY	19[redacted]
OTHER: HEMORRHOIDS	20[redacted]
OTHER: LYCHEN SIMPLEX	20[redacted]
OTHER: OCCASIONAL MIGRAINE HEADACHES	20[redacted]
OTHER: ROSACEA	20[redacted]
OTHER: STYE	20[redacted]
OTHER: UTERINE FIBROIDS	20[redacted]
OTHER: VITAMIN A DEFICENCY	20[redacted]
OTHER: VITAMIN E DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: BARTHOLIN CYST REMOVAL	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.25 PACK	20	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 54	54
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 55	[redacted]20[redacted] / 427	373
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 428		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ASCORBIC ACID;CALCIUM PHOSPHATE;COLECALCIFEROL;COPPER; CYANOCOBALAMIN;DL-ALPHA TOCOPHEROL;FOLIC ACID;IODINE;IRON;MANGANESE;NICOTINAMIDE;PANTOTHENIC ACID;PYRIDOXINE;RETINOL;RIBOFLAVIN;THIAMINE;ZINC	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted]
HYDROCORTISONE	100 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]-[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted]
FISH OIL	500 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4.8 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	800 mg	QD	Y-M: 20[redacted]-[redacted]
HYDROCORTISONE	100 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]-[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ASCORBIC ACID;CALCIUM PHOSPHATE;COLECALCIFEROL; COPPER;CYANOCOBALAMIN;DL-ALPHA TOCOPHEROL;FOLIC ACID;IODINE;IRON;MANGANESE ;NICOTINAMIDE;PANTOTHENIC ACID;PYRIDOXINE;RETINOL;RIB OFLAVIN;THIAMINE;ZINC	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Not reported
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
FISH OIL	500 mg	QD	Y-M: 20[redacted]	ONGOING
ULIPRISTAL	5 mg	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 210
BISACODYL	3 OTHER: TABLETS	OTHER: ONCE	Y-M: 20[redacted] / 334	Y-M: 20[redacted] / 334
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: SATCHETS	OTHER: ONCE	Y-M: 20[redacted] / 334	Y-M: 20[redacted] / 334
FENTANYL	75 ug	OTHER: ONCE	Y-M: 20[redacted] / 335	Y-M: 20[redacted] / 335
MESALAZINE	2.4 g	QD	Y-M: 20[redacted] / 335	Not reported
MIDAZOLAM	3 mg	OTHER: ONCE	Y-M: 20[redacted] / 335	Y-M: 20[redacted] / 335
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 335	Y-M: 20[redacted] / 342
ESCITALOPRAM	10 mg	QD	Y-M: 20[redacted] / 342	Not reported
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 391
HYDROCORTISONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 413	Y-M: 20[redacted] / 420
MINOCYCLINE	100 mg	QD	Y-M: 20[redacted] / 485	Y-M: 20[redacted] / 577
ANESTHETICS, GENERAL	UNKNOWN OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / 674	Y-M: 20[redacted] / 674
CEFAZOLIN	2 g	OTHER: ONCE	Y-M: 20[redacted] / 674	Y-M: 20[redacted] / 674
HYDROMORPHONE	0.4 mg	PRN	Y-M: 20[redacted] / 674	Y-M: 20[redacted] / 674
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 674	Y-M: 20[redacted] / 674
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 674	Y-M: 20[redacted] / 674
TINZAPARIN	8,000 IU	OTHER: QHS	Y-M: 20[redacted] / 674	Y-M: 20[redacted] / 675

Event #1: Serious Adverse Event

Event Description	WORSENING OF UTERINE FIBROIDS
Preferred term	子宮平滑筋腫
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 547 / 120
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 674): TOTAL HYSTERECTOMY AND BILATERAL SAPLINGECTOMIES: TOTAL REMOVAL OF UTERUS AND OVARIES WITH NO COMPLICATIONS.

AE Stopped Initial Rx Day / Rx Day	1101 / 674
Duration of AE	555 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UTERINE FIBROIDS ARE PART OF MEDICAL HISTORY FOR THIS SUBJECT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はカナダの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，子宮類線維症の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，子宮類線維症，元喫煙者（1 日 0.25 箱を 20 年間）及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与547日後＊ ，被験者は子宮類線維症の悪化を発現した。投与1101日後＊ ，子宮類線維症の悪化は消失した。

投与1101日後＊，子宮類線維症（投与の約3年前＊–）による異常出血があり，子宮全摘術及び両側卵管摘除術を受けるために入院した。被験者は fiberstal を試したが，効果は認められなかった。被験者の最新の超音波検査では，左側面の子宮筋腫が最大で 8 × 7.4 × 6 cm，後側の子宮筋腫が 3 × 2 × 3 cm であった。被験者には，本事象に関連する危険因子及び家族歴はなかった。投与

1103日後＊，被験者は，合併症もなく退院した。

投与された薬剤は，tramacet，tinzaparin，セファゾリン，maxeran，zofran 及びヒドロモルフォンであった。

The patient's past medications include:

CORTENEMA for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

SALOFALK ENEMA for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

FIBRISTAL for UTERINE FIBROIDS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Uterine fibroids aggravated (10048417) (Uterine leiomyoma (10046798)) [v.23.1] [10048417]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF UTERINE FIBROIDS

- Investigator: Uterine fibroids are part of medical history for this subject

- AbbVie: More likely related to pre-existing uterine fibroids.

Relevant Laboratory & Other Diagnostic Tests

Unknown date ULTRASOUND: LEFT LATERAL FIBROID MEASURED UP TO 8 X 7.4 X 6 CM. POSTERIOR FIBROID OF 3 X 2 X 3 CM

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19 肺炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	5[redacted]	MALE	WHITE

Medical History	Onset Year
COLD SORES	19[redacted]
DRY COUGH	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
LOWER BACK PAIN	19[redacted]
NON INSULIN DEPENDANT DIABETES	20[redacted]
SLEEP APNEA	20[redacted]
SLEEP DISTURBANCE	20[redacted]
STEROID INDUCED FOLLICULITIS	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	20	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 56	[redacted] / 417	362
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted] / 419		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1000 mg	QD	Y-M: [redacted]
MESALAZINE	2400 mg	QD	Y-M: [redacted]
METFORMIN	800 mg	BID	Y-M: [redacted]
BUDESONIDE	3 mg	QD	Y-M: [redacted]
BUDESONIDE	6 mg	QD	Y-M: [redacted]
ZOPICLONE	7.5 mg	PRN	Y-M: [redacted] / -84
ACETYLSALICYLIC ACID	81 mg	QD	Y: [redacted]
VITAMINS NOS	1 OTHER: TAB	QD	Y: [redacted]
VITAMIN D NOS	1000 IU	QD	Y: [redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	2400 mg	QD	Y-M: [redacted]	Not reported
METFORMIN	800 mg	BID	Y-M: [redacted]	Not reported
ZOPICLONE	7.5 mg	PRN	Y-M: [redacted] / -84	Not reported
ACETYLSALICYLIC ACID	81 mg	QD	Y: [redacted]	Not reported
VITAMINS NOS	1 OTHER: TAB	QD	Y: [redacted]	Not reported
VITAMIN D NOS	1000 IU	QD	Y: [redacted]	Not reported

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	COVID 19 PNEUMONIA
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted] / 824 / 406
Age at AE Onset	[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 412): NPTST087-CULTURES: NO GROWTH IN 5 DAYS [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 413): Hematocrit: 0.4 [0.41 - 0.52] FRACTION OF 1; Lymphocytes: 0.4 [1 - 4.5] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 412): BLOOD NPTST047-BLOOD CULTURES: Negative-NO GROWTH IN 5 DAYS FROM TIME OF RECEIPT IN LABORATORY

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 412): CHEST X-RAY, 2 VIEWS: CARDIAC OUTLINE IS NORMAL. THERE IS AORTIC UNFOLDING. HYPERINFLATION SUSPECTED. DEVELOPMENT OF CONFLUENT AREA OF OPACIFICATION IN THE LATERAL SEGMENT OF RIGHT MIDDLE LOBE, LEFT LUNG REMAINS CLEAR. RIG HT MIDDLE LOBE PNEUMONIA HAS DEVELOPED SINCE [redacted] 20[redacted]. COPD SUSPECTED.; ECG: NORMAL ECG; [redacted]20[redacted] (RX DAY 415): CHEST X-RAY 2 VIEWS: FINDINGS INDICATING RIGHT MIDDLE LOBE PNEUMONIA AGAIN DEMONSTRATED THERE ARE SLIGHT DECREASED OPACIFICATION SINCE THE PREVIOUS EXAM. THERE ARE A FEW PATCHY AREAS OF PNEUMONIA ALSO SEEN IN THE LEFT LOW ER LOBE, WHICH IN RETROSPECT CAN BE SEEN ON THE PREVIOUS EXAM. HYPERINFLATION AGAIN SEEN.

AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はカナダの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，COVID-19 肺炎の事象を発現した。関連する病歴は，元喫煙者（1 日 0.5 箱を 20 年間），高血圧，非インスリン依存性糖尿病，潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与824日後＊，被験者は COVID-19 肺炎を発現した。

＊新薬承認情報提供時に置き換え

投与824日後＊，被験者は高熱（摂氏41℃），疲労，体の痛み，持続性の咳嗽，及び胸部うっ血を経験し始めた。肺の聴診では，右中肺野に轟音が認められた。COVID-19 感染が確認された。投与830日後＊　，被験者は入院した。胸部 X 線検査では，COVID 関連の肺炎が認められた。入院 4 日目及び 5 日目に劇的な改善が認められ，酸素飽和度は室内気で 90%以上を維持していた。被験者は酸素吸入を開始しなかった。投与835日後＊，被験者は退院した。

投与された薬剤は，ロセフィン及び zithromax であった。

The patient's past medications include:

SALOFALK SUPPOSITORIES for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　COVID-19 pneumonia (10084380)　(COVID-19 pneumonia (10084380))　[v.24.0]　[10084380]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID 19 PNEUMONIA

- Investigator: Not applicable

- AbbVie: Event is more likely related to the COVID-19 pandemic outbreak.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **BLOOD CULTURES:** Negative - No growth in 5 days from time of receipt in laboratory

[redacted] 20[redacted] **BMI:** 33.6 kg/m2

[redacted] 20[redacted] **BODY TEMPERATURE:** 41 Degrees C

[redacted] 20[redacted] **BODY WEIGHT:** 11[redacted] KG

[redacted] 20[redacted] **CHEST X-RAY:** Cardiac outline is normal There is aortic unfolding. Hyperinflation suspected. Development of confluent area of opacification in the lateral segment of right middle lobe, left lung remains clear. Right middle lobe pneumonia has developed since [redacted] 20[redacted], COPD suspected.

[redacted] 20[redacted] **CHEST X-RAY:** Findings indicate right middle lobe pneumonia again demonstrated, there is slight decreased opacification since the previous exam. There are a few patchy areas of pneumonia also seen in the left lower lobe, which in retrospect can be seen on previous exam. Hyperinflation again seen.

[redacted] 20[redacted] **COVID-19 VIRUS TEST:** Tested positive

[redacted] 20[redacted] **ECG:** Normal

[redacted] 20[redacted] **HCT:** 0.40 L/L (normal 0.41 to 0.52)

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 0.4 X10**9/L (normal 1.0 to 4.5)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
消化管感染	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	3[redacted]	MALE	WHITE

Medical History	Onset Year
ACNE	20[redacted]
ANEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GINGIVITIS	20[redacted]
ORAL APHTHOUS ULCERS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: CHEST X-RAY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56

M14-675 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 112	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 113	[redacted]20[redacted] / 177	65
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 178	[redacted]20[redacted] / 415	238

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	OTHER: 3 TIMES A DAY	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	600 mg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1 g	OTHER: 3 TIMES A DAY	Y-M: 20[redacted]	ONGOING
PREDNISONE	20 mg	QD	Y-M: 20[redacted]	ONGOING
CIPROFLOXACIN	200 mg	QD	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 233
METRONIDAZOLE	500 mg	QD	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 233

Event #1: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	INTESTINAL INFECTION
Preferred term	消化管感染
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 403 / 226
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 226): Basophils: 0.08 [0 - 1] 10^9/L; Basophils/Leukocytes: 0.7 [0 - 1] %; Eosinophils: 0.1 [0 - 1] 10^9/L; Eosinophils/Leukocytes: 0.1 [0 - 1] %; Erythrocytes: 4.78 [4.5 - 6.3] 10^12/L; Hematocrit: 0.407 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 124 [130 - 175] G/L; Leukocytes: 11.3 [4 - 10] 10^9/L; Lymphocytes: 1.59 [1 - 4] 10^9/L; Lymphocytes/Leukocytes: 14.1 [25 - 40] %; Monocytes: 0.69 [0 - 1] 10^9/L; Monocytes/Leukocytes: 6.1 [2 - 8] %; NPTST085-CRP: 4.4 [0.1 - 0.5] MG/DL; Neutrophils: 8.83 [2 - 8] 10^9/L; Neutrophils/Leukocytes: 78.1 [40 - 75] %; Platelets: 459 [140 - 450] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 226): CT SCAN ABDOMINAL: INTESTINAL INFECTION

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FREE FLUID IN EDEMATOUS INTESTINAL WALL, WITHOUT EVIDENCE OF PERFORATION OR SIGNS OF INTESTINAL OBSTRUCTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はチリの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腸管感染症の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与403日後＊，被験者は腸管感染症を発現した。

投与403日後＊　，被験者は，下痢，血便及び嘔吐を伴わない腹痛のために入院した。被験者は緊急の診察を受け，検体検査及び診断が行われた。投与410日後＊，被験者は退院した。

投与された薬剤は，メトロニダゾール及び ciprofloxacino であった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Gastrointestinal infection (10017964) (Gastrointestinal infection (10017964)) [v.24.0] [10017964]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of INTESTINAL INFECTION

- Investigator: Free fluid in edematous intestinal wall, without evidence of perforation or signs of intestinal obstruction.

- AbbVie: Gastrointestinal tract infections are common in both developing and developed countries and are produced by a wide variety of enteropathogens, including bacteria, viruses and parasites.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABSOLUTE BASOPHIL COUNT:** 0.08 X10**3/MCL (normal 0 to 1)

[redacted] **ABSOLUTE EOSINOPHIL COUNT:** 0.1 X10**3/MCL (normal 0 to 1)

[redacted] **ABSOLUTE LYMPHOCYTE COUNT:** 1.59 X10**3/MCL (normal 1 to 4)

[redacted] **ABSOLUTE MONOCYTE COUNT:** 0.69 X10**3/MCL (normal 0 to 1)

[redacted] **ABSOLUTE NEUTROPHIL COUNT:** 8.83 X10**3/MCL (normal 2 to 8)

[redacted] **BASOPHIL COUNT:** 0.7 % (normal 0 to 1)

[redacted] **CRP:** 4.4 mg/dL (normal 0.1 to 0.5)

[redacted] **ABDOMINAL CT SCAN:** Intestinal infection

[redacted] **EOSINOPHIL COUNT:** 0.1 % (normal 0 to 1)

[redacted] **20[redacted] HEMATOCRIT:** 40.7 L/L (normal 40 to 52)

[redacted] **20[redacted] HEMOGLOBIN:** 12.4 G/DL (normal 13 to 17.5)

[redacted] **20[redacted] LYMPHOCYTE COUNT:** 14.1 % (normal 25 to 40)

[redacted] **20[redacted] MONOCYTES:** 6.1 % (normal 2 to 8)

[redacted] **20[redacted] NEUTROPHIL COUNT:** 78.1 % (normal 40 to 75)

[redacted] **20[redacted] PLATELET COUNT:** 459 X10**3/MCL (normal 140 to 450)

[redacted] **20[redacted] RBC:** 4.78 X10**6/MCL (normal 4.5 to 6.3)

[redacted] **20[redacted] WBC:** 11.3 X10**3/MCL (normal 4 to 10)

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
帯状疱疹	X	X		X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	3[redacted]	MALE	ASIAN

Medical History	Onset Year
ANEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HYPELURICEMIA	20[redacted]
INTERNAL HEMORRHOIDS	20[redacted]
TRACHEITIS	20[redacted]
URINE PROTEIN POSITIVE	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 208	153

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 209	[redacted]20[redacted] / 457	249

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	500 mg	TID	Y-M: 20[redacted]
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
CEFOPERAZONE;SULBACTAM	3 g	TID	Y-M: 20[redacted]
HYDROCORTISONE	80 mg	QD	Y-M: 20[redacted]
METRONIDAZOLE	0.5 g	BID	Y-M: 20[redacted]
SODIUM CHLORIDE	100 mL	TID	Y-M: 20[redacted]
BLINDED THERAPY	40 mL	OTHER: BIWEEKLY	Y-M: 20[redacted]
PIPERACILLIN;TAZOBACTAM	4.5 g	TID	Y-M: 20[redacted]
SODIUM CHLORIDE	100 mL	TID	Y-M: 20[redacted]
MESALAZINE	2 g	QD	Y-M: 20[redacted] / -252
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -68
MESALAZINE	1 g	QD	Y: 20[redacted]
MESALAZINE	1 g	QID	Y: 20[redacted]
RIFAXIMIN	200 mg	QID	Y: 20[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	500 mg	TID	Y-M: 20[redacted]	ONGOING
ANGELICA DAHURICA;ARISAEMA SPP.;BOMBYX MORI;GASTRODIA ELATA;NOTOPTERYGIUM SPP.;PANAX NOTOGINSENG;SAPOSHNIKOVIA DIVARICATA;TYPHONIUM GIGANTEUM	0.56 g	TID	Y-M: 20[redacted] / 250	Y-M: 20[redacted] / 252
FAMCICLOVIR	0.25 g	TID	Y-M: 20[redacted] / 250	Y-M: 20[redacted] / 252
OTHER DERMATOLOGICAL PREPARATIONS	NA OTHER: NA	BID	Y-M: 20[redacted] / 250	Y-M: 20[redacted] / 252

PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 250	Y-M: 20[redacted] / 252
RABBIT VACCINIA EXTRACT	2 OTHER: TROCHE	BID	Y-M: 20[redacted] / 250	Y-M: 20[redacted] / 252
DIHYDROCODEINE;PARACETAMOL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 251	Y-M: 20[redacted] / 252
BRIVUDINE	125 mg	QD	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 258
CIPROFLOXACIN	10 g	OTHER: NA	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 264
COBAMAMIDE	1.5 mg	QD	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 263
GANODERMA LUCIDUM	4 mL	QD	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 263
INTERFERON ALFA-2B	10 g	OTHER: NA	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 264
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 252	ONGOING
THIAMINE	10 mg	TID	Y-M: 20[redacted] / 252	ONGOING
UNSPECIFIED HERBAL	NA OTHER: NA	BID	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 260
UNSPECIFIED HERBAL	NA OTHER: TOPICAL TREATMENT	OTHER: TOPICAL TREATMENT	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 264
MESALAZINE	0.5 g	QD	Y-M: 20[redacted] / 253	ONGOING
CLINDAMYCIN;METRONIDAZOLE	10 g	OTHER: NA	Y-M: 20[redacted] / 255	ONGOING
SODIUM CHLORIDE	20 mL	OTHER: NA	Y-M: 20[redacted] / 255	Y-M: 20[redacted] / 262
BOVINE BASIC FIBROBLAST GROWTH FACTOR	NA OTHER: NA	OTHER: NA	Y-M: 20[redacted] / 264	ONGOING
GANCICLOVIR	NA OTHER: NA	OTHER: NA	Y-M: 20[redacted] / 264	ONGOING
MECOBALAMIN	0.5 mg	TID	Y-M: 20[redacted] / 264	ONGOING
PRANOPROFEN	NA OTHER: NA	OTHER: NA	Y-M: 20[redacted] / 264	ONGOING
UROGASTRONE	NA OTHER: NA	OTHER: NA	Y-M: 20[redacted] / 264	ONGOING
MESALAZINE	1 g	QID	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 456 / 248
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 253): NPTST001-(PUS BULB) STOOL: 8-10 [NOT REPORTED - NOT REPORTED] /HP; NPTST058-C-REACTIVE PROTEIN: 22.12 [0 - 10] MG/L; NPTST100-ERYTHROCYTE SEDIMENTATION RATE: 23 [0 - 15] MM/H; NPTST214-RED BLOOD CELLS (STOOL): 1-2 [NOT REPORTED - NOT REPORTED] /HP; NPTST228-SERUM AMYLOID A: 267.76 [0 - 10] MG/L