

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██-██
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	14.6 g	QD	Y-M: 20██-██ / -64
PREDNISONE	50 mg	QD	Y: 20██

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
MESALAZINE	1 g	TID	Y-M: 20██-██	ONGOING
CEFUROXIME	500 mg	BID	Y-M: 20██-██ / 247	Y-M: 20██-██ / 254
PYRANTEL	3 OTHER: TABL	QD	Y-M: 20██-██ / 250	Y-M: 20██-██ / 250
GLUCOSE	UNK mL	OTHER: DAILY	Y-M: 20██-██ / 254	Y-M: 20██-██ / 259
GLUCOSE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	UNK mL	OTHER: DAILY	Y-M: 20██-██ / 254	Y-M: 20██-██ / 259
OCTENIDINE;PHENOXYETHANOL	UNK mL	OTHER: DAILY	Y-M: 20██-██ / 254	Y-M: 20██-██ / 259
OMEPRAZOLE	UNK mg	OTHER: DAILY	Y-M: 20██-██ / 254	Y-M: 20██-██ / 259
PREDNISONE	25 mg	QD	Y-M: 20██-██ / 254	Y-M: 20██-██ / 274
TIMONACIC	UNK mg	OTHER: DAILY	Y-M: 20██-██ / 254	Y-M: 20██-██ / 259
OMEPRAZOLE	20 mg	QD	Y-M: 20██-██ / 260	ONGOING
TIMONACIC	100 mg	TID	Y-M: 20██-██ / 260	ONGOING
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	14.6 g	QD	Y-M: 20██-██ / 307	Y-M: 20██-██ / 307

Event #1: Event of Interest - Hepatic Disorder

Event Description	HEPATITIS DUE TO MONONUCLEOSIS
Preferred term	肝炎
AE Onset Date / Initial Rx Day	███-██-20██ / 303
Age at AE Onset	2█
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
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

Event #2: 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	20 / 303
Age at AE Onset	2

Laboratory Testing

20 (RX DAY 255): Bilirubin: 0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Erythrocytes: 4+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Erythrocytes: 4.54 [3.8 - 5.1] 10¹²/L; Glucose: 0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hematocrit: 0.393 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 132 [117 - 155] G/L; Ketones: 0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 6.71 [4.5 - 11] 10⁹/L; Leukocytes: 0 [4.5 - 11] 10⁹/L; Lymphocytes/Leukocytes: 70.2 [20 - 44] %; NPTST258-GRANULOCYTES: 12.5 [NOT REPORTED - NOT REPORTED] %; NPTST334-MCV: 86.6 [NOT REPORTED - NOT REPORTED] fL; Nitrite: 0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 312 [150 - 400] 10⁹/L; Protein: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Specific Gravity: 1.015 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Urobilinogen: 0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; pH: 6 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; 20 (RX DAY 256): Erythrocytes: 4.52 [3.8 - 5.1] 10¹²/L; Hematocrit: 0.389 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 132 [117 - 155] G/L; Leukocytes: 7.55 [4.5 - 11] 10⁹/L; Lymphocytes/Leukocytes: 69.8 [20 - 44] %; NPTST258-GRANULOCYTES: 14.5 [NOT REPORTED - NOT REPORTED] %; NPTST334-MCV: 86.1 [NOT REPORTED - NOT REPORTED] fL; Platelets: 319 [150 - 400] 10⁹/L; 20 (RX DAY 259): Erythrocytes: 4.36 [3.8 - 5.1] 10¹²/L; Hematocrit: 0.375 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 126 [117 - 155] G/L; Leukocytes: 6.76 [4.5 - 11] 10⁹/L; Lymphocytes/Leukocytes: 58.3 [20 - 44] %; NPTST194-EBV-IGM: 160 [NOT REPORTED - NOT REPORTED] U/mL; NPTST258-GRANULOCYTES: 22.8 [NOT REPORTED - NOT REPORTED] %; NPTST334-MCV: 86 [NOT REPORTED - NOT REPORTED] fL; Platelets: 330 [150 - 400] 10⁹/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	320
Duration of AE	18 DAYS
Severity	MODERATE
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

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Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者はポーランドの 2 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、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、ジルベール症候群、非喫煙者及び非飲酒者であった。

Event 2 の臨床経過：

投与303日後＊，被験者は伝染性単核症を発現した。投与320日後＊，伝染性単核症は消失した。

投与303日後＊，被験者は入院した。被験者は単核症による咽頭痛及び肝腫大（いずれも非重篤）を呈していた。被験者の症状は治療後に元に戻った。投与320日後＊，被験者は退院した。

投与された薬剤は、octanisept, encorton, 複合電解質溶液及び bioracef であった。

Causality for ABT-494 (Blinded)

1) Infectious mononucleosis (10021914) (Infectious mononucleosis (10021914)) [v.21.0]
[10021914]

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 ABT-494 (Blinded)

Event of INFECTIOUS MONONUCLEOSIS

- **Investigator:** Viral infection.

- **AbbVie:** Event is common in the general population. Additional risk factor includes subject's age.

Relevant Laboratory & Other Diagnostic Tests

██████ 20██ URINE RED BLOOD CELLS: 4+

██████ 20██ WBC: 6.71 G/L

██████ 20██ WBC: 7.55 G/L

██████ 20██ WBC: 6.76 G/L

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Hepatitis(██████ 20██): Due to Mononucleosis. Study drug interrupted. Symptoms included hepatomegaly, increase of ALT, AST, and GGT. History of 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
COVID-19	X			X

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

Medical History	Onset Year
ASTHMA	20 [REDACTED]
CHICKENPOX	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	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 55	55
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	[REDACTED] 20 [REDACTED] / 56	[REDACTED] 20 [REDACTED] / 108	53
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	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
MESALAZINE	1 g	QD	Y-M: 20███
MESALAZINE	4 g	QD	Y-M: 20███
MESALAZINE	3 g	QD	Y-M: 20███
PREDNISOLONE	40 mg	QD	Y-M: 20███ / -355
MESALAZINE	3 g	QD	Y-M: 20███ / -256
MESALAZINE	4 g	QD	Y-M: 20███ / -207
PANTOPRAZOLE	20 mg	BID	Y-M: 20███ / -2
CYPROTERONE	2 mg	QD	Y: 20███
ETHINYLESTRADIOL	0,035 mg	QD	Y: 20███
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 20███

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
PANTOPRAZOLE	20 mg	BID	Y-M: 20███ / -2	ONGOING
CYPROTERONE	2 mg	QD	Y-M: 20███ / 122	ONGOING
ETHINYLESTRADIOL	0,035 mg	QD	Y-M: 20███ / 122	ONGOING
BENZYL PENICILLIN	300 000 IU	OTHER: ONCE	Y-M: 20███ / 228	Y-M: 20███ / 228
BENZYL PENICILLIN	600 000 IU	OTHER: ONCE	Y-M: 20███ / 228	Y-M: 20███ / 228
BENZYL PENICILLIN	2.4 MIU	OTHER: ONCE	Y-M: 20███ / 229	Y-M: 20███ / 229
DOMPERIDONE	10 mg	PRN	Y-M: 20███ / 229	Y-M: 20███ / 236
PARACETAMOL	1 g	QID	Y-M: 20███ / 229	Y-M: 20███ / 240
PREDNISOLONE	20 mg	QD	Y-M: 20███ / 229	Y-M: 20███ / 235
IPRATROPIUM	0.25/2 OTHER: MG/ML	BID	Y-M: 20███ / 231	ONGOING
SALBUTAMOL	5 OTHER: MG/ML	PRN	Y-M: 20███ / 231	ONGOING
BENZYL PENICILLIN	2.4 MIU	OTHER: ONCE	Y-M: 20███ / 232	Y-M: 20███ / 232

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

Event Description	WORSENING OF COVID-19 INFECTION
Preferred term	COVID-19
AE Onset Date / Initial Rx Day	20███ / 339
Age at AE Onset	3█
Laboratory Testing	20███ (RX DAY 231): Alanine Aminotransferase: 16 [NOT REPORTED - 36] U/L; Albumin: 37 [35 - 50] G/L; Alkaline Phosphatase: 94 [42 - 98] U/L; Aspartate Aminotransferase: 17 [10 - 40] U/L; Basophils/Leukocytes: 0 [0.5 - 1] %;

Bilirubin: 0.3 [NOT REPORTED - 1.1] mg/dL; Chloride: 106 [96 - 115] MMOL/L; Creatine Kinase: 57 [21 - 173] U/L; Creatine Kinase MB: 0.3 [NOT REPORTED - 3.1] ng/mL; Creatinine: 61.882282 [44.20163 - 79.562934] UMOL/L; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4.3 [4.55 - 6.55] 10¹²/L; Glucose: 6.050263 [3.33042 - 6.10577] MMOL/L; Hematocrit: 0.379 [0.36 - 0.46] FRACTION OF 1; Hemoglobin: 130 [120 - 160] G/L; Leukocytes: 5.8 [4.5 - 11] 10⁹/L; Lymphocytes/Leukocytes: 9.4 [20 - 40] %; Monocytes/Leukocytes: 8.1 [2 - 8] %; NPTST186-DIRECT BILIRUBIN: 0.15 [NOT REPORTED - 0.2] mg/dL; NPTST243-GAMMA-GLUTAMYL TRANSFERASE: 35 [5 - 36] U/L; NPTST246-GFR: 102.4 [NOT REPORTED - NOT REPORTED] mL/min/1.73m²; NPTST313-LACTATE DEHYDROGENASE: 208 [125 - 220] U/L; NPTST331-MCH: 30.2 [27 - 32] PG; NPTST332-MCHC: 34.2 [30 - 36] G/DL; NPTST334-MCV: 88.4 [76 - 96] FL; NPTST352-MPV: 9.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST416-PROCALCITONIN: 0.0 [NOT REPORTED - 0.05] ng/mL; NPTST439-RDW: 13.2 [11 - 15] %; NPTST522-TROPONIN I: <1.9 [0 - 15.6] PG/ML; NPTST532-UREA: 19 [NOT REPORTED - 50] mg/dL; Neutrophils/Leukocytes: 82.5 [40 - 60] %; Platelets: 202 [150 - 400] 10⁹/L; Potassium: 4.2 [3.5 - 5.5] MMOL/L; Protein: 67 [64 - 83] G/L; Sodium: 139 [135 - 145] MMOL/L

Microbiology

20 (RX DAY 231): URINE NPTST319-LEGIONELLA PNEUMOPHILA AG: NEGATIVE; URINE NPTST494-STREPTOCOCCUS PNEUMONIAE: NEGATIVE

AE Stopped Initial Rx Day	340
Duration of AE	2 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SARS-COV-2 VIRUS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者はポルトガルの 3 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、COVID-19 感染の悪化の事象を発現した。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339日後＊，被験者は COVID-19 感染の悪化を発現した。投与340日後＊，COVID-19 感染の悪化は消失した。

本事象発現前の投与337日後＊，COVID-19感染（非重篤）と診断され、本事象により治験薬の投与が中止された。

投与339日後＊，被験者は刺激性の咳嗽，呼吸困難及び疲労感のために入院した。被験者には発熱はなかったが，頻呼吸があり，血圧が 131/90 mmHg，心拍数が 80 bpm，酸素飽和度が 98%，及び体温が摂氏 36.6℃であった。身体検査では，肺の聴診で，包括的に肺胞音が減少していることが確認された。残りの入院期間中，被験者は発熱がなかった。投与340日後＊，被験者は安定した状態で退院した。

投与された薬剤は，benzathine penicillin，ベンジルペニシリン，procaine benzylpenicillin，プレドニゾロン，イプラトロピウム臭化物，サルブタモール，ドンペリドン及び paracetamol であった。

The patient's past medications include:

MESALAZINE for ULCERATIVE COLITIS (20 - 20, 20 - 20, 20 - 20, 20 - 20)

PREDNISOLONE for ULCERATIVE COLITIS (20 - 20)

Causality for UPADACITINIB (Blinded)

1) COVID-19 aggravated (10084657) (COVID-19 (10084268)) [v.24.0] [10084657]

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 OF COVID-19 INFECTION

- **Investigator:** SARS-COV-2 VIRUS

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

Relevant Laboratory & Other Diagnostic Tests

20	BLOOD PRESSURE: . 131/90 mmHg
20	CHEST CT: SCATTERED BILATERAL GROUND GLASS AREAS COMPATIBLE WITH COVID INFECTION. NO CONSOLIDATIONS OR SUSPICIOUS EXPANSIVE INJURIES. NO HILAR OR MEDIASTINAL ADENOPATHIES. NO PLEURAL OR PERICARDIAL EFFUSION. NO OTHER RELEVANT CHANGES IN THE EMERGENCY SERVICE CONTEXT
20	CHEST XRAY: DISCRETE BILATERAL HILAR REINFORCEMENT
20	GAMMA-GLUTAMYL TRANSFERASE: 35 U/L (normal 5 to 36)
20	GFR: 102.4 ML/MIN/1.73M^2
20	GLUCOSE: 109 mg/dL (normal 60 to 110)
20	HEART RATE: 80 /min
20	HEMATOCRIT: 37.9 % (normal 36.0 to 46.0)
20	HEMOGLOBIN: 13.0 G/L (normal 12.0 to 16.0)
20	LACTATE DEHYDROGENASE: 208 U/L (normal 125 to 220)
20	MONOCYTES %: 8.10 % (normal 2.0 to 8.0)
20	MPV: 9.0 no units
20	NASOPHARYNGEAL SWAB: Positive for Covid-19
20	NEUTROPHILS %: 82.5 % (normal 40 to 60)
20	OXYGEN SATURATION: 98 %
20	PLATELET COUNT: 202 X10**3/MM**3 (normal 150 to 400)
20	RED BLOOD CELLS: 4.3 10^6/mm3 (normal 4.55 to 6.55)
20	TEMPERATURE: 36.6 Degrees C
20	TROPONIN I: <1.9 PG/ML
20	URINE LEGIONELLE PNEUMOPHILA AG: NEGATIVE

20 ■ URINE STREPTOCOCCUS PNEUMONIAE: NEGATIVE

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
Placebo	4[REDACTED]	MALE	WHITE

Medical History	Onset Year
COXOFEMORAL JOINT DISLOCATION	20[REDACTED]
LEFT SIDED UC	20[REDACTED]
VASOMOTOR RHINITIS	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	0.25 PACK	10	20[REDACTED]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration						
Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 20[REDACTED] / 1	[REDACTED] 20[REDACTED] / 58	58
M14-234 SS3 Placebo (MAIN)		ORAL	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
SULFASALAZINE	2 g	BID	Y-M: 20██-██
SULFASALAZINE	1 g	BID	Y-M: 20██-██
HYDROCORTISONE	125 mg	QD	Y-M: 20██-██
SULFASALAZINE	2 g	BID	Y-M: 20██-██
MESALAZINE	500 mg	BID	Y-M: 20██-██
SULFASALAZINE	1 g	BID	Y-M: 20██-██
DEXAMETHASONE	48 mg	QD	Y-M: 20██-██
SULFASALAZINE	1 g	BID	Y-M: 20██-██
SULFASALAZINE	2 g	BID	Y-M: 20██-██
MESALAZINE	500 mg	QD	Y-M: 20██-██ / -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 / Stop Year-Month / RX Day	RX Day
SULFASALAZINE	1 g	BID	Y-M: 20██-██	ONGOING
CEFTRIAXONE	2.0 g	BID	Y-M: 20██-██ / 118	Y-M: 20██-██ / 127
LEVOFLOXACIN	500 mg	BID	Y-M: 20██-██ / 118	Y-M: 20██-██ / 127
AMBROXOL	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
ASCORBIC ACID	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
DEXAMETHASONE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
ENOXAPARIN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
INOSINE;MEGLUMINE;METHIONI NE;NICOTINAMIDE;SUCCINIC ACID	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
INOSINE;NICOTINAMIDE;RIBOFL AVIN;SUCCINIC ACID	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
LOPINAVIR;RITONAVIR	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
OMEPRAZOLE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
SODIUM CHLORIDE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 93	Y-M: 20██-██ / 153
AMBROXOL	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 123	Y-M: 20██-██ / 153

APIXABAN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 123 Y-M: 20██-██ / 153
VANCOMYCIN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 123 Y-M: 20██-██ / 153
AMIKACIN	500 mg	BID	Y-M: 20██-██ / 128 Y-M: 20██-██ / 131

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	2020-01-16 / 165
Age at AE Onset	41
Laboratory Testing	2020-01-18 (RX DAY 108): NPTST450-RNA2019-NCOV: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; 2020-01-19 (RX DAY 127): Alanine Aminotransferase: 69 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 41 [NOT REPORTED - NOT REPORTED] U/L; Creatinine: 106 [80 - 115] UMOL/L; Hemoglobin: 145 [132 - 173] G/L; Leukocytes: 5.7 [4.5 - 11] 10^9/L; NPTST307-INR: 1.221 [NOT REPORTED - NOT REPORTED] RATIO; NPTST450-RNA2019-NCOV: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 351 [150 - 400] 10^9/L; 2020-01-20 (RX DAY 130): NPTST450-RNA2019-NCOV: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; 2020-01-21 (RX DAY 134): Alanine Aminotransferase: 83 [NOT REPORTED - NOT REPORTED] U/L; 2020-01-22 (RX DAY 137): Creatinine: 101 [80 - 115] UMOL/L
Microbiology	NOT REPORTED
AE Stopped Initial Rx Day	196
Duration of AE	32 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID-19, VIRUS IDENTIFIED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [REDACTED] 20[REDACTED]:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者はロシア連邦の 41 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 0.25 箱を 10 年間）、潰瘍性大腸炎及び非飲酒者であった。

Event 1 の臨床経過：

投与165日後＊，被験者は COVID-19 肺炎を発現した。投与196日後＊，COVID-19 肺炎は消失した。

投与165日後＊，被験者は咽頭痛，鼻水，摂氏 38.5°C までの発熱，乾性咳嗽，関節痛，全身の脱力感及び胸痛を経験し始めた。投与166日後＊，鼻咽頭ぬぐい液での COVID-19 検査で陽性であった。被験者は，COVID-19 感染（非重篤）と診断された。被験者は外来で治療を受けた。

投与174日後＊，被験者は良好な臨床経過が認められないため，隔離の条件下で，治療のために入院した。入院時の症状は，咳嗽及び摂氏 38.5°C までの高体温症であった。被験者の状態は，継続的な治療により安定していた。臨床経過として，投与184日後＊ に実施したマルチスライス（スパイラル）コンピュータ断層撮影の結果では，投与175日後＊ に実施した結果と比較して，密閉された空気の容積が減少し，網状の変化が優位であり，CT 画像では消失しつつある両側の多分節性肺炎が確認された。治療により，良好な臨床経過が達成された。被験者は，投与185日後＊ 及び投与188日後＊ に実施した 2 回の鼻咽頭ぬぐい液での検査で，COVID-19 ウイルス陰性の結果が確認されたため，フォローアップケアを行う病院に移った。被験者の状態は安定しており，投与189日後＊ 以降，高熱は認められず，酸素飽和度は安定しており（95%–99%），呼吸不全の徴候も認められなかった。身体検査では，肺の安定した画像が確認された。投与196日後＊，被験者は良好な状態で退院した。

投与された薬剤は，エノキサパリン，セフトリアキソン，ビタミン C，remaxol，cytoflavin，塩化ナトリウム 0.9%水溶液，デキサメタゾン，オメプラゾール，アミカシン，バンコマイシン，エリキュース，bronchorus，カレトラ，アンブロキシソール及びレボフロキサシンであった。

The patient's past medications include:

SULFASALAZINE for ULCERATIVE COLITIS (2000 - 2000, 2000 - 2000, 2000 - 2000)

HYDROCORTISONE for ULCERATIVE COLITIS (2000 - 2000)

DEXAMETHASONE for ULCERATIVE COLITIS (2000 - 2000)

SALOFALK [AMINOSALICYLIC ACID] for ULCERATIVE COLITIS (2000 - 2000)

Causality for UPADACITINIB (Blinded)

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: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 PNEUMONIA

- **Investigator:** COVID-19 virus identified

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

Relevant Laboratory & Other Diagnostic Tests

20 ALT: 69 U/L (normal 6 to 34)

20 ALT: 83 U/L (normal 6 to 34)

20 AST: 41 U/L (normal 9 to 34)

20 BMI: 30.48 kg/m2

20 BODY TEMPERATURE: 38.5 Degrees C

20 BODY TEMPERATURE: 38.5 Degrees C

20 COVID-19 VIRUS TEST: nasopharyngeal swab: positive

20 COVID-19 VIRUS TEST: nasopharyngeal swab; negative

20 COVID-19 VIRUS TEST: nasopharyngeal swab; negative

20 CREATININE: 106 MMOL/L (normal 31 to 101)

- 20 CREATININE: 101 MMOL/L (normal 31 to 101)
- 20 ECG: Sinus rhythm, heart rate 73 per minute, EOC horizontally. No marked metabolic changes.
- 20 HEMOGLOBIN: 145 G/L (normal 116 to 164)
- 20 INR: 1.221 units (normal 0.85 to 1.15)
- 20 OXYGEN SATURATION: 95 - 99%
- 20 PLATELET COUNT: 351 X10**9/L (normal 140 to 400)
- 20 SPIRAL COMPUTED TOMOGRAPHY OF THE CHEST: Lungs: On both sides, half-segmentally, multiple foci of infiltration of lung tissue of the "ground glass" type are determined, the lesion volume is less than 50%. Trachea and large bronchi are not changed. No pleural effusion was found.
- 20 SPIRAL COMPUTED TOMOGRAPHY OF THE CHEST: In dynamics, a decrease in the size of pneumatic seals, the predominance of reticular changes. Positive dynamics compared to 20/20.
- 20 WBC: 5.7 X10**9/L (normal 4.0 to 10.0)

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
COVID-19 肺炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	3 [REDACTED]	FEMALE	WHITE

Medical History	Onset Year
ANKYLOSING SPONDYLITIS	20 [REDACTED]
ARTHRITIS	20 [REDACTED]
ENTHESITIS	20 [REDACTED]
ESOPHAGITIS	20 [REDACTED]
GASTROESOPHAGEAL REFLUX	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	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration						
Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 56	56

M14-675 ABT-494 (OL)	45 mg	ORAL	QD	20 / 57	20 / 118	62
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	20 / 1	20 / 364	364

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	50 mg	BID	Y-M: 20 /
BUDESONIDE	6 mg	QD	Y-M: 20 /
MESALAZINE	2 g	BID	Y-M: 20 /
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20 /
PREDNISONE	15 mg	QD	Y-M: 20 /
GOLIMUMAB	50.000 mg	NOT REPORTED	Y-M: 20 /
MESALAZINE	1.2 g	TID	Y-M: 20 /
ESTRADIOL;NOMEGESTROL	2.5 mg	QD	Y: 20

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	TID	Y-M: 20 /	ONGOING
FAVIPIRAVIR	1.6 g	BID	Y-M: 20 / 278	Y-M: 20 / 278
FAVIPIRAVIR	0.6 g	BID	Y-M: 20 / 279	Y-M: 20 / 280
ESTRADIOL;NOMEGESTROL	2.5 mg	QD	Y: 20	ONGOING

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

Event Description	POLYSEGMENTAL BILATERAL COVID-19 PNEUMONIA
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day	2020 / 394
Age at AE Onset	3
Laboratory Testing	
	2020 (RX DAY 276): NPTST449-RNA 2019 -NCOV: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED
Microbiology	
	NOT REPORTED
AE Stopped Initial Rx Day	406
Duration of AE	13 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID-19 PANDEMIC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: 2020:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者はロシア連邦の 3 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、多分節性両側 COVID-19 肺炎の事象を発現した。関連する病歴は、潰瘍性大腸炎、強直性脊椎炎及び非喫煙者であった。

Event 1 の臨床経過：

投与394日後＊，被験者は多分節性両側 COVID-19 肺炎を発現した。投与406日後＊，多分節性両側 COVID-19 肺炎は消失した。

投与395日後＊，被験者は障害のステータスの拡大に必要な書類を作成するため、消化器科に入院した。入院中にコロナウイルス（COVID-19）塗抹陽性が確認された。この検査を除いては、COVID-19 に関連する徴候又は症状は認められなかった。被験者は COVID-19 の治療のため

移送された。投与396日後＊，被験者は COVID-19 の治療薬を開始したが，その治療に耐えることができなかった。CT スキャン検査が実施され，被験者はウイルス性多分節性両側肺炎と診断された。投与398日後＊に治療は中止された。投与406日後＊，被験者は良好な状態で退院した。

投与された薬剤は，ファビピラビルであった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

METIPRED for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

SALOFALK for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

BUDESONIDE for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

PREDNISONE for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

GOLIMUMAB for ULCERATIVE COLITIS (■■■■■ 20■■■ - ■■■■■ 20■■■)

Causality for UPADACITINIB (Blinded)

1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.24.1] [10084380]

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 POLYSEGMENTAL BILATERAL COVID-19 PNEUMONIA

- **Investigator:** COVID-19 pandemic

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

Relevant Laboratory & Other Diagnostic Tests

201 ■ **BODY MASS INDEX:** 17.8 kg/m²

201 ■ **CHEST CT:** Changes in the lungs can be regarded as viral polysegmental bilateral pneumonia.
The amount of damage on both sides is not more than 6 percent.

201 ■ **SARS-COV-2 TEST:** Nasopharyngeal swab positive

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
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
ARTERIAL HYPERTENSION	20 [REDACTED]
ATHEROSCLEROSIS	20 [REDACTED]
CATARACT BILATERAL	20 [REDACTED]
CORONARY HEART DISEASE	20 [REDACTED]
DUODENAL ULCER	20 [REDACTED]
EXTENSIVE UC/PANCOLITIS	20 [REDACTED]
NEPHROLITHIASIS	20 [REDACTED]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: CORONARY ARTERY BYPASS GRAFTING	20 [REDACTED]
PRIOR PROCEDURES: SURGICAL TREATMENT OF CATARACTS	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	20	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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 55	55
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	20 / 56	20 / 112	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	20 / 1	20 / 365	365

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	1.5 g	QD	Y-M: 20 -
MESALAZINE	1 g	OTHER: USED PERIODICALLY FOR A WEEK IN 2-3 MONTHS	Y-M: 20 -
PREDNISOLONE	30 mg	QD	Y-M: 20 -
AMLODIPINE	5 mg	QD	Y-M: 20 -
ATORVASTATIN	20 mg	QD	Y-M: 20 -
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20 -
MESALAZINE	4 g	QD	Y-M: 20 - / - 275
PREDNISOLONE	10 mg	QD	Y: 20
MESALAZINE	4 g	QD	Y: 20

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	Stop Year-Month / RX Day
AMLODIPINE	5 mg	QD	Y-M: 20██-██	ONGOING
ATORVASTATIN	20 mg	QD	Y-M: 20██-██	ONGOING
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20██-██	ONGOING
MESALAZINE	4 g	QD	Y-M: 20██-██ / -275	ONGOING
INSULIN	ACCORDING TO NEED IU	OTHER: ACCORDING TO NEED	Y-M: 20██-██ / 183	Y-M: 20██-██ / 213
AMOXICILLIN;CLAVULANIC ACID	500 mg	BID	Y-M: 20██-██ / 200	Y-M: 20██-██ / 205
UMIFENOVIR	200 mg	BID	Y-M: 20██-██ / 200	Y-M: 20██-██ / 205
DEXAMETHASONE	20 mg	QD	Y-M: 20██-██ / 206	Y-M: 20██-██ / 208
FAVIPIRAVIR	200 mg	QD	Y-M: 20██-██ / 206	Y-M: 20██-██ / 216
LEVOFLOXACIN	500 mg	BID	Y-M: 20██-██ / 206	Y-M: 20██-██ / 216
RIVAROXABAN	10 mg	QD	Y-M: 20██-██ / 206	Y-M: 20██-██ / 230
DEXAMETHASONE	10 mg	QD	Y-M: 20██-██ / 209	Y-M: 20██-██ / 213

Event #1: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	██-██-20██ / 113
Age at AE Onset	6█
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	171
Duration of AE	59 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	COVID-19 PNEUMONIA
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day	2020/ / 311
Age at AE Onset	6
Laboratory Testing	
NOT REPORTED	
Microbiology	
2020 (RX DAY 203): OTHER NASOPHARYNGEAL SWAB NPTST360-NASOPHARYNGEAL SWAB (COVID-19): NEGATIVE	
AE Stopped Initial Rx Day	328
Duration of AE	18 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID-19
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: 2020:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者はロシア連邦の 6 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 1 箱を 20 年間）、動脈性高血圧、アテローム性動脈硬化症、冠動脈性心疾患、潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与311日後＊、被験者は、COVID-19 肺炎を発現した。投与328日後＊、COVID-19 肺炎は消失した。

入院前、被験者は発熱を経験していた。

投与318日後＊，被験者は体温の上昇，衰弱，息切れ及び鼻閉のために入院した。被験者はウイルス性肺炎と診断された。投与328日後＊，発熱及び呼吸困難は著しく改善した。同日，被験者は退院した。

投与された薬剤は，avifavir，イグザレルト，arbidol，レボフロキサシン，amoksiklav（アモキシシリン・クラブラン酸合剤）及びデキサメタゾンであった。

The patient's past medications include:

PREDNISOLON for ULCERATIVE COLITIS (20■■ - 20■■, ■■ 20■■ - ■■ 20■■)

SULFASALAZIN for ULCERATIVE COLITIS (■■ 20■■ - ■■ 20■■)

Causality for UPADACITINIB (Blinded)

1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.24.0] [10084380]

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 COVID-19 PNEUMONIA

- **Investigator:** COVID-19

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

Relevant Laboratory & Other Diagnostic Tests

■■■ 20■■ BMI: 29 kg/m2

20 ■ BODY TEMPERATURE: Up to 39 degree C

20 ■ BODY WEIGHT: 9 ■ KG

20 ■ COVID -19 TEST: (NASOPHARYNGEAL SWAB) Negative

20 ■ CT SCAN: LUNGS: polysegmental bilateral pneumonia, lesion 15%

20 ■ CT SCAN: LUNGS: polysegmental bilateral pneumonia, lesion 5-10%

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
急性心筋梗塞	X	X		X

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

Medical History	Onset Year
CARDIAC ARRHYTHMIA: RBBB	20 [REDACTED]
DIABETES MELLITUS: TYP 2	20 [REDACTED]
HYPERLIPIDEMIA: HYPERLIPIDEMIA	20 [REDACTED]
HYPERTENSION	20 [REDACTED]
LATENT TB	20 [REDACTED]
LEFT SIDED UC	20 [REDACTED]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): FLEXIBLE SIGMOIDOSCOPY	20 [REDACTED]
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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 58	58
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20 / 1	20 / 319	319

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19 /
MESALAZINE	500 mg	OTHER: 3X3	Y-M: 20 /
BISOPROLOL	2.5 mg	BID	Y-M: 20 /
GLICLAZIDE	30 mg	QD	Y-M: 20 /
HYDROCHLOROTHIAZIDE;RAMIPRIL	5+25 mg	QD	Y-M: 20 /
ISONIAZID	300 mg	QD	Y-M: 20 /
LERCANIDIPINE	5 mg	QD	Y-M: 20 /
METFORMIN	1000 mg	BID	Y-M: 20 /
RAMIPRIL	5 mg	QD	Y-M: 20 /
MONOCLONAL ANTIBODIES	876.000 mg	PER EVERY 4 WEEKS	Y-M: 20 /
FENOFIBRATE	160 mg	QD	Y-M: 20 / -236
MESALAZINE	500 mg	TID	Y-M: 20 / -210
PREDNISONE	40 mg	QD	Y-M: 20 / -184
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	74 g	BID	Y-M: 20 / -65
INDAPAMIDE	1.5 mg	QD	Y-M: 20 / -66
LERCANIDIPINE	10 mg	BID	Y-M: 20 / -66
MOXONIDINE	0.2 mg	BID	Y-M: 20 / -66
TELMISARTAN	60 mg	QD	Y-M: 20 / -66
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	74 g	BID	Y-M: 20 / -9

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
BISOPROLOL	2.5 mg	BID	Y-M: 20 /	ONGOING

GLICLAZIDE	30 mg	QD	Y-M: 20■■■	ONGOING
METFORMIN	1000 mg	BID	Y-M: 20■■■	ONGOING
FENOFIBRATE	160 mg	QD	Y-M: 20■■■ / -236	ONGOING
MESALAZINE	500 mg	TID	Y-M: 20■■■ / -210	ONGOING
INDAPAMIDE	1.5 mg	QD	Y-M: 20■■■ / -66	ONGOING
LERCANIDIPINE	10 mg	BID	Y-M: 20■■■ / -66	ONGOING
MOXONIDINE	0.2 mg	BID	Y-M: 20■■■ / -66	ONGOING
TELMISARTAN	60 mg	QD	Y-M: 20■■■ / -66	ONGOING
ROSUVASTATIN	20 mg	QD	Y-M: 20■■■ / 288	ONGOING
BROMAZEPAM	1.5 mg	QD	Y-M: 20■■■ / 319	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20■■■ / 319 Y-M: 20■■■ / 327	
PANTOPRAZOLE	20 mg	QD	Y-M: 20■■■ / 319	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated MACE *

Event Description	NON ST ELEVATION MYOCARDIAL INFARCT
Preferred term	急性心筋梗塞
AE Onset Date / Initial Rx Day	■■■20■■■ / 377
Age at AE Onset	6■
Laboratory Testing	■■■20■■■ (RX DAY 319): NPTST285-HS- TROPONIN: 69 [0 - 14] NG/L
Microbiology	NOT REPORTED
AE Stopped Initial Rx Day	394 (17 DAYS AFTER LAST TREATMENT)
Duration of AE	18 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CONDITIONS LISTED IN MEDICAL HISTORY AT SCREENING (HYPERTENSION, DIABETES MELLITUS, CARDIAC ARRHYTHMIA, HYPERLIPIDEMIA)
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Generated: [REDACTED] 20[REDACTED]:11:02

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。本被験者はセルビアの 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、非 ST 上昇型心筋梗塞の事象を発現した。関連する病歴は、潰瘍性大腸炎、2 型糖尿病、高血圧、右脚ブロック、高脂血症、非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与377日後＊，被験者は非 ST 上昇型心筋梗塞を発現した。投与394日後＊，非 ST 上昇型心筋梗塞は消失した。

投与377日後＊，被験者は左肩及び左腕に拡散する圧迫感のある胸痛があり、入院した。被験者は、悪心、左腕の刺痛、空気不足の感覚及び労作性狭心症も訴えた。検体検査及び診断が行われ、非 ST 上昇型心筋梗塞の診断が確定した。外科的な再治療の必要性が示された。投与378日後＊、右経橈骨動脈アプローチでの冠動脈造影検査で、主幹である LKA が関与する 3 枝の冠動脈疾患が確認され、SYNTAX スコアは 46 であった。処置は合併症なく行われ、止血は適切であり、穿刺部位は落ち着いていた。被験者の入院中、狭心症やうっ血性疾患はなく、血行動態は安定していると考えられた。投与394日後＊、被験者は退院した。

被験者の治験は中止された。

投与された薬剤は、プラビックス及び roxera であった。

The patient's past medications include:

MESALAZIN for ULCERATIVE COLITIS ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

AMPRIL for HYPERTENSION ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

AMPRIL HD for HYPERTENSION ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

LERCANIL for HYPERTENSION ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

ANTI OX40 MONOCLONAL ANTIBODY for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

PRONISON for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

Causality for UPADACITINIB (Blinded)

1) Non ST segment elevation myocardial infarction (10064347) (Acute myocardial infarction (10000891)) [v.23.0] [10064347]

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 NON ST ELEVATION MYOCARDIAL INFARCT

- **Investigator:** CONDITIONS LISTED IN MEDICAL HISTORY AT SCREENING (HYPERTENSION, DIABETES MELLITUS, CARDIAC ARRHYTHMIA, HYPERLIPIDEMIA)

- **AbbVie:** Event likely due to pre-existing diabetes mellitus type 2, hypertension, hyperlipidemia and underlying cardiac disease (right bundle branch block on screening EKG).

Relevant Laboratory & Other Diagnostic Tests

■■■■ 20■■ **ABDOMINAL ECHO:** ABDOMEN METEORISTIC. LIVER OF THE USUAL SIZE AND ECHOTEXTURE, VISIBLE LESIONS ARE THE HOMOGENEOUS, WITHOUT ISOLATION OF FOCAL CHANGES. SEVERAL SMALL CALCULUS AND ONE LARGER DIAMETER 6MM. THE GALLBLADDER IS NOT DILATED. THE PANCREAS IN THE SEEN AREA IS HOMOGENEOUS. NORMAL-SIZED SPLEEN, HOMOGENEOUS. NORMAL SIZE KIDNEYS, PRESERVED CORTICAL THICKNESS, LEFT WITHOUT PATH. RIGHT ADRENAL, AT THE LOWER POLE OF A 72MM AMETER ABD. AORTA OF NORMAL LUMEN WIDTH AND FLOW. NO FREE FLUID IS OBSERVED IN THE ABDOMEN AND PELVIS. M. BLADDER INSUFFICIENTLY FILLED WITH ANECHOIC CONTENT

20 ■ **CORONAROGRAPHY:** RCA dominant, occluded in the proximal segment. Homo and heterocolateral are visualized. In distal segment suboccluded before crux. LCA-IM ostially narrowed 70-90%. LAD diffuse atheromatous alternating and calcified, proximal narrowed 50%, medially in the long segment atheromatous alternating and narrowed 70-90%. LAD ostially narrowed 70-90% (medina 0,0,1). ACX in distal segment narrowed 70-90%.

20 ■ **DOPPLER BLOOD VESSELS:** CDS KS shows minimal atherosclerotic changes are present in the investigated arteries of both carotid trees. Left fibrolipid plaque present that narrows the lumen of ACI 20-25%. Right in the bifurcation and towards the ACI retreat there is a fibrolipid plaque that narrows the lumen of the ACI 30-35%. The vertebral arteries are of antegrade flow. The subclavian arteries are of the normal protrusion. Jugular veins compressible.

20 ■ **ECHOCARDIOGRAM:** AORTA IS OF NORMAL DIMENSIONS AT THE ROOT, EASILY DILATED IN THE ASCENDING PART, THREE VEINS, PRESERVED SEPARATIONS IN THE SYSTOLE, FLOW NEAT, WITHOUT AR. LP EASILY DILATED, NO FOREIGN MASSES. MV NEAT MORPHOLOGY, FLOW NEAT, MR 1+. LV OF NEAT DIMENSIONS, NEAT WALL THICKNESS, PRESERVED SYSTOLIC, DISTURBED DIASTOLIC FUNCTIONS. AKINESIA APICALLY, HYPO TO AKINESIA APICASEPTALLY. PRESERVED SYSTOLIC FUNCTION LV, EF 50-55%. MR 1+ INTO EASILY DILATED LP. INITIALLY DILATED ASC.AORTA

20 ■ **EKG:** SCREENING EKG: Right bundle branch block

20 ■ **TROPONIN:** 69 NG/L (normal 0 to 14)

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
Placebo	4 [REDACTED]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20 [REDACTED]
GASTRODUODENITIS	20 [REDACTED]
NODD. HEMORROIDALES	20 [REDACTED]
PSEUDOPOLYPOSIS COLONIS	20 [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	FORMER	1 PACK	17	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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 60	60
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 368	368

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1500 mg	BID	Y-M: 20██-██
METRONIDAZOLE	400 mg	QID	Y-M: 20██-██ / -149
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	74 g	BID	Y-M: 20██-██ / -65
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	74 g	BID	Y-M: 20██-██ / -1
AZATHIOPRINE	150 mg	QD	Y: 20██

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	1500 mg	BID	Y-M: 20██-██	ONGOING
METRONIDAZOLE	400 mg	TID	Y-M: 20██-██ / 22	Y-M: 20██-██ / 32
SACCHAROMYCES BOULARDII	250 mg	PRN	Y-M: 20██-██ / 22	ONGOING
ALFACALCIDOL	50 mg	BID	Y-M: 20██-██ / 43	ONGOING
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20██-██ / 43	Y-M: 20██-██ / 48
PANTOPRAZOLE	40 mg	QD	Y-M: 20██-██ / 43	ONGOING
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20██-██ / 49	Y-M: 20██-██ / 51
PREDNISONE	30 mg	QD	Y-M: 20██-██ / 52	Y-M: 20██-██ / 77
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	74 g	BID	Y-M: 20██-██ / 55	Y-M: 20██-██ / 55
PREDNISONE	25 mg	QD	Y-M: 20██-██ / 78	Y-M: 20██-██ / 82
PREDNISONE	20 mg	QD	Y-M: 20██-██ / 83	Y-M: 20██-██ / 89
PREDNISONE	15 mg	QD	Y-M: 20██-██ / 90	Y-M: 20██-██ / 96
PREDNISONE	10 mg	QD	Y-M: 20██-██ / 97	Y-M: 20██-██ / 103
PREDNISONE	7.5 mg	QD	Y-M: 20██-██ / 103	Y-M: 20██-██ / 110
PREDNISONE	5 mg	QD	Y-M: 20██-██ / 111	Y-M: 20██-██ / 117
PREDNISONE	2.5 mg	QD	Y-M: 20██-██ / 118	Y-M: 20██-██ / 125

Event #1: Serious Adverse Event

Event Description	UC EXACERBATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	20 / 101
Age at AE Onset	4
Laboratory Testing	
	20 (RX DAY 43): NPTST098-CALPROTECTIN: 1000 [50 - 200] MG/KG; NPTST165-CRP: 75.4 [0 - 5] MG/L
Microbiology	
	20 (RX DAY 50): OTHER GASTRIC BIOPSY SAMPLE NPTST249-GIMSI COLORING FOR HELICOBACTER: NEGATIVE
AE Stopped Initial Rx Day	185
Duration of AE	85 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PROGRESSION OF BASIS DEASEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者はセルビアの 4 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、元喫煙者（1 日 1 箱を 17 年間）、潰瘍性大腸炎、胃十二指腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与101日後＊，被験者は潰瘍性大腸炎の悪化を発現した。投与185日後＊，潰瘍性大腸炎の悪化は消失した。

被験者は腹痛及び体重減少のために医師を訪れた。身体検査が行われ、検査のために採血が行われた。投与103日後＊，被験者は腹痛及び液状便があり、入院した。検体検査、腹部超音

波検査, 結腸内視鏡検査及び MRI 検査が行われた。投与117日後*, 被験者は退院した。

投与された薬剤は, metilprednisolone, prednisone, pronison 及び pantoprazol であった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS (20 - 20)

METRONIDASOL for ULCERATIVE COLITIS (20 - , 20 - 20 -)

Causality for UPADACITINIB (Blinded)

1) UC aggravated (10045283) (Colitis ulcerative (10009900)) [v.24.0] [10045283]

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 UC EXACERBATION

- **Investigator:** Progression of basis disease

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

Relevant Laboratory & Other Diagnostic Tests

 20 ABDOMEN XRAY: Normal

20 COLONOSCOPY: Active form of ulcerative colitis of ascendant and transversal colon

20 CRP: 75.4 MG/L (normal 0 to 5)

-
- 20 ■ **ECHO OF ABDOMEN:** Normal
 - 20 ■ **EGDS:** Normal
 - 20 ■ **FECALCALPROTECTIN:** Result of 1000 mg/kg with a normal low of greater than 50
 - 20 ■ **GASTRIC BIOPSY SAMPLE:** Negative-Gimsi coloring for Helicobacter Pylori
 - 20 ■ **MRI ENTEROGRAPHY:** Active form of ulcerative colitis of ascendant and transversal colon
 - 20 ■ **PA CHEST XRAY:** Normal

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
急性心内膜炎	X	X		X

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

Medical History	Onset Year
ARTERIAL HYPERTENSION	20 [REDACTED]
DEPRESSION	20 [REDACTED]
LEFT SIDED UC	20 [REDACTED]
OSTEOPOROSIS	20 [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	FORMER	1 PACK	10	20 [REDACTED]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	2 - 4 DRINKS

Study Drug Administration						
Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 55	55
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 6	6

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	150 mg	QD	Y-M: 20██-██
PREDNISONE	40 mg	QD	Y-M: 20██-██
MESALAZINE	1 g	OTHER: EVERY OTHER DAY	Y-M: 20██-██ / -253
MESALAZINE	2 g	OTHER: EVERY OTHER DAY	Y-M: 20██-██ / -253
MESALAZINE	1 g	QD	Y-M: 20██-██ / -183
MESALAZINE	3.6 g	QD	Y-M: 20██-██ / -183
MIDAZOLAM	4 mg	PRN	Y-M: 20██-██ / -61
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	2 OTHER: SACHET	PRN	Y-M: 20██-██ / -62
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	2 OTHER: SACHET	PRN	Y-M: 20██-██ / -1

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
MESALAZINE	3.6 g	QD	Y-M: 20██-██ / -183	ONGOING
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	2 OTHER: SACHET	PRN	Y-M: 20██-██ / -1	Y-M: 20██-██ / -1
PARACETAMOL	10 OTHER: MG/ML	PRN	Y-M: 20██-██ / 7	Y-M: 20██-██ / 7
METAMIZOLE	2.5/5 OTHER: G/ML	PRN	Y-M: 20██-██ / 36	Y-M: 20██-██ / 38
ALENDRONIC ACID	70 mg	OTHER: ONCE A WEEK	Y-M: 20██-██ / 46	ONGOING
AMILORIDE;HYDROCHLOROTHIAZIDE	25/2.5 mg	QD	Y-M: 20██-██ / 46	ONGOING
BISOPROLOL	5 mg	QD	Y-M: 20██-██ / 46	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20██-██ / 46	ONGOING
MIRTAZAPINE	30 mg	QD	Y-M: 20██-██ / 46	ONGOING
PANTOPRAZOLE	20 mg	QD	Y-M: 20██-██ / 46	ONGOING
PRAVASTATIN	20 mg	QD	Y-M: 20██-██ / 46	ONGOING
RAMIPRIL	5 mg	BID	Y-M: 20██-██ / 46	ONGOING

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

Event Description	ACUTE ENDOCARDITIS
Preferred term	急性心内膜炎
AE Onset Date / Initial Rx Day	20 / 62 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6
Laboratory Testing	20 (RX DAY 7): Alanine Aminotransferase: 12 [0 - 41] U/L; Albumin: 36 [35 - 52] G/L; Alkaline Phosphatase: 62 [40 - 129] U/L; Aspartate Aminotransferase: 12 [0 - 40] U/L; Bilirubin: 8.1 [5 - 21] UMOL/L; Blood Urea Nitrogen: 4.7 [2.5 - 8.3] MMOL/L; Creatinine: 84 [53 - 132] UMOL/L; Erythrocytes: 3.46 [4 - 5.5] 10¹²/L; Hematocrit: 0.341 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 106 [130 - 170] G/L; Leukocytes: 6.5 [4.8 - 10.8] 10⁹/L; Lymphocytes: 0.97 [0.9 - 5.2] 10⁹/L; Lymphocytes/Leukocytes: 14.9 [20 - 46] %; NPTST165-CRP: 129.4 [0 - 5] MG/L; Neutrophils: 4.93 [1.9 - 8] 10⁹/L; Neutrophils/Leukocytes: 75.8 [45 - 72] %; Platelets: 230 [150 - 450] 10⁹/L; Potassium: 3.8 [3.4 - 5.1] MMOL/L; Sodium: 146 [136 - 146] MMOL/L; 20 (RX DAY 10): Blood Urea Nitrogen: 3 [2.5 - 8.3] MMOL/L; Creatinine: 76 [53 - 132] UMOL/L; Erythrocytes: 3.83 [4 - 5.5] 10¹²/L; Hematocrit: 0.37 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 118 [130 - 170] G/L; Leukocytes: 9.8 [4.8 - 10.8] 10⁹/L; Lymphocytes: 2.73 [0.9 - 5.2] 10⁹/L; Lymphocytes/Leukocytes: 28 [20 - 46] %; NPTST165-CRP: 168.6 [0 - 5] MG/L; NPTST165-CRP: 168 [0 - 5] MG/L; Neutrophils: 6.15 [1.9 - 8] 10⁹/L; Neutrophils/Leukocytes: 63 [45 - 72] %; Potassium: 3.5 [3.4 - 5.1] MMOL/L; Sodium: 145 [136 - 146] MMOL/L; 20 (RX DAY 15): Leukocytes: 10.6 [4.8 - 10.8] 10⁹/L; 20 (RX DAY 45): Leukocytes: 8.7 [4.8 - 10.8] 10⁹/L; NPTST165-CRP: 16.1 [0 - 5] MG/L
Microbiology	20 (RX DAY 7): STOOL NPTST090-C.DIFFICILE: NEGATIVE; STOOL NPTST155-COPROCULTURE: NEGATIVE; OTHER SWAB NPTST211-FARINGEAL SWAB: NEGATIVE; BLOOD NPTST260-HAEMOCULTURE: NEGATIVE; OTHER SWAB NPTST359-NASAL SWAB: NEGATIVE; STOOL NPTST383-PARASITES: NEGATIVE; URINE NPTST541-URINECULTURE: NEGATIVE
AE Stopped Initial Rx Day	101 (40 DAYS AFTER LAST TREATMENT)
Duration of AE	40 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SYGMOIDOSCOPY JUST BEFORE THE SYMPTOM ONSET AND POTENTIAL IMMUNOSUPRESION CAUSED BY IP.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者はセルビアの 6 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、急性心内膜炎の事象を発現した。関連する病歴は、動脈性高血圧、元喫煙者（1 日 1 箱を 10 年間）、潰瘍性大腸炎及び元飲酒者（1 日 2-4 杯）であった。

Event 1 の臨床経過：

投与62日後＊，被験者は急性心内膜炎を発現した。投与101日後＊，急性心内膜炎は消失した。

投与62日後＊，被験者は摂氏 39℃ までの発熱，食欲不振及び疲労が 7 日間続き，入院した。被験者は，3 日間続く下痢も経験した。投与65日後＊，心エコー検査が行われ，心内膜炎と確認された。投与101日後＊，被験者は退院した。本事象により，被験者の治験は中止された。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS (20 - 20)

METIL-PREDNISOLON for ULCERATIVE COLITIS (20 - 20)

Causality for UPADACITINIB (Blinded)

1) Acute endocarditis (10049001) (Acute endocarditis (10049001)) [v.22.1] [10049001]

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 ACUTE ENDOCARDITIS

- **Investigator:** SYGMOIDOSCOPY JUST BEFORE THE SYMPTOM ONSET AND POTENTIAL IMMUNOSUPRESION CAUSED BY IP.

- **AbbVie:** risk factors include inflammatory bowel disease and recent sigmoidoscopy prior to symptom onset per PI.

Relevant Laboratory & Other Diagnostic Tests

20 ■ **BLOOD CULTURE:** negative

20 ■ **CRP:** 129.4 MG/L (normal <5)

20 ■ **CRP:** 168.6 MG/L

20 ■ **CRP:** 16.1 MG/L (normal 0 to 5)

20 ■ **ECHOCARDIOGRAM:** CONCLUSION: AORTIC AND MITRAL VALVULAR ENDOCARDITIS INDICATED PATIENT TRANSITION TO CARDIOLOGY DEPARTMENT FOR FURTHER TREATMENT.

20 ■ **HCT:** 34.1 % (normal 40 to 52)

20 ■ **NASAL SWAB:** negative

20 ■ **PHARYNGEAL SWAB:** negative

20 ■ **PLATELET COUNT:** 23 X10**9/L (normal 150 to 450)

20 ■ **RBC:** 3.46 X10**12/L (normal 4.0 to 5.5)

20 ■ **STOOL C DIFFICILE:** negative

20 ■ **STOOL COPROCULTURE:** negative

20 ■ **STOOL PARASITES:** negative

■■■■ 20 ■■■■ TEMPERATURE: 37 Degrees C
■■■■ 20 ■■■■ TEMPERATURE: 39 Degrees C
■■■■ 20 ■■■■ TEMPERATURE: 38.3 Degrees C
■■■■ 20 ■■■■ TEMPERATURE: 38 Degrees C
■■■■ 20 ■■■■ TEMPERATURE: 37 Degrees C
■■■■ 20 ■■■■ URINE CULTURE: negative
■■■■ 20 ■■■■ WBC: 6.5 X10**9/L (normal 4.8 to 10.8)
■■■■ 20 ■■■■ WBC: 9.8 X10**9/L (normal 4.8 to 10.8)
■■■■ 20 ■■■■ WBC: 10.6 X10**9/L (normal 4.8 to 18.8)
■■■■ 20 ■■■■ WBC: 8.7 X10**9/L (normal 4.8 to 18.8)

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
発熱	X	X		

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	19 [REDACTED]
NEPHROLZTHIASIS	19 [REDACTED]
PSEUDOPOLYPS	20 [REDACTED]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20 [REDACTED]
ENDOSCOPY (UC): COLONOSCOPY	20 [REDACTED]
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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration						
Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 60	60

M14-234 SS3 ORAL QD █████ 20██ / 1 █████ 20██ / 52 52
Placebo (MAIN)

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100 mg	QD	Y-M: 20██-██
PREDNISONE	20 mg	QD	Y-M: 20██-██
SULFASALAZINE	3 g	TID	Y-M: 20██-██

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
SULFASALAZINE	3 g	TID	Y-M: 20██-██	ONGOING
SULFAMETHOXAZOLE;TRIMETHOPRIM	480 mg	BID	Y-M: 20██-██ / 42	Y-M: 20██-██ / 50
CEFIXIME	400 mg	QD	Y-M: 20██-██ / 50	Y-M: 20██-██ / 51
CEFTRIAZONE	2 g	QD	Y-M: 20██-██ / 51	Y-M: 20██-██ / 52
DICLOFENAC	75 mg	PRN	Y-M: 20██-██ / 52	Y-M: 20██-██ / 63
FLUCONAZOLE	400 mg	QD	Y-M: 20██-██ / 52	Y-M: 20██-██ / 66
MEROPENEM	1 g	TID	Y-M: 20██-██ / 52	Y-M: 20██-██ / 56
VANCOMYCIN	1 g	BID	Y-M: 20██-██ / 52	Y-M: 20██-██ / 62
PIPERACILLIN;TAZOBACTAM	4.5 g	TID	Y-M: 20██-██ / 56	Y-M: 20██-██ / 62

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

Event Description FEBRILE STATE

Preferred term 発熱

AE Onset Date / Initial Rx Day █████ 20██ / 112

Age at AE Onset 5█

Laboratory Testing

█████ 20██ (RX DAY 52): Erythrocytes: 3.48 [4.3 - 5.8] 10¹²/L; Hematocrit: 0.31 [0.41 - 0.56] FRACTION OF 1; Hemoglobin: 106 [120 - 180] G/L; Leukocytes: 6.6 [4 - 9] 10⁹/L; Lymphocytes/Leukocytes: 13.6 [20 - 50] %; Monocytes/Leukocytes: 0.1 [1 - 10] %; NPTST087-C-REACTIVE PROTEIN: 268.1 [0 - 5] MG/L; NPTST349-MICROSCOPY OF URIN: FEW BACTERIAS [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils/Leukocytes: 80.8 [44 - 72] %

Microbiology

█████ 20██ (RX DAY 52): BLOOD NPTST201-ELISA CHLAMIDIA PNEUMONIAE IGG: NEGATIVE; BLOOD NPTST202-ELISA MYCOPLASMA PNEUMONIAE IGG: NEGATIVE; BLOOD NPTST265-HEMOCULTURE: NEGATIVE

AE Stopped Initial Rx Day 125 (13 DAYS AFTER LAST TREATMENT)

Duration of AE	14 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]:11:02

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。本被験者はセルビアの 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、発熱状態の事象を発現した。関連する病歴は、広範囲な潰瘍性大腸炎、非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与112日後＊，被験者は発熱状態を発現した。投与125日後＊，発熱状態は消失した。

本事象発現前の投与96日後＊ から投与111日後＊，被験者は発熱状態（非重篤）を経験していた。

投与112日後＊，被験者は摂氏 40°C の発熱があり入院した。投与125日後＊，被験者は発熱もなく退院した。

投与141日後＊，被験者の治験は中止された。

投与された薬剤は、diklofenak，panceph，メロペネム，バンコマイシン，ジフルカン及び longaceph であった。

The patient's past medications include:

IMURAN for ULCERATIVE COLITIS ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED], [REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

Causality for UPADACITINIB (Blinded)

1) Fever (10016558) (Pyrexia (10037660)) [v.22.0] [10016558]

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 (Blinded)

Event of FEBRILE STATE

- **Investigator:** Not applicable

- **AbbVie:** Common in the general population. Additional risk factor includes pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

██████ 20██ ██████ 20██: 106 G/L (normal 120 to 180)

Unknown date ABDOMINAL CT SCAN: RTG PULMO ET COR

██████ 20██ **AXILARY TEMPERATURE:** 37.1 Degrees C

██████ 20██ **AXILARY TEMPERATURE:** 38.5 Degrees C

██████ 20██ **BODY TEMPERATURE:** 40 Degrees C

██████ 20██ **C-REACTIVE PROTEIN:** 268.1 MG/L (normal 0.0 to 5.0)

██████ 20██ **CHEST X RAY:** Normal

██████ 20██ **CT OF ABDOMEN:** Few cysts of left kidney

██████ 20██ **ECHOCARDIOGRAPHY:** Normal finding

20	ELISA CHLAMIDIA PNEUMONIAE IGG IGM: Negative
20	ELISA MYCOPLASMA PNEUMONIAE IGG IGM: Negative
20	HEMATOCRIT: 0.31 (0.99% ~~Y~~ L/L)
20	HEMOCULTURE: Negative
20	LYMPHOCYTES %: 13.6 % (normal 20.0 to 50.0)
20	LYMPHOCYTES ABS: $1.2 \times 10^9/L$
20	MONOCYTES %: 0.1 % (normal 1.0 to 10.0)
20	NEUTROPHILS %: 80.8 % (normal 44 to 72)
20	NEUTROPHILS ABS: $7.5 \times 10^9/L$
20	RED BLOOD CELLS: $3.48 \times 10^{12}/L$ (normal 4.30 to 5.80)
20	RTG PULMO ET COR: Decreased transparency in both lungs
20	SYGMOIDOSCOPY: Decreased vascular pattern of mucosa, few pseudopolyps
20	URINALYSIS: Negative for protein, occult blood, urobilinogen, glucose, and bilirubin.
20	URINE CULTURE: FEW BACTERIAS
20	URINE PH: 6.0 no unit
20	URINE SPECIFIC GRAVITY: 1.020 no unit
20	URINE WHITE BLOOD CELLS: 1-2
20	WHITE BLOOD CELLS: $8.9 \times 10^9/L$

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
ABT-494 15 mg	61	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
DYSPEPSIA	2011
ECG:LEFT BUNDLE BRANCH BLOCK	2011
HYPERTENSION	2011
LEFT SIDED UC	2011
PAIN MANAGEMENT	2011
POSTMENOPAUSAL	1998
PSEUDOPOLYPS	2011
TACHYCARDIA	2011

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	2011
ENDOSCOPY (UC): COLONOSCOPY	2011
PRIOR PROCEDURES: COLON BIOPSIES FOR HISTOLOGY	11/2011
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	2011

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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 58	58
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	20 / 1	20 / 159	159

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMLODIPINE	10 mg	QD	Y-M: 20 / -
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20 / -
LANSOPRAZOLE	30 mg	QD	Y-M: 20 / -
AZATHIOPRINE	50 mg	QD	Y-M: 20 / -
PREDNISON	30 mg	QD	Y-M: 20 / -
SULFASALAZINE	1.5 g	BID	Y-M: 20 / -
ISONIAZID	300 mg	QD	Y-M: 20 / -77
PYRIDOXINE	25 mg	QD	Y-M: 20 / -77
ALFENTANIL	1 MG mg	OTHER: STAT DOSE	Y-M: 20 / -84
OSMOTICALLY ACTING LAXATIVES	2 SACHETS DAILY OTHER: 2 SACHETS	QD	Y-M: 20 / -86
ALFENTANIL	1 MG mg	OTHER: STAT	Y-M: 20 / -1
OSMOTICALLY ACTING LAXATIVES	2 SACHETS DAILY OTHER: 2 SACHETS	QD	Y-M: 20 / -3
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19
FOLIC ACID	5 mg	QD	Y: 20
VITAMIN D NOS	500000 IU	OTHER: WEEKLY	Y: 20

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
AMLODIPINE	10 mg	QD	Y-M: 20 / ONGOING
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20 / ONGOING
LANSOPRAZOLE	30 mg	QD	Y-M: 20 / ONGOING
PYRIDOXINE	25 mg	QD	Y-M: 20 / -77 Y-M: 20 / 159
FOLIC ACID	5 mg	QD	Y: 20 / ONGOING

VITAMIN D NOS 500000 IU OTHER: Y: 20 ONGOING
WEEKLY

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 INVASIVE CARCINOMA OF THE RIGHT BREAST
Preferred term 浸潤性乳癌
AE Onset Date / Initial Rx Day 20 / 217
Age at AE Onset 6
Laboratory Testing
20 (RX DAY 159): NPTST280-HISTOLOGY: INVASIVE BREAST CANC [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED
Microbiology
NOT REPORTED
AE Stopped Initial Rx Day ONGOING
Duration of AE ONGOING
Severity SEVERE
Relation to Study Drug by Investigator NO REASONABLE POSSIBILITY
Investigator Alternative Etiology IDIOPATHIC
Discontinued Study Drug Due to the Event YES
SAE Criteria IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は南アフリカの 6 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、右乳房の浸潤性乳癌の事象を発現した。関連する病歴は、偽ポリープ、潰瘍性大腸炎、非喫煙者及び禁酒であった。

Event 1 の臨床経過：

投与217日後＊、被験者は右乳房の浸潤性乳癌を発現した。

投与217日後＊，被験者は救急科を受診し，入院した。被験者は，約1週間前に右乳房にしこりを感じたと報告した。被験者は閉経しており，過去に乳房撮影を行っていなかった。身体検査では，右乳房の上部4分の1に固いしこりを触知した。腋窩のリンパ節腫脹，乳頭からの分泌，及び乳頭退縮は認められなかった。その後，被験者は乳腺クリニックに紹介された。乳房撮影及び生検により，右乳房の浸潤癌が確認された。その後，被験者は治療のために乳腺科によるトリアージを受けた。投与252日後＊，被験者は予定された外科手術のために入院した。投与255日後＊，被験者は右乳房の切除術を受けた。合併症の報告はなく，潰瘍性大腸炎の症状もなかった。投与256日後＊，被験者は退院した。投与261日後＊，被験者の右腋窩のドレーンが抜去された。

この被験者の治験は完全に中止された。

被験者は4■歳で閉経が始まった。被験者には3人の子供がおり，最も若い子供は3■歳であった。被験者には，癌の家族歴はなかった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS (■■■ 20■■■ - ■■■ 20■■■)

PREDNISONE for ULCERATIVE COLITIS (■■■ 20■■■ - ■■■ 20■■■)

SALAZOPYRINE for ULCERATIVE COLITIS (■■■ 20■■■ - ■■■ 20■■■)

Causality for UPADACITINIB (Blinded)

1) Invasive breast carcinoma (10075713) (Invasive breast carcinoma (10075713)) [v.23.0]
[10075713]

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 INVASIVE CARCINOMA OF THE RIGHT BREAST

- **Investigator:** Idiopathic

- **AbbVie:** In South Africa, breast cancer is the most common cancer in women, with a lifetime risk of 1 in 27. Additionally, the subject's age is a risk factor and there is a weak temporal association given that the subject's only had 7 months of exposure to study drug.

Relevant Laboratory & Other Diagnostic Tests

■■■■ 20 ■■■ **HISTOLOGY:** Invasive breast cancer

■■■■ 20 ■■■ **MAMMOGRAPHY:** Right breast- BIRADS 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
子宮頸部上皮異形成	X			

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

Medical History	Onset Year
COGNITIVE OR PSYCHIATRIC DISORDER: POST TRAUMATIC STRESS DISORDER	20 [REDACTED]
DEPRESSION: DUE TO TRAUMATIC EVENT	20 [REDACTED]
DRUG ABUSE: INTERMITTENT COCAINE USE STOPPED 1 YEAR AGO	20 [REDACTED]
LEFT SIDED UC	20 [REDACTED]
OTHER: ACNE	20 [REDACTED]
OTHER: INTERMITTENT SINUS CONGESTION	19 [REDACTED]
OTHER: JOINT PAIN ANKLES AND KNEES	20 [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	CURRENT	0.05 PACK	15	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 57	57
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	20 / 1	20 / 308	308

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 /
BUDESONIDE	1 OTHER: ENEMA	BID	Y-M: 20 /
METHOTREXATE	25 mg	OTHER: WEEKLY	Y-M: 20 / -108
PROBIOTICS NOS	1 OTHER: TABLET	QD	Y-M: 20 / -130
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	OTHER: WEEKLY	Y-M: 20 / -130
CIPROFLOXACIN	500 mg	BID	Y-M: 20 / -78
METRONIDAZOLE	500 mg	BID	Y-M: 20 / -78
SODIUM PHOSPHATE;SODIUM PHOSPHATE MONOBASIC (ANHYDROUS)	135 mL	OTHER: STAT	Y-M: 20 / -59
DROSPIRENONE;ETHINYLESTRADIOL	1 OTHER: TABLET	QD	Y: 20

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
METHOTREXATE	25 mg	OTHER: WEEKLY	Y-M: 20 / -108	ONGOING
PROBIOTICS NOS	1 OTHER: TABLET	QD	Y-M: 20 / -130	ONGOING
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	OTHER: WEEKLY	Y-M: 20 / -130	Y-M: 20 / 273
FOLIC ACID	1 OTHER: TABLET	QD	Y-M: 20 / 34	ONGOING
CIPROFLOXACIN	500 mg	TID	Y-M: 20 / 170	Y-M: 20 / 173
BUPIVACAINE;EPINEPHRINE	1.8 mL	OTHER: STAT	Y-M: 20 / 182	Y-M: 20 / 182
FENTANYL	100 mg	OTHER: STAT	Y-M: 20 / 182	Y-M: 20 / 182
GRANISETRON	1 mg	OTHER: STAT	Y-M: 20 / 182	Y-M: 20 / 182
MIDAZOLAM	0.35 mg/kg	OTHER: STAT	Y-M: 20 / 182	Y-M: 20 / 182
PARACETAMOL;TRAMADOL	2 OTHER: TABLETS	PRN	Y-M: 20 / 182	ONGOING
PROPOFOL	5 mL	OTHER: STAT	Y-M: 20 / 182	Y-M: 20 / 182
SEVOFLURANE	100 mL	OTHER: STAT	Y-M: 20 / 182	Y-M: 20 / 182

DROSPIRENONE;ETHINYLESTRA 1 OTHER: TABLET QD Y: 20 ONGOING
DIOL

Event #1: Serious Adverse Event

Event Description	CIN-1
Preferred term	子宮頸部上皮異形成
AE Onset Date / Initial Rx Day	20 / 237
Age at AE Onset	3
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	239
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HPV POSITIVE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: 20 :11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は南アフリカの 3 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、子宮頸部上皮内腫瘍（CIN1）の事象を発現した。関連する病歴は、うつ病、潰瘍性大腸炎、現喫煙者（1 日 0.05 箱を 15 年間）及び現飲酒者（1 日 2-4 杯）であった。

Event 1 の臨床経過：

投与237日後＊、被験者は子宮頸部上皮内腫瘍（CIN1）を発現した。投与239日後＊、子宮頸部上皮内腫瘍（CIN1）は消失した。

投与237日後＊，被験者の PAP スミアは LSIL を示し，リスクであるヒトパピローマウイルスが陽性であり，CIN1 細胞を認めた。投与239日後＊，被験者は大口径ループ型電極を用いた移行帯切除（LLETZ）の処置のために入院した。入院時には，膣カンジダ症及び尿路感染症が認められた。処置後，CIN1 細胞は完全に切除された。同日，被験者は退院した。

投与された薬剤は，tramacet であった。

Causality for ABT-494 (Blinded)

1) Cervical intraepithelial neoplasia I (10049700) (Cervical dysplasia (10008263)) [v.21.1]
[10049700]

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 CERVICAL INTRAEPITHELIAL NEOPLASIA 1

- Investigator: HPV POSITIVE

- AbbVie: EVENT'S ETIOLOGY IS COMMONLY ASSOCIATED WITH POSITIVE HPV INFECTION. ADDITIONAL RISK FACTORS INCLUDE SUBJECT'S AGE AND CURRENT SMOKING STATUS.

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
潰瘍性大腸炎	X			

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	6 [REDACTED]	FEMALE	MULTIPLE

Medical History	Onset Year
FIBROIDS	20 [REDACTED]
IRON DEFICIENCY ANAEMIA	20 [REDACTED]
LEFT SIDED UC	20 [REDACTED]
MENOPAUSE	19 [REDACTED]
OSTEOPENIA	20 [REDACTED]
RIGHT SUBCONJUNCTIVAL HEAMORRHAGE	20 [REDACTED]
ULCERATIVE COLITIS	20 [REDACTED]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20 [REDACTED]
ENDOSCOPY (UC): COLONOSCOPY	20 [REDACTED]
PRIOR PROCEDURES: CESAREAN SECTION	19 [REDACTED]
PRIOR PROCEDURES: CESAREAN SECTION	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 78	78
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20 / 1	20 / 372	372

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100 mg	QD	Y-M: 20 / -
MESALAZINE	2.4 g	QD	Y-M: 20 / -
INFLIXIMAB	250.000 mg	WEEK 0, 2, 6	Y-M: 20 / -
ADALIMUMAB	160.000 mg	EVERY OTHER WEEK	Y-M: 20 / -
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20 / - 272
MIDAZOLAM	1 mg	QD	Y-M: 20 / - 100
PROPOFOL	3 mL	QD	Y-M: 20 / - 100
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	TID	Y-M: 20 / - 101
CALCIUM CARBONATE;COLECALCIFEROL;MENAQUINONE	45/500/1000 OTHER: UG/MG/IU	QD	Y-M: 20 / - 122
IRON	100 mg	QD	Y-M: 20 / - 122
AMLODIPINE	5 mg	QD	Y-M: 20 / - 70
ENALAPRIL	5 mg	BID	Y-M: 20 / - 76
ISONIAZID	300 mg	QD	Y-M: 20 / - 78
PYRIDOXINE	25 mg	QD	Y-M: 20 / - 78
PHOLCODINE	10 mL	BID	Y-M: 20 / - 32
AMOXICILLIN;CLAVULANIC ACID	1 g	BID	Y-M: 20 / - 49
AMOXICILLIN;CLAVULANIC ACID	1 g	BID	Y-M: 20 / - 20

MIDAZOLAM	1 mg	QD	Y-M: 20██-██ / -24
PROPOFOL	3 mL	QD	Y-M: 20██-██ / -24
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	TID	Y-M: 20██-██ / -25
ALENDRONIC ACID	70 mg	OTHER: ONCE WEEKLY	Y-M: 20██-██ / -27
CICLESONIDE	1 OTHER: SPRAY	QD	Y-M: 20██-██ / -28

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	Stop Year-Month / RX Day
MESALAZINE	2.4 g	QD	Y-M: 20██-██	Y-M: 20██-██ / 317
CALCIUM CARBONATE;COLECALCIFEROL; MENAQUINONE	45/500/1000 OTHER: UG/MG/IU	QD	Y-M: 20██-██ / -122	ONGOING
ALENDRONIC ACID	70 mg	OTHER: ONCE WEEKLY	Y-M: 20██-██ / -27	ONGOING
CICLESONIDE	1 OTHER: SPRAY	QD	Y-M: 20██-██ / -28	ONGOING
ASCORBIC ACID;COPPER;GLYCINE;LYSINE; PROLINE;RUTOSIDE;ZINC	1 OTHER: TABLET	QD	Y-M: 20██-██ / 85	ONGOING
GLYCINE MAX;PERSEA AMERICANA	1 OTHER: TABLET	QD	Y-M: 20██-██ / 85	ONGOING
ASCORBIC ACID;CALCIUM PHOSPHATE;COLECALCIFEROL; COPPER;CYANOCOBALAMIN;DL-ALPHA TOCOPHEROL;IODINE;IRON;MAGNESIUM OXIDE;MANGANESE;NICOTINAMIDE;PANTOTHENIC ACID;POTASSIUM SULFATE;PYRIDOXINE;RETINOL; RIBOF	1 OTHER: TABLET	QD	Y-M: 20██-██ / 135	Y-M: 20██-██ / 238
LOSARTAN	50 mg	QD	Y-M: 20██-██ / 194	ONGOING
ACETYLCYSTEINE	2 OTHER: TABLETS	BID	Y-M: 20██-██ / 282	Y-M: 20██-██ / 369
ERGOCALCIFEROL	50 000 IU	OTHER: WEEKLY	Y-M: 20██-██ / 282	ONGOING
LORATADINE	10 mg	QD	Y-M: 20██-██ / 282	Y-M: 20██-██ / 308
IRON	1000 mg	OTHER: STAT	Y-M: 20██-██ / 286	Y-M: 20██-██ / 286

PANTOPRAZOLE	40 mg	QD	Y-M: 20■■■ / 309	ONGOING
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	TID	Y-M: 20■■■ / 316	Y-M: 20■■■ / 317
HYDROCORTISONE	100 mg	QID	Y-M: 20■■■ / 317	Y-M: 20■■■ / 320
MIDAZOLAM	1 mg	QD	Y-M: 20■■■ / 317	Y-M: 20■■■ / 317
PROPOFOL	3 mL	QD	Y-M: 20■■■ / 317	Y-M: 20■■■ / 317
RED BLOOD CELLS	1 OTHER: UNIT	BID	Y-M: 20■■■ / 317	Y-M: 20■■■ / 318
ASCORBIC ACID;CYANOCOBALAMIN;ERGO CALCIFEROL;FOLIC ACID;NICOTINAMIDE;PANTOTH ENIC ACID;PYRIDOXINE;RETINOL;RIB OFLAVIN;THIAMINE;TOCOPHER OL	1 OTHER: TABLET	QD	Y-M: 20■■■ / 318	ONGOING
MESALAZINE	4.8 g	QD	Y-M: 20■■■ / 318	ONGOING
PREDNISONE	60 mg	QD	Y-M: 20■■■ / 320	Y-M: 20■■■ / 327
PREDNISONE	55 mg	QD	Y-M: 20■■■ / 328	Y-M: 20■■■ / 334
PREDNISONE	50 mg	QD	Y-M: 20■■■ / 335	Y-M: 20■■■ / 341
PREDNISONE	45 mg	QD	Y-M: 20■■■ / 342	Y-M: 20■■■ / 348
MESALAZINE	1 g	QD	Y-M: 20■■■ / 345	ONGOING
PREDNISONE	40 mg	QD	Y-M: 20■■■ / 349	Y-M: 20■■■ / 355
PREDNISONE	35 mg	QD	Y-M: 20■■■ / 356	Y-M: 20■■■ / 362
PREDNISONE	30 mg	QD	Y-M: 20■■■ / 363	Y-M: 20■■■ / 368
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	TID	Y-M: 20■■■ / 365	Y-M: 20■■■ / 366
MIDAZOLAM	1 mg	QD	Y-M: 20■■■ / 366	Y-M: 20■■■ / 366
PROPOFOL	3 mL	QD	Y-M: 20■■■ / 366	Y-M: 20■■■ / 366
PREDNISONE	25 mg	QD	Y-M: 20■■■ / 369	ONGOING

Event #1: Event of Interest - Anemia

Event Description	ANAEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	■■■■20■■■ / 329
Age at AE Onset	6■
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	

AE Stopped Initial Rx Day	447
Duration of AE	119 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	SEVERE, ACUTE ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	20 / 395
Age at AE Onset	6

Laboratory Testing

20 (RX DAY 317): Albumin: 25 [35 - 52] G/L; Hematocrit: 0.28 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 91 [115 - 155] G/L; NPTST165-CRP: 12.9 [0 - 5] MG/L; NPTST471-SERUM IRON: 4.3 [10.7 - 32.2] UMOL/L; NPTST516-TRANSFERRIN: 1.81 [2 - 3.6] G/L; NPTST518-TRANSFERRIN SATURATION: 9 [16 - 50] %; 20 (RX DAY 318): Hemoglobin: 88 [115 - 155] G/L; 20 (RX DAY 319): Hemoglobin: 112 [115 - 155] G/L; 20 (RX DAY 320): Hemoglobin: 113 [115 - 155] G/L

Microbiology

NOT REPORTED

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	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Generated: 20 :11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は南アフリカの 6 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、重症及び急性の潰瘍性大腸炎の再燃の事象を発現した。関連する病歴は、閉経、潰瘍性大腸炎（左側）、鉄欠乏性貧血、非喫煙者及び非飲酒者であった。

Event 2 の臨床経過：

投与395日後＊，被験者は重症及び急性の潰瘍性大腸炎の再燃を発現した。投与479日後＊，重症及び急性の潰瘍性大腸炎の再燃は消失した。

投与の約12ヵ月後＊，被験者は潰瘍性大腸炎の悪化（非重篤）を経験していた。

投与395日後＊，被験者は1日10回以上の血便、緩便及び粘液便があり、入院した。結腸内視鏡検査では、強度の潰瘍性大腸炎が確認された。被験者は大腸を失う危険性があると告げられた。胃内視鏡検査は正常であった。治療後、被験者の状態は改善した。投与398日後＊，被験者は直腸出血及び腹痛はなく、1日5回緩便がある状態で退院した。

投与された薬剤及び処置は、ペンタサ坐剤、prednisone、mezavant、ヒドロコルチゾン及び輸血であった。

The patient's past medications include:

AZATHIOPRINE for ULCERATIVE COLITIS (20 - 20)

REVELLEX for ULCERATIVE COLITIS (20 - 20)

HUMIRA for ULCERATIVE COLITIS (20 - 20)

MEDROL for ULCERATIVE COLITIS (20 - 20)

Causality for UPADACITINIB (Blinded)

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

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 SEVERE, ACUTE ULCERATIVE COLITIS FLARE

- **Investigator:** Not applicable.

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

Relevant Laboratory & Other Diagnostic Tests

20 ■ ABDOMINAL X-RAY: Normal

20 ■ ALBUMIN: 25 G/L (normal 35 to 52)

20 ■ COLONOSCOPY: Severe, acute pancolitis. Pseudopolyps present.

20 ■ CRP: 12.9 MG/L (normal 0.0 to 5.0)

20 ■ GASTROSCOPY: Normal

20 ■ HEMATOCRIT: 0.28 L/L (normal 0.35 to 0.45)

20 ■ HEMOGLOBIN: 9.1 G/DL (normal 11.5 to 15.5)

20 ■ HEMOGLOBIN: 8.8 G/DL (normal 11.5 to 15.5)

20 ■ HEMOGLOBIN: 11.2 G/DL (normal 11.5 to 15.5)

20 ■ HEMOGLOBIN: 11.3 G/DL (normal 11.5 to 15.5)

20 ■ SERUM IRON: 4.3 MCMOL/L (normal 10.7 to 32.2)

20 ■ TRANSFERRIN: 1.81 G/L (normal 2.00 to 3.60)

20 ■ TRANSFERRIN SATURATION: 9 % (normal 16 to 50)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Anaemia: Iron studies and Vitamin B 12.

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
股関節部骨折	X			

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	71	FEMALE	WHITE

Medical History	Onset Year
ANXIETY	2011
BACKACHE	1998
DRUG INDUCED CAECAL COLITIS	2008
LEFT HEMIPLEGIA	2008
LEFT SIDED UC	2008
PENICILLIN ALLERGY	1998
POST MENOPAUSAL	1998
RESTLESS LEG SYNDROME	2008
RIGHT ANKLE INJURY	2008
ULCERATIVE COLITIS	2008

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	2008
PRIOR PROCEDURES: COLONOSCOPY	2008
PRIOR PROCEDURES: ILIOCOLONOSCOPY	2008
PRIOR PROCEDURES: ILIOCOLONOSCOPY IN 2008, 2008, 2008	2008
PRIOR PROCEDURES: LAMINECTOMY	1998
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	2008

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 PACK	50	2008
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4 DRINKS

Study Drug Administration						
Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		ORAL	QD	20 / 1	20 / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20 / 1	20 / 364	364

Previous Therapy - Prior to baseline/enrollment			
Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	BID	Y-M: 20 / -
SULPIRIDE	500 mg	BID	Y-M: 20 / -
VITAMINS NOS	10 mL	QD	Y-M: 20 / -
CORTICOSTEROIDS	60 mg	QID	Y-M: 20 / -273
OFLOXACIN	400 mg	TID	Y-M: 20 / -273
MESALAZINE	1 g	QD	Y-M: 20 / -286
MESALAZINE	2 g	BID	Y-M: 20 / -286
KETAMINE	20 ug	OTHER: ONCE	Y-M: 20 / -62
PROPOFOL	250 mg	OTHER: ONCE	Y-M: 20 / -62
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	15.5 g	PRN	Y-M: 20 / -63
PREDNISONE	30 mg	QD	Y-M: 20 / -25
ACETYLSALICYLIC ACID	75 mg	QD	Y: 20
PRAMIPEXOLE	0.25 mg	QD	Y: 20
THIAMINE	100 mg	QD	Y: 20

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
SULPIRIDE	500 mg	BID	Y-M: 20 / -	ONGOING
VITAMINS NOS	10 mL	QD	Y-M: 20 / -	ONGOING
MESALAZINE	2 g	BID	Y-M: 20 / -286	ONGOING
METOCLOPRAMIDE	10 mg	TID	Y-M: 20 / 54	Y-M: 20 / 59
MORPHINE	5 mg	QID	Y-M: 20 / 54	Y-M: 20 / 55
NALOXONE;OXYCODONE	10/5 mg	BID	Y-M: 20 / 54	Y-M: 20 / 59

OXYCODONE	5 mg	BID	Y-M: 20███ / 54	Y-M: 20███ / 59
PARACETAMOL	1 g	QID	Y-M: 20███ / 54	Y-M: 20███ / 59
TRAMADOL	100 mg	TID	Y-M: 20███ / 54	Y-M: 20███ / 59
CLINDAMYCIN	300 mg	QID	Y-M: 20███ / 55	Y-M: 20███ / 56
MORPHINE	10 mg	QID	Y-M: 20███ / 55	Y-M: 20███ / 59
ACETYLSALICYLIC ACID	75 mg	QD	Y: 20██	ONGOING
PRAMIPEXOLE	0.25 mg	QD	Y: 20██	ONGOING
THIAMINE	100 mg	QD	Y: 20██	ONGOING

Event #1: Serious Adverse Event

Event Description	LEFT HIP FRACTURE
Preferred term	股關節部骨折
AE Onset Date / Initial Rx Day	20 / 109
Age at AE Onset	7
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	111
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	A FALL AT HOME AFTER BEING KNOCKED OVER BY HER DOG.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [REDACTED] 20[REDACTED]:11:02

Program Source Code:

Investigator No.: [REDACTED]

Subject Number: [REDACTED]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は南アフリカの 71 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、左股関節部骨折の事象を発現した。関連する病歴は、閉経後、左片麻痺、元喫煙者（1 日 20 箱を 50 年間）、潰瘍性大腸炎及び現飲酒者（1 日 2-4 杯）であった。

Event 1 の臨床経過：

投与109日後＊，被験者は左股関節部骨折を発現した。投与111日後＊，左股関節部骨折は消失した。

投与109日後＊，被験者は転倒後に痛みがあり、立ち上がれない状態であった。X 線検査で股関節部骨折が確認された。投与111日後＊，被験者は、髄内固定用の釘及びねじを用いた左大腿骨の観血的整復固定術を受けた。投与115日後＊，被験者は退院した。

投与された薬剤は、クレキサン、モビコール、cernevit、セレネース、perfalgan、トラマドール、maxalon、モルヒネ、targinact、クリンダマイシン及びオキノームであった。

The patient's past medications include:

CORTICOSTEROID for ULCERATIVE COLITIS ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

OFLOXACIN for ULCERATIVE COLITIS ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

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

PENICILLIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

1) Hip fracture (10020100) (Hip fracture (10020100)) [v.23.0] [10020100]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, outcome unknown

Alternative Etiology for UPADACITINIB (Blinded)

Event of LEFT HIP FRACTURE

- **Investigator:** A fall at home after being knocked over by her dog.

- **AbbVie:** Event is more likely related to fall after being knocked over by her dog as reported per investigator.

Relevant Laboratory & Other Diagnostic Tests

20 ■ LUMBAR SPINE XRAY: INTRAMEDULLARY NAIL WITH INTERLOCKING SCREWS
SEEN

20 ■ X-RAY PELVIS, HIP AND LUMBAR SPINE: Comminuted intertrochanteric left proximal
femoral fracture

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
子宮頸部上皮異形成	X			

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

Medical History	Onset Year
ATYPICAL SQUAMOUS CELLS - LOW GRADE INTRAEPITHELIAL LESION	20 [REDACTED]
ECZEMA LEFT FOOT	20 [REDACTED]
EXTENSIVE UC/PANCOLITIS	20 [REDACTED]
HPV HIGH RISK	20 [REDACTED]
HYPERGLYCAEMIA	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	FORMER	0.5 PACK	10	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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 56	56

M14-234 SS3 30 mg ORAL QD 20 / 1 20 / 368 368
ABT-494 (MAIN)

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 /
PREDNISONE	40 mg	QD	Y-M: 20 / -190
MESALAZINE	2 g	BID	Y-M: 20 / -160
AZATHIOPRINE	100 mg	QD	Y: 20
MESALAZINE	1.5 g	BID	Y: 20
CLOBETASOL	2 g	PRN	Y: 20

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
MESALAZINE	2 g	BID	Y-M: 20 / -160	ONGOING
CEFPROZIL	2 g	OTHER: ONCE	Y-M: 20 / 34	Y-M: 20 / 34
DEXAMETHASONE	8 mg	OTHER: ONCE	Y-M: 20 / 34	Y-M: 20 / 34
GRANISETRON	1 mg	OTHER: ONCE	Y-M: 20 / 34	Y-M: 20 / 34
KETAMINE	50 mg	OTHER: ONCE	Y-M: 20 / 34	Y-M: 20 / 34
OXYCODONE	10 mg	OTHER: ONCE	Y-M: 20 / 34	Y-M: 20 / 34
PARACETAMOL	1 g	OTHER: ONCE	Y-M: 20 / 34	Y-M: 20 / 34
PROPOFOL	150 mg	OTHER: ONCE	Y-M: 20 / 34	Y-M: 20 / 34
CLOBETASOL	2 g	PRN	Y: 20	ONGOING

Event #1: Serious Adverse Event

Event Description	FOCAL CIN I - II IN CERVIX
Preferred term	子宮頸部上皮異形成
AE Onset Date / Initial Rx Day	20 / 90
Age at AE Onset	4
Laboratory Testing	
NOT REPORTED	
Microbiology	
20 (RX DAY 34): OTHER OPEN FRAGMENT OF CERVIX NPTST281-HISTOPATHOLOGY: POSITIVE-FOCAL CIN I-II AND FULL THICKNESS HPV INFECTION AT SQUAMOCOLUMNAR JUNCTION AND WITHIN STRIPPED ECTOCERVICAL SQUAMOPUS EPITHELIUM. NO EVIDENCE OF CIN III OR INVASIVE MALIGNANCY. ABN AREA FULLY EXCISED	
AE Stopped Initial Rx Day	91

Duration of AE	2 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HUMAN PAPILOMAVIRUS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

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Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は南アフリカの 4 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、局所的な子宮頸部上皮内腫瘍（CIN1 及び CIN2）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 10 年間）、潰瘍性大腸炎及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与90日後＊，被験者は局所的な子宮頸部上皮内腫瘍（CIN1 及び CIN2）を発現した。
投与91日後＊，局所的な子宮頸部上皮内腫瘍（CIN1 及び CIN2）は消失した。

被験者は、定期的な診察時の PAP スミアで異常が認められたが、無症状であった。投与90日後＊，被験者はヒトパピローマウイルスに関連する CIN1 及び CIN2 のために入院した。投与90日後＊，被験者はループ式電気外科円錐切除法（LLETZ）を受け、合併症は認められなかった。組織学的に CIN1 及び CIN2 が完全に切除されたことが確認された。

The patient's past medications include:

AZIOTHYPRINE for ULCERATIVE COLITIS (20 - 20)

PREDNISONE for ULCERATIVE COLITIS and ECZEMA (20 - , 20 - 20)

Causality for UPADACITINIB (Blinded)

1) Cervical intraepithelial neoplasia (10056576) (Cervical dysplasia (10008263)) [v.23.1]
[10056576]

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 FOCAL CIN I - II IN CERVIX

- **Investigator:** human papillomavirus

- **AbbVie:** Events is more likely related to HPV infection; Human papillomavirus (HPV) is central to the development of cervical neoplasia and can be detected in 99.7 percent of cervical cancers.

Relevant Laboratory & Other Diagnostic Tests

20 **HISTOPATHOLOGY:** Focal CIN I-II and full thickness HPV infection at squamocolumnar junction and within stripped ectocervical squamous epithelium. No evidence of CIN III or invasive malignancy. Abnormal area fully excised

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
腹部膿瘍	X	X		X
大腸穿孔		X		X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	3 [REDACTED]	MALE	ASIAN

Medical History	Onset Year
ASTHMA	19 [REDACTED]
BEE STING ALERGY	20 [REDACTED]
EXTENSIVE UC/PANCOLITIS	20 [REDACTED]
HEMORRHOIDECTOMY	20 [REDACTED]
INTERMITTEND ISNUSITIS	20 [REDACTED]
OBESITY	20 [REDACTED]
PILES	20 [REDACTED]
POLYPECTOMY	20 [REDACTED]
SHORTSIGHTEDNESS	20 [REDACTED]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: HEMORRHOIDECTOMY	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	8	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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20██ / 1	20██ / 49	49
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20██ / 1	20██ / 240	240

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100.00 mg	QD	Y-M: 20██-██
PERINDOPRIL	5 mg	QD	Y-M: 20██-██ / -10
FOLIC ACID	5.000 mg	QD	Y: 20██
HYOSCINE	1.000 OTHER: TABLET	PRN	Y: 20██
LOPERAMIDE	1.000 OTHER: TABLET	PRN	Y: 20██
SULFASALAZINE	2.00 g	TID	Y: 20██
MESALAZINE	500 mg	BID	Y: 20██

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
PERINDOPRIL	5 mg	QD	Y-M: 20██-██ / -10 ONGOING
PREDNISONE	5.00 mg	QD	Y-M: 20██-██ / 178 Y-M: 20██-██ / 240
HYDROCORTISONE	100 mg	OTHER: 8 HOURLY	Y-M: 20██-██ / 239 Y-M: 20██-██ / 240
ONDANSETRON	4 mg	OTHER: 8 HOURLY	Y-M: 20██-██ / 239 Y-M: 20██-██ / 240
TRAMADOL	100 mg	OTHER: 6 HOURLY	Y-M: 20██-██ / 239 Y-M: 20██-██ / 240
AMLODIPINE	10 mg	QD	Y-M: 20██-██ / 242 ONGOING
CAFFEINE;CODEINE;MEPROBAMATE;PARACETAMOL	2 OTHER: TABS	PRN	Y-M: 20██-██ / 242 Y-M: 20██-██ / 257
ENOXAPARIN	40 mg	QD	Y-M: 20██-██ / 242 Y-M: 20██-██ / 257
FLUCONAZOLE	400 mg	BID	Y-M: 20██-██ / 242 Y-M: 20██-██ / 257
GRANISETRON	1 g	OTHER: 8 HOURLY	Y-M: 20██-██ / 242 Y-M: 20██-██ / 254
MAGNESIUM CHLORIDE	2 OTHER: TABS	BID	Y-M: 20██-██ / 242 ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20██-██ / 242 Y-M: 20██-██ / 257

PARACETAMOL	1 g	OTHER: 8 HOURLY	Y-M: 20■■■■ / 242 Y-M: 20■■■■ / 257
PIPERACILLIN;TAZOBACTAM	45 g	QID	Y-M: 20■■■■ / 242 Y-M: 20■■■■ / 257
CEFTRIAZONE	4 g	OTHER: STAT	Y-M: 20■■■■ / 243 Y-M: 20■■■■ / 243
DEXAMETHASONE	8 mg	OTHER: STAT	Y-M: 20■■■■ / 243 Y-M: 20■■■■ / 243
HYDROCORTISONE	200 mg	OTHER: STAT	Y-M: 20■■■■ / 243 Y-M: 20■■■■ / 243
MAGNESIUM SULFATE	UNKNOWN OTHER: UNKNOWN	OTHER: STAT	Y-M: 20■■■■ / 243 Y-M: 20■■■■ / 243
MORPHINE	10 mg	OTHER: STAT	Y-M: 20■■■■ / 243 Y-M: 20■■■■ / 243
PROPOFOL	200 mL	OTHER: STAT	Y-M: 20■■■■ / 243 Y-M: 20■■■■ / 243
ROCURONIUM	200 mg	OTHER: STAT	Y-M: 20■■■■ / 243 Y-M: 20■■■■ / 243
SUGAMMADEX	2 mL	OTHER: STAT	Y-M: 20■■■■ / 243 Y-M: 20■■■■ / 243
AMOXICILLIN;CLAVULANIC ACID	1.2 g	QID	Y-M: 20■■■■ / 253 Y-M: 20■■■■ / 255
AMOXICILLIN;CLAVULANIC ACID	1 g	BID	Y-M: 20■■■■ / 255 Y-M: 20■■■■ / 256
MESALAZINE	500 mg	BID	Y: 20■■■■ Y-M: 20■■■■ / 240

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections, Event of Interest - Adjudicated Gastrointestinal Perforations

Event Description	ABDOMINAL ABSCESS
Preferred term	腹部膿瘍
AE Onset Date / Initial Rx Day	■■■■20■■■■ / 289
Age at AE Onset	3■
Laboratory Testing	■■■■20■■■■ (RX DAY 240): NPTST162-COVID19 PCR: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; ■■■■20■■■■ (RX DAY 246): Potassium: 4.2 [3.5 - 5.1] MMOL/L; Sodium: 137 [136 - 145] MMOL/L; ■■■■20■■■■ (RX DAY 248): NPTST333-MCS: NORMAL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; ■■■■20■■■■ (RX DAY 250): NPTST333-MCS: ABNORMAL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED
Microbiology	■■■■20■■■■ (RX DAY 243): OTHER COLON NPTST348-MICROSCOPY: POSITIVE-DISTAL CHRONIC ACTIVE COLITIS WITH A PERFORATION AND A FOREIGN BODY RESPONSE TO FAECAL MATERIAL MOST IN KEEPING WITH PERFORATED ULCERATIVE COLITIS
AE Stopped Initial Rx Day	336 (47 DAYS AFTER LAST TREATMENT)
Duration of AE	48 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PROBABLY BACTERIAL INFECTION

Discontinued Study Drug Due to the Event YES

SAE Criteria HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Gastrointestinal Perforations

Event Description	PERFORATION OF SIGMOID COLON
Preferred term	大腸穿孔
AE Onset Date / Initial Rx Day	20 / 289
Age at AE Onset	3
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	334 (45 DAYS AFTER LAST TREATMENT)
Duration of AE	46 DAYS
Severity	SEVERE
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

Generated: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は南アフリカの 3 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、腹部膿瘍の事象を発現した。関連する病歴は、元喫煙者（1 日 0.5 箱を 8 年間）、潰瘍性大腸炎、肥満及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与289日後＊、被験者は腹部膿瘍を発現した。

投与の約5ヵ月後*から、被験者は腹部の圧痛を経験していた。

投与287日後*，被験者は腹部に疑わしい腫瘍があり，それに伴う腹痛を訴えて来院した。被験者は消化器内科医に紹介され，腹部膿瘍が疑われた。投与288日後*，被験者は腹部の腫瘍に伴う腹痛があり，入院した。投与289日後*，腹部及び骨盤のCT スキャン検査が行われた。被験者は，潰瘍性大腸炎の急性増悪（非重篤）と診断された。投与292日後*，被験者は別の病院に移され，膿瘍のドレナージ及び末端の回腸瘻造設を伴う結腸切除術を受けた。

本事象により，治験薬の投与は完全に中止された。投与336日後*，腹部膿瘍は消失した。

投与された薬剤は，ソル・コーテフ，zofran，クレキサン，pantoloc，stilpane，kytril，perfalgan，タゾシン，フルコナゾール，オーグメンチン，ranclav，dexone 及びヒドロコルチゾンであった。

The patient's past medications include:

SULPHASALAZINE for ULCERATIVE COLITIS (20■■ - 20■■)

AZAPRESS for ULCERATIVE COLITIS and EXACERBATION OF COLITIS (■■■■ 20■■ - ■■■■ 20■■, ■■■■ 20■■ - ■■■■ 20■■)

Causality for UPADACITINIB (Blinded)

1) Abdominal abscess (10060921) (Abdominal abscess (10060921)) [v.23.1] [10060921]

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 ABDOMINAL ABSCESS

- **Investigator:** Probably bacterial infection

- **AbbVie:** Event is more likely a complication of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

20 ■ **ABDOMEN AND PELVIS CT:** Perforation of the sigmoid colon (non serious): extravasation of oral contrast from the sigmoid colon anterior large Collection: associated infraumbilical hernia (non serious)

20 ■ **COVID 19 TEST:** Negative

20 ■ **HISTOPATHOLOGY COLECTOMY SPECIMEN:** Distal chronic active colitis with a perforation and a foreign body response to faecal material most in keeping with perforated ulcerative colitis

20 ■ **POTASSIUM:** 4.2 MMOL/L (normal 3.5 to 5.1)

20 ■ **PUS MCS:** Abnormal

20 ■ **SODIUM:** 137 MMOL/L (normal 136 to 145)

20 ■ **URINE MCS:** Normal

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
大腸炎	X			

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	3 [REDACTED]	MALE	ASIAN

Medical History	Onset Year
ANEMIA, UNSPECIFIED	20 [REDACTED]
AXIAL ARTHROPATHY (INCLUDING SACROILIITIS OR ANKYLOSING SPONDYLITIS)	20 [REDACTED]
BENIGN NEOPLASM OF SKIN, SITE UNSPECIFIED	20 [REDACTED]
CONTACT DERMATITIS	20 [REDACTED]
DISEASE OF STOMACH AND DUODENUM, UNSPECIFIED	20 [REDACTED]
DISORDERS OF FUNCTION OF STOMACH	20 [REDACTED]
ECZEMA	20 [REDACTED]
HEADACHE	20 [REDACTED]
INSOMNIA, UNSPECIFIED	20 [REDACTED]
LEFT SIDED UC	20 [REDACTED]
LEFT-SIDED ULCERATIVE (CHRONIC) COLITIS	20 [REDACTED]
MIXED SIMPLE AND MUCOPURULENT CHRONIC BRONCHITIS	20 [REDACTED]
NONINFECTIVE GASTROENTERITIS AND COLITIS, UNSPECIFIED	20 [REDACTED]
OTHER ACNE	20 [REDACTED]
OTHER CHRONIC BRONCHITIS	20 [REDACTED]
OTHER SPECIFIED DYSPEPSIA	20 [REDACTED]
OTHER URTICARIA	20 [REDACTED]
PAIN IN UNSPECIFIED JOINT	20 [REDACTED]
REFLUX ESOPHAGITIS	20 [REDACTED]
SEBORRHEIC DERMATITIS	20 [REDACTED]
UNSPECIFIED CONTACT DERMATITIS, UNSPECIFIED CAUSE	20 [REDACTED]
UNSPECIFIED CONTACT DERMATITIS, UNSPECIFIED CAUSE	20 [REDACTED]
UNSPECIFIED FUNCTIONAL DISORDER OF INTESTINE	20 [REDACTED]
UNSPECIFIED LOCAL INFECTION OF SKIN AND SUBCUTANEOUS TISSUE	20 [REDACTED]
URTICARIA, UNSPECIFIED	20 [REDACTED]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20██
ENDOSCOPY (UC): COLONOSCOPY	20██
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20██

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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	██████20██ / 1	██████20██ / 57	57
M14-234 SS3 Placebo (MAIN)		ORAL	QD	██████20██ / 1	██████20██ / 258	258

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██-██
MESALAZINE	2000 mg	BID	Y-M: 20██-██
PREDNISOLONE	10 mg	BID	Y-M: 20██-██
MESALAZINE	500 mg	BID	Y-M: 20██-██
MESALAZINE	1000 mg	BID	Y-M: 20██-██
MESALAZINE	2000 mg	BID	Y-M: 20██-██
MESALAZINE	1000 mg	BID	Y-M: 20██-██
PREDNISOLONE	10 mg	BID	Y-M: 20██-██
MESALAZINE	2000 mg	BID	Y-M: 20██-██
PREDNISOLONE	5 mg	BID	Y-M: 20██-██
PREDNISOLONE	10 mg	BID	Y-M: 20██-██
PREDNISOLONE	5 mg	BID	Y-M: 20██-██

PREDNISOLONE	5 mg	BID	Y-M: 20██
PREDNISOLONE	10 mg	TID	Y-M: 20██
AZATHIOPRINE	50 mg	BID	Y-M: 20██
MESALAZINE	1000 mg	BID	Y-M: 20██
PREDNISOLONE	5 mg	BID	Y-M: 20██
PREDNISOLONE	5 mg	BID	Y-M: 20██
AZATHIOPRINE	50 mg	BID	Y-M: 20██
AZATHIOPRINE	50 mg	BID	Y-M: 20██
PREDNISOLONE	10 mg	BID	Y-M: 20██
AZATHIOPRINE	50 mg	BID	Y-M: 20██
PREDNISOLONE	10 mg	BID	Y-M: 20██
MESALAZINE	500 mg	BID	Y-M: 20██
MESALAZINE	1000 mg	BID	Y-M: 20██
PREDNISOLONE	5 mg	BID	Y-M: 20██
PREDNISOLONE	10 mg	QD	Y-M: 20██
AZATHIOPRINE	50 mg	BID	Y-M: 20██
MESALAZINE	2 g	OTHER: QOD	Y-M: 20██
PREDNISOLONE	5 mg	BID	Y-M: 20██
AZATHIOPRINE	50 mg	BID	Y-M: 20██
PREDNISOLONE	5 mg	BID	Y-M: 20██
ADALIMUMAB	40.000 mg	Q2W	Y-M: 20██
MESALAZINE	500 mg	BID	Y-M: 20██
MESALAZINE	1000 mg	BID	Y-M: 20██
TRIAMCINOLONE	15 g	BID	Y-M: 20██ / -79
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	16.2 g	OTHER: STAT	Y-M: 20██ / -64
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	16.2 g	OTHER: STAT	Y-M: 20██ / -6

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	Stop Year-Month / RX Day
MESALAZINE	1000 mg	BID	Y-M: 20██	ONGOING
DIMETICONE	40 mg	BID	Y-M: 20██ / 139	ONGOING
OTILONIUM	40 mg	BID	Y-M: 20██ / 195	Y-M: 20██ / 222
ALGINIC ACID;ALUMINIUM HYDROXIDE;MAGNESIUM CARBONATE;SILICA GEL	1 DF	TID	Y-M: 20██ / 223	Y-M: 20██ / 244

ALUMINIUM HYDROXIDE- MAGNESIUM CARBONATE GEL;ALUMINIUM MAGNESIUM SILICATE;GLUCOSE;GLYCYRRHI ZA GLABRA	3 g	BID	Y-M: 20■■■■ / 223 Y-M: 20■■■■ / 244
BENZONATATE	100 mg	TID	Y-M: 20■■■■ / 223 Y-M: 20■■■■ / 230
LEVOCETIRIZINE	5 mg	QD	Y-M: 20■■■■ / 223 Y-M: 20■■■■ / 230
OTILONIUM	40 mg	TID	Y-M: 20■■■■ / 223 Y-M: 20■■■■ / 244
CODEINE	30 mg	QD	Y-M: 20■■■■ / 230 Y-M: 20■■■■ / 245
LOPERAMIDE	2 mg	QD	Y-M: 20■■■■ / 230 Y-M: 20■■■■ / 244
FLOMOXEF	1 g	OTHER: Q8H	Y-M: 20■■■■ / 236 Y-M: 20■■■■ / 242
FLOMOXEF	1 g	OTHER: STAT	Y-M: 20■■■■ / 236 Y-M: 20■■■■ / 237
POTASSIUM	1190 mg	TID	Y-M: 20■■■■ / 236 Y-M: 20■■■■ / 242
HYDROCORTISONE	100 mg	OTHER: Q6H	Y-M: 20■■■■ / 240 Y-M: 20■■■■ / 242
HYDROCORTISONE	100 mg	OTHER: Q8H	Y-M: 20■■■■ / 242 Y-M: 20■■■■ / 245
FUSIDIC ACID	2 %	BID	Y-M: 20■■■■ / 245 Y-M: 20■■■■ / 252
MOMETASONE	0.1 %	BID	Y-M: 20■■■■ / 245 Y-M: 20■■■■ / 252
PREDNISOLONE	10 mg	TID	Y-M: 20■■■■ / 245 Y-M: 20■■■■ / 248
SERTACONAZOLE	2 %	OTHER: BIW	Y-M: 20■■■■ / 245 ONGOING

Event #1: Serious Adverse Event

Event Description	WORSENING OF LEFT SIDED COLITIS WITHOUT COMPLICATIONS
Preferred term	大腸炎
AE Onset Date / Initial Rx Day	■■■■20■■ / 293
Age at AE Onset	3■
Laboratory Testing	■■■■20■■ (RX DAY 236): Blood Urea Nitrogen: 2.14182 [2.49879 - 8.92425] MMOL/L; Erythrocytes: 4.53 [4.5 - 5.7] 10^12/L; Hemoglobin: 102 [137 - 170] G/L; Leukocytes: 11.9 [3.6 - 11.2] 10^9/L; Lymphocytes/Leukocytes: 11.8 [16 - 43.5] %; ■■■■20■■ (RX DAY 240): Blood Urea Nitrogen: 1.07091 [2.49879 - 8.92425] MMOL/L; Creatinine: 65.418412 [61.882282 - 114.924238] UMOL/L; Hemoglobin: 100 [137 - 170] G/L; Leukocytes: 10.9 [3.6 - 11.2] 10^9/L
Microbiology	■■■■20■■ (RX DAY 240): STOOL NPTST216-FECAL: NEGATIVE
AE Stopped Initial Rx Day	302
Duration of AE	10 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]:11:02

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。本被験者は台湾の 3 [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、合併症を伴わない大腸炎（左側）の悪化の事象を発現した。関連する病歴は、胃の機能障害、消化不良、潰瘍性大腸炎（左側、慢性）、特定不能の腸の機能障害、貧血、特定不能の胃及び十二指腸の疾患、特定不能の非感染性胃腸炎及び大腸炎、非喫煙者並びに非飲酒者であった。

Event 1 の臨床経過：

投与293日後＊，被験者は合併症を伴わない大腸炎（左側）の悪化を発現した。投与302日後＊，合併症を伴わない大腸炎（左側）の悪化は消失した。

本事象発現前に、被験者は 1-2 週間にわたり、嘔吐及び血性下痢を経験した。投与290日後＊，被験者は食後の腹痛及び断続的な発熱を新たに経験し始めた。

投与293日後＊，被験者は入院した。身体検査では、左下腹部に圧痛があった。局所的な神経性の徴候、胸痛、肋骨脊椎角の打診時の痛み、灼熱感や異常な呼吸音はなかった。投与302日後＊，被験者は退院した。

投与された薬剤は、グルコン酸カリウム、フロモキシセフナトリウム、ヒドロコルチゾン及びプレドニゾロンであった。

The patient's past medications include:

[illegible]

AZATHIOPRINE 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])

ADALIMUMAB for ULCERATIVE COLITIS (■■■■■ 20■■ - ■■■■ 20■■)

Causality for UPADACITINIB (Blinded)

1) Colitis aggravated (10009890) (Colitis (10009887)) [v.23.0] [10009890]

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 WORSENING OF LEFT SIDED COLITIS WITHOUT COMPLICATIONS

- Investigator: Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

20 BLOOD PRESSURE: 127/83 mmHg

20 BODY TEMPERATURE: 36.6 Degrees C

20	BUN: 6 mg/dL (normal 7 to 25)
20	BUN: 3 mg/dL (normal 7 to 25)
20	CHEST X-RAY: No active lung lesion. No prominent pleural effusion.
20	CREATININE: 0.74 mg/dL (normal 0.7 to 1.3)
20	EKG: sinus tachycardia
20	FECAL TEST: negative
20	GLASGOW COMA SCALE: 15 no units
20	HEART RATE: 107 /min
20	HEMOGLOBIN: 10.2 G/DL (normal 13.7 to 17.0)
20	HEMOGLOBIN: 10.0 G/DL (normal 13.7 to 17.0)
20	KUB: Calcified density noted in right pelvis; maybe phlebolith or lower ureteral stone, narrowing of sacroiliac joint. No presence of free air.
20	LYMPHOCYTES: 11.8 % (normal 16 to 43.5)
20	POTASSIUM: 3.0 no units
20	RED BLOOD CELLS: 4.53 X10**6/MCL (normal 4.5 to 5.7)
20	RESPIRATORY RATE: 18 /min
20	WHITE BLOOD CELLS: 11.9 X10**3/MCL (normal 3.6 to 11.2)
20	WHITE BLOOD CELLS: 10.9 X10**3/MCL (normal 3.6 to 11.2)

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
痔瘻	X			

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

Medical History	Onset Year
DISEASE OF DIGESTIVE SYSTEM, UNSPECIFIED	20 [REDACTED]
EXTENSIVE UC/PANCOLITIS	20 [REDACTED]
FUNCTIONAL DYSPEPSIA	20 [REDACTED]
GASTRO-ESOPHAGEAL REFLUX DISEASE WITH ESOPHAGITIS	20 [REDACTED]
INFLAMMATORY LIVER DISEASE, UNSPECIFIED	20 [REDACTED]
MIXED HEMORRHOID	20 [REDACTED]
MYOPIA, UNSPECIFIED EYE	20 [REDACTED]
OTHER HYPERLIPIDEMIA	20 [REDACTED]
ULCERATIVE (CHRONIC) PANCOLITIS WITHOUT COMPLICATIONS	20 [REDACTED]
UNSPECIFIED CONJUNCTIVITIS	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	5 PACK	20	20 [REDACTED]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 57	57
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	20 / 1	20 / 363	363

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1000 mg	TID	Y-M: 20 /
PREDNISOLONE	10 mg	TID	Y-M: 20 /
MESALAZINE	1000 mg	TID	Y-M: 20 /
ADALIMUMAB	80.000 mg	QD	Y-M: 20 /
AZATHIOPRINE	50 mg	QD	Y-M: 20 /
MESALAZINE	1000 mg	BID	Y-M: 20 /
MERCAPTOPYRINE	50 mg	QD	Y-M: 20 /
MESALAZINE	1000 mg	BID	Y-M: 20 /
DIMETICONE	40 mg	BID	Y-M: 20 / -211
AMOXICILLIN;CLAVULANIC ACID	1 g	BID	Y-M: 20 / -83
MESALAZINE	1000 mg	TID	Y-M: 20 / -99

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	1000 mg	TID	Y-M: 20 / -99 ONGOING
AMOXICILLIN;CLAVULANIC ACID	1 g	BID	Y-M: 20 / 180 Y-M: 20 / 193
BACITRACIN;NEOMYCIN;POLYM YXIN B	10 g	QD	Y-M: 20 / 193 Y-M: 20 / 224
BUPIVACAINE	20 mg	OTHER: STAT	Y-M: 20 / 193 Y-M: 20 / 193
MAGNESIUM OXIDE	250 mg	QID	Y-M: 20 / 193 Y-M: 20 / 210
SENNOSIDE A+B	20 mg	OTHER: HS	Y-M: 20 / 193 Y-M: 20 / 210
PARACETAMOL	500 mg	QID	Y-M: 20 / 194 Y-M: 20 / 210

Event #1: Serious Adverse Event

Event Description	ANAL FISTULA
Preferred term	痔瘻
AE Onset Date / Initial Rx Day	20 / 250

Age at AE Onset	5
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	251
Duration of AE	2 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ULCERATIVE PANCOLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は台湾の 5 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、痔瘻の事象を発現した。

Event 1 の臨床経過：

投与250日後＊，被験者は痔瘻を発現した。投与251日後＊，痔瘻は消失した。

本事象発現前に，被験者は痔瘻（非重篤）を経験していた。

投与250日後＊，被験者は肛門痛及び排膿のために入院した。結腸直腸外科の外来を受診した。診断は，左肛門括約筋間の瘻孔，つまり左陰嚢壁とその5時方向にある左肛門壁との間の単純な線状の瘻孔であり，括約筋間にある種類の瘻孔であった。発熱，悪心/嘔吐，腹痛，便通の変化，及び体重減少は認められなかった。被験者は入院し，肛門瘻孔切開術を受けた。投与251日後＊，被験者は退院した。

投与された薬剤は、アセトアミノフェン、酸化マグネシウム、sennosides 及び spersin oint であった。

The patient's past medications include:

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

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

MERCAPTOPURINE for ULCERATIVE COLITIS ([REDACTED] 20 [REDACTED] - [REDACTED] 20 [REDACTED])

Causality for UPADACITINIB (Blinded)

1) Anal fistula (10002156) (Anal fistula (10002156)) [v.22.1] [10002156]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, outcome unknown

Alternative Etiology for UPADACITINIB (Blinded)

Event of ANAL FISTULA

- Investigator: ulcerative pancolitis

- AbbVie: event is most likely related to pre-existing ulcerative colitis and its peri-anal involvement.

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
インフルエンザ	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	4 [REDACTED]	MALE	ASIAN

Medical History	Onset Year
AGORAPHOBIA	20 [REDACTED]
INFLAMMATORY SPONDYLOPATHIES	20 [REDACTED]
INTERNAL HEMORRHOIDS	20 [REDACTED]
LEFT SIDED UC	20 [REDACTED]
MYOFASCIAL PAIN SYNDROME	20 [REDACTED]
PANIC ATTACKS	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration						
Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 56	56

M14-234 SS3 15 mg ORAL QD 20 / 1 20 / 365 365
ABT-494 (MAIN)

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	OTHER: HS	Y-M: 20 /
ENTEROCOCCUS FAECALIS	1.000 g	OTHER: TIDPC	Y-M: 20 /
LANSOPRAZOLE	30.000 mg	OTHER: QDAC	Y-M: 20 /
DICYCLOVERINE	10.000 mg	TID	Y-M: 20 /
MESALAZINE	2400 mg	QD	Y-M: 20 /
MAGNESIUM OXIDE	250.000 mg	TID	Y-M: 20 /
PREDNISOLONE	40 mg	QD	Y-M: 20 /
CINCHOCAINE;POLICRESULEN	100.000 mg	QD	Y-M: 20 /
AZATHIOPRINE	50 mg	QD	Y-M: 20 /

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	2400 mg	QD	Y-M: 20 / ONGOING
AMBROXOL	30 mg	TID	Y-M: 20 / 104 Y-M: 20 / 104
CEFUROXIME	1500 mg	OTHER: Q8H	Y-M: 20 / 104 Y-M: 20 / 104
FEXOFENADINE	60 mg	BID	Y-M: 20 / 104 Y-M: 20 / 104
PARACETAMOL	500 mg	PRN	Y-M: 20 / 104 Y-M: 20 / 104
SODIUM CHLORIDE	0.9 %	QD	Y-M: 20 / 104 Y-M: 20 / 105
ACETYLSALICYLIC ACID	0.5 g	QD	Y-M: 20 / 105 Y-M: 20 / 105
BENZONATATE	100 mg	TID	Y-M: 20 / 106 Y-M: 20 / 106
LEVOCETIRIZINE	5 mg	OTHER: QE	Y-M: 20 / 106 Y-M: 20 / 106

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

Event Description	INFLUENZA TYPE A INFECTION
Preferred term	インフルエンザ
AE Onset Date / Initial Rx Day	20 / 160
Age at AE Onset	4
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	165

Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INFLUENZA TYPE A INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [REDACTED] 20[REDACTED]:11:02

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。本被験者は台湾の 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、A 型インフルエンザ感染の事象を発現した。関連する病歴は、潰瘍性大腸炎（左側）、非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与160日後＊，被験者は A 型インフルエンザ感染を発現した。投与165日後＊，A 型インフルエンザ感染は消失した。

投与160日後＊，被験者は A 型インフルエンザ感染及び発熱（数値は提供されていない）があり、入院した。徴候及び症状には、2 週間前に始まった咳嗽が含まれた。投与164日後＊，被験者は退院した。

投与された薬剤は、mubroxol, フェキソフェナジン, fucole paran, lyacety, 生理食塩水, ザイザル, furoxime 及び zcough cap であった。

The patient's past medications include:

PREDONINE for ULCERATIVE COLITIS ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

IMURAN for ULCERATIVE COLITIS ([REDACTED] 20[REDACTED] - [REDACTED] 20[REDACTED])

Causality for UPADACITINIB (Blinded)

1) Influenza A virus infection (10022002) (Influenza (10022000)) [v.22.1] [10022002]

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 INFLUENZA TYPE A INFECTION

- **Investigator:** Influenza type a infection

- **AbbVie:** event is a common viral infection in the general population.

Relevant Laboratory & Other Diagnostic Tests

██████ 20██ X-RAY: Not reported

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
人工流産	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	21	FEMALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	2011
ULCERATIVE COLITE	2011

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	2011
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	2011

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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 2011 / 1	[REDACTED] 2011 / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[REDACTED] 2011 / 1	[REDACTED] 2011 / 225	225

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FENTANYL	50 OTHER: MGC	QD	Y-M: 20██-██ / -70
KETAMINE	25 mg	QD	Y-M: 20██-██ / -70
MIDAZOLAM	2 mg	QD	Y-M: 20██-██ / -70
PROPOFOL	100 mg	QD	Y-M: 20██-██ / -70
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: DOSE	BID	Y-M: 20██-██ / -71
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: DOSE	BID	Y-M: 20██-██ / -1
MESALAZINE	3000 mg	TID	Y: 20██
MESALAZINE	4 g	BID	Y: 20██
MESALAZINE	4 g	QD	Y: 20██
MESALAZINE	4000 mg	BID	Y: 20██

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
MESALAZINE	3000 mg	TID	Y: 20██	Not reported

Event #1: Serious Adverse Event

Event Description	ELECTIVE ABORTION
Preferred term	人工流産
AE Onset Date / Initial Rx Day	██-██-20██ / 309 (28 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2█
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	309 (28 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAY
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PATIENT DECISION FOR PREGNANCY TERMINATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者はトルコの 2 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、人工妊娠中絶及び妊娠時の母体の曝露（非重篤）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、非飲酒者及びコンドームでの避妊であった。

Event 1 の臨床経過：

年月不明日に、被験者は妊娠時の母体の曝露（非重篤）を発現した。投与309日後＊，人工妊娠中絶を発現した。

投与283日後＊，治験実施施設は被験者の妊娠を認識した。胎児は、受胎前及び妊娠第一期の間、ウパダシチニブの母体内での使用（子宮内での使用）に曝露されていた。分娩予定日（EDD）は投与の約17ヵ月後＊であった。ウパダシチニブの母体内での使用を中止した。投与309日後＊，被験者は人工妊娠中絶を受けた。

The patient's past medications include:

ASACOL (MESALAZIN) for ULCERATIVE COLITIS (20 - 20)

ASACOL LAVMAN (ENEMA) for ULCERATIVE COLITIS (20 - 20)

SALOFALK LAVMAN for ULCERATIVE COLITIS (20 - 20)

Causality for UPADACITINIB (Blinded)

1) Elective abortion (10082264) (Abortion induced (10000220)) [v.23.1] [10082264]

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

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

Dechallenge: Not Applicable

2) Maternal exposure during pregnancy (10071408) (Maternal exposure during pregnancy (10071408))
[v.23.1] [10071408]

Causality as per reporter (Drug/Vaccine): Not Reported

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of ELECTIVE ABORTION

- **Investigator:** Patient decision for pregnancy termination

- **AbbVie:** Event is more likely related to the subject's choice to terminate the pregnancy.

Event of MATERNAL EXPOSURE DURING PREGNANCY

- **Investigator:** Not reported.

- **AbbVie:** Special situation of maternal use of active pharmaceutical ingredient.

Relevant Laboratory & Other Diagnostic Tests

20 COVID-19 VIRUS TEST: Nasopharyngeal swab: Negative

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
肺塞栓症	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	4 [REDACTED]	FEMALE	WHITE

Medical History	Onset Year
GASTROESOPHAGEAL REFLUX DISEASE	20 [REDACTED]
HYPERTENSION	20 [REDACTED]
LEFT SIDED UC	19 [REDACTED]
NEPHROLITHIASIS	19 [REDACTED]
OSTEOPOROSIS	20 [REDACTED]
OTHER: BENZO ADDICTION	20 [REDACTED]
OTHER: BIPOLAR DISORDER	20 [REDACTED]
OTHER: BOWEL OBSTRUCTION	20 [REDACTED]
OTHER: ENDOMETRIOSIS	19 [REDACTED]
OTHER: FIBROMYALGIA	20 [REDACTED]
OTHER: IRRITABLE BOWEL SYNDROME	19 [REDACTED]
OTHER: RECURRENT UTIS	20 [REDACTED]
OTHER: SCREENING PHYSICAL EXAM: DIFFUSE POSTERIOR THORAX AND BACK TENDERNESS	20 [REDACTED]
OTHER: SCREENING PHYSICAL EXAM: MODERATE DIFFUSE ABDOMINAL TENDERNESS. NO MASSES. NO REBOUND	20 [REDACTED]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20 [REDACTED]
ENDOSCOPY (UC): COLONOSCOPY	20 [REDACTED]
SAE SUPPLEMENTAL PROCEDURE: CT HEAD WO CONTRAST	20 [REDACTED]
SAE SUPPLEMENTAL PROCEDURE: XR CHEST	20 [REDACTED]
SURGERY: APPENDECTOMY	20 [REDACTED]
SURGERY: C-SECTION	19 [REDACTED]
SURGERY: C-SECTION	19 [REDACTED]
SURGERY: CHOLECYSTECTOMY	20 [REDACTED]

SURGERY: HERNIA REPAIR	20██
SURGERY: HYSTERECTOMY	20██
SURGERY: LEFT ANKLE SURGERY	20██
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20██

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	1	20██
CIGARS	NEVER			
E-CIGARETTES	CURRENT	10 SESSIONS	1	
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	██████20██ / 1	██████20██ / 59	59
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	██████20██ / 1	██████20██ / 312	312

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100 mg	QD	Y-M: 20██-██ / -136
INFLIXIMAB	5.000 mg/kg	EVERY 2 WEEKS	Y-M: 20██-██ / -136
CIPROFLOXACIN	500 mg	BID	Y-M: 20██-██ / -136
METRONIDAZOLE	500 mg	BID	Y-M: 20██-██ / -136
PREDNISONE	20 mg	QD	Y-M: 20██-██ / -136
CIPROFLOXACIN	400 mg	BID	Y-M: 20██-██ / -140
METRONIDAZOLE	500 mg	TID	Y-M: 20██-██ / -140
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20██-██ / -141
SULFASALAZINE	1000 mg	TID	Y-M: 20██-██ / -141
GABAPENTIN	600 mg	TID	Y-M: 20██-██ / -161
PROMETHAZINE	25 mg	PRN	Y-M: 20██-██ / -161
PREDNISONE	20 mg	QD	Y-M: 20██-██ / -73

PREDNISONE	60 mg	OTHER: ONCE ONLY	Y-M: 20██-██ / -74
CIPROFLOXACIN	500 mg	QD	Y-M: 20██-██ / -91
ACETYLSALICYLIC ACID;CAFFEINE	1 OTHER: PACKET	PRN	Y-M: 20██-██ / -56
TRAMADOL	50 mg	PRN	Y-M: 20██-██ / -69
OXYCODONE	5 mg	PRN	Y-M: 20██-██ / -29
PARACETAMOL	325 mg	PRN	Y-M: 20██-██ / -29
CIPROFLOXACIN	400 mg	OTHER: ONCE ONLY	Y-M: 20██-██ / -32
PIPERACILLIN;TAZOBACTAM	4.5 g	OTHER: ONCE ONLY	Y-M: 20██-██ / -32
SODIUM CHLORIDE	2,409 mL	OTHER: ONCE ONLY	Y-M: 20██-██ / -32
LIDOCAINE	40 mg	OTHER: ONCE	Y-M: 20██-██ / -4
PROPOFOL	800 mg	OTHER: ONCE	Y-M: 20██-██ / -4
MACROGOL 3350	238 g	OTHER: ONCE	Y-M: 20██-██ / -5

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	Stop Year-Month / RX Day
SULFASALAZINE	1000 mg	TID	Y-M: 20██-██ / -141	ONGOING
GABAPENTIN	600 mg	TID	Y-M: 20██-██ / -161	ONGOING
PROMETHAZINE	25 mg	PRN	Y-M: 20██-██ / -161	ONGOING
ACETYLSALICYLIC ACID;CAFFEINE	1 OTHER: PACKET	PRN	Y-M: 20██-██ / -56	Y-M: 20██-██ / 167
LORAZEPAM	1 mg	BID	Y-M: 20██-██ / 52	ONGOING
BISACODYL	5 mg	PRN	Y-M: 20██-██ / 57	ONGOING
OXYCODONE;PARACETAMOL	10 mg	BID	Y-M: 20██-██ / 85	Y-M: 20██-██ / 158
CIPROFLOXACIN	500 mg	BID	Y-M: 20██-██ / 134	Y-M: 20██-██ / 145
PREDNISONE	20 mg	QD	Y-M: 20██-██ / 136	Y-M: 20██-██ / 138
HYOSCYAMINE	125 mg	QD	Y-M: 20██-██ / 137	ONGOING
PREDNISONE	40 mg	QD	Y-M: 20██-██ / 138	Y-M: 20██-██ / 138
OXYCODONE;PARACETAMOL	5 mg	QID	Y-M: 20██-██ / 153	Y-M: 20██-██ / 290
ENOXAPARIN	30 mg	OTHER: ONCE ONLY	Y-M: 20██-██ / 166	Y-M: 20██-██ / 166
LORAZEPAM	2 mg	PRN	Y-M: 20██-██ / 166	Y-M: 20██-██ / 168
APIXABAN	5 mg	QD	Y-M: 20██-██ / 167	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Initial Rx Day	20 / 225
Age at AE Onset	4
Laboratory Testing	20 (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; NPTST143-CO2: 23 [22 - 32] MEQ/L; NPTST431-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
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

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Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 4 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 1 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 ヶ月間，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 (■■■■ 20■■ - ■■■■ 20■■)

REMICADE for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

SOLUMEDROL for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

CIPRO for ULCERATIVE COLITIS, URINARY TRACT INFECTION and SEPSIS (■■■■ 20■■ - ■■■■ 20■■, ■■■■ 20■■ - ■■■■ 20■■, ■■■■ 20■■ - ■■■■ 20■■, ■■■■ 20■■ - ■■■■ 20■■)

PREDNISONE for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■, ■■■■ 20■■ - ■■■■ 20■■, ■■■■ 20■■ - ■■■■ 20■■)

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)

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

20 ■ **BASOPHILS ABS:** 0.1 TH/mm3 (normal <0.1)

20 ■ **BLOOD PRESSURE:** 143/89 mmHg

20 ■ **BODY TEMPERATURE:** 36.6 Degrees C

20 ■ **BUN:** 14 mg/dL (normal 6 to 24)

20 ■ **CALCIUM:** 9.3 mg/dL

20 ■ **CHEST X-RAY:** Norma no acute cardiopulmonary pathology

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

20 ■ **CHLORIDE:** 108 MMOL/L (normal 97 to 109)

20 ■ **CO2:** 23 MMOL/L

20 ■ **CREATININE:** 0.87 mg/dL

20 ■ **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.

20 ■ **ECHOCARDIOGRAM:** The left ventricular systolic function is normal (55-65%). Grade 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

20 ■ **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 nubbins of a Q-wave in 3.

20 ■ **ELECTROCARDIOGRAM:** Normal

20 ■ **EOSINOPHILS ABS:** 0 (normal <0.7)

20 ■ **GLUCOSE:** 102 mg/dL

20 ■ **HEMATOCRIT:** 37.4 % (normal 34.0 to 46.0)

20 ■ **HEMOGLOBIN:** 12.4 G/DL (normal 11.1 to 15.9)

20 ■ **INR:** 0.9 No units (normal 0.8 to 1.1)

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

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

20 ■ **POTASSIUM:** 3.6 MMOL/L (normal 3.5 to 5.2)

20 ■ **PULSE:** 100 bpm

Unknown date **QUANTIFERON-TB:** Negative

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

20 ■ **RESPIRATORY RATE:** 18 /min

20 ■ **SODIUM:** 144 MMOL/L (normal 134 to 145)

20 SPO2 (Room Air): 94 %

20 WBC: $6.4 \times 10^3/\mu\text{L}$ (normal 3.4 to 10.8)

20 WBC: $8.8 \times 10^3/\mu\text{L}$ (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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	20 / 1	20 / 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 /
MESALAZINE	1.2 mg	QD	Y-M: 20 /
PREDNISONE	10 mg	QD	Y-M: 20 /
PARACETAMOL	650.000 mg	PRN	Y-M: 20 / -324
ADALIMUMAB	40.000 mg/kg	ONCE A WEEK	Y-M: 20 / -341
PREDNISONE	40 mg	QD	Y-M: 20 / -170
IBUPROFEN	800 mg	PRN	Y-M: 20 / -46
CEFALEXIN	500 mg	BID	Y-M: 20 / -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 /	ONGOING
PREDNISONE	10 mg	QD	Y-M: 20 /	Y-M: 20 / -1
PREDNISONE	5 mg	QD	Y-M: 20 / 1	Y-M: 20 / 15
PREDNISONE	2.5 mg	QD	Y-M: 20 / 16	Y-M: 20 / 30
METHYLPREDNISOLONE	4 mg	OTHER: TID X 3 DAYS,BIDX 3 DAYS,QDX 3 DAYS AND OFF	Y-M: 20 / 31	Y-M: 20 / 39
OMEPRAZOLE	20 mg	PRN	Y-M: 20 / 31	ONGOING
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20 / 43	ONGOING
CAFFEINE;CODEINE;PARACETAMOL;PIPERYLONE	1 PACK mL	TID	Y-M: 20 / 195	Y-M: 20 / 203

Event #1: Serious Adverse Event

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

Age at AE Onset	2
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
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

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Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 2 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 (■■■■ 20■■ - ■■■■ 20■■)

HUMIRA for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

Causality for ABT-494 (Blinded)

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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 57	57

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

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 / Stop Year-Month / RX Day	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	20 / 57
Age at AE Onset	5
Laboratory Testing	
20 (RX DAY -1): NPTST495-SURGICAL PATHOLOGY: FOCAL HIGH GRADE DYS [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED	
Microbiology	
NOT REPORTED	
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 Venous Thromboembolic Event

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Initial Rx Day	20 / 88 (29 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5
Laboratory Testing	
NOT REPORTED	
Microbiology	
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	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]:11:02

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 (■■■■ 20■■ - ■■■■ 20■■)

ENTYVIO for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

VENOFER for ULCERATIVE COLITIS / IRON DEFICIENCY ANEMIA and ULCERATIVE COLITIS / IRON DEFICIENCY ANEMIA (■■■■ 20■■ - ■■■■ 20■■)

MESALAMINE for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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

■■■■ 20■■ **BICARB:** 23 no units

■■■■ 20■■ **BIOPSY, COLON:** Left colon, focal high grade dysplasia

■■■■ 20■■ **BODY TEMPERATURE:** 98.5 degrees F

20 BUN: 12 no units

20 CALCIUM: 8.9 no units

20 CL: 101 no units

20 COLONOSCOPY: High grade dysplasia

20 CREATININE: 0.99 no units

20 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.

20 HCT: 35 no units

20 HGB: 11.3 no units

20 K: 3.9 no units

20 NA: 140 no units

20 PLT: 348 no units

20 WBC: 10.8 no units

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 5 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██ - ████ 20██)

HUMIRA for ULCERATIVE COLITIS (████ 20██ - ████ 20██)

REMICADE for ULCERATIVE COLITIS (████ 20██ - ████ 20██, ████ 20██ - ████ 20██)

PREDNISONE for WORSENING OF ULCERATIVE COLITIS SYMPTOMS (████ 20██ - ████ 20██, ████ 20██ - ████ 20██, ████ 20██ - ████ 20██, ████ 20██ - ████ 20██, ████ 20██ - ████ 20██, ████ 20██ - ████ 20██, ████ 20██ - ████ 20██)

ENTYVIO for ULCERATIVE COLITIS (████ 20██ - ████ 20██)

ACETAMINOPHEN for WORSENING OF ULCERATIVE COLITIS SYMPTOMS and FEVER (████ 20██ - ████ 20██)

VENOFER for ULCERATIVE COLITIS and IRON DEFICIENCY ANEMIA (████ 20██ - ████ 20██)

Causality for ABT-494 (Blinded)

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

20 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.

20 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-VEINUS: 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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 54	54
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20 / 1	20 / 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 / -175
MESALAZINE	1600 mg	BID	Y-M: 20 / -91
MESALAZINE	800.000 mg	NOT REPORTED	Y-M: 20 / -91
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	5.86 g	OTHER: ONCE	Y-M: 20 / -64
MACROGOL 3350	17 g	PRN	Y-M: 20 / -74
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	5.86 g	OTHER: ONCE	Y-M: 20 / -1
NAPROXEN	500 mg	OTHER: BIDPRN	Y-M: 20 / -2
SIMVASTATIN	20 mg	QD	Y: 20
TOPIRAMATE	200 mg	BID	Y: 20
TRAZODONE	50 mg	QD	Y: 20
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y: 20
FLUPHENAZINE	25 mg	OTHER: Q MONTHLY	Y: 20
VENLAFAXINE	75 mg	QD	Y: 20
BENZATROPINE	1 mg	QD	Y: 20
GOLIMUMAB	200.000 mg	QMONTH	Y: 20

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	Stop Year-Month / RX Day
GABAPENTIN	300 mg	QD	Y-M: 20██-██ / -175	ONGOING
PARACETAMOL	1000 mg	OTHER: Q8 HRS PRN	Y-M: 20██-██ / 59	ONGOING
RIZATRIPTAN	10 mg	PRN	Y-M: 20██-██ / 79	ONGOING
ZOLPIDEM	5 mg	QD	Y-M: 20██-██ / 117	ONGOING
SIMVASTATIN	20 mg	QD	Y: 20██	ONGOING
TOPIRAMATE	200 mg	BID	Y: 20██	ONGOING
TRAZODONE	50 mg	QD	Y: 20██	Y-M: 20██-██ / 117
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y: 20██	ONGOING
FLUPHENAZINE	25 mg	OTHER: Q MONTHLY	Y: 20██	ONGOING
VENLAFAXINE	75 mg	QD	Y: 20██	ONGOING
BENZATROPINE	1 mg	QD	Y: 20██	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	20 / 167
Age at AE Onset	3
Laboratory Testing	20 (RX DAY -10): Chloride: 104 [102 - 112] MMOL/L; 20 (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; NPTST029-ANION GAP: 10.0 [3 - 11] MMOL/L; NPTST080-BUN/CREA RATIO: 15 [7 - 25] MG/DL; NPTST093-CA CORRECTED: 9.2 [8.7 - 10.7] MG/DL; NPTST197-EGFR AFRICAN AMERICAN: > 60 [60 - 60] UNIT NOT REPORTED; NPTST198-EGFR NON AFRICAN: >60 [60 - 60] UNIT NOT REPORTED; NPTST251-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	20 (RX DAY 113): OTHER TOXICOLOGY NPTST513-TOXICOLOGY: POSITIVE-MDS MDMA UR QL; URINE NPTST536-URINALYSIS: NEGATIVE-UR WBC AUTO RESULT 28/HPE. UR RBC AUTO RESULT 15/HPE
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

Event #2: 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	20 / 167
Age at AE Onset	3
Laboratory Testing	20 (RX DAY -10): Chloride: 104 [102 - 112] MMOL/L; 20 (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; NPTST029-ANION GAP: 10.0 [3 - 11] MMOL/L; NPTST080-BUN/CREA RATIO: 15 [7 - 25] MG/DL; NPTST093-CA CORRECTED: 9.2 [8.7 - 10.7] MG/DL; NPTST197-EGFR AFRICAN AMERICAN: > 60 [60 - 60] UNIT NOT REPORTED; NPTST198-EGFR NON AFRICAN: >60 [60 - 60] UNIT NOT REPORTED; NPTST251-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	20 (RX DAY 113): OTHER TOXICOLOGY NPTST513-TOXICOLOGY: POSITIVE-MDS MDMA UR QL; URINE NPTST536-URINALYSIS: NEGATIVE-UR WBC AUTO RESULT 28/HPE. UR RBC AUTO RESULT 15/HPE
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

Event #3: 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	20 / 167
Age at AE Onset	3
Laboratory Testing	20 (RX DAY -10): Chloride: 104 [102 - 112] MMOL/L; 20 (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; NPTST029-ANION GAP: 10.0 [3 - 11] MMOL/L; NPTST080-BUN/CREA RATIO: 15 [7 - 25] MG/DL; NPTST093-CA CORRECTED: 9.2 [8.7 - 10.7] MG/DL; NPTST197-EGFR AFRICAN AMERICAN: > 60 [60 - 60] UNIT NOT REPORTED; NPTST198-EGFR NON AFRICAN: >60 [60 - 60] UNIT NOT REPORTED; NPTST251-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	20 (RX DAY 113): OTHER TOXICOLOGY NPTST513-TOXICOLOGY: POSITIVE-MDS MDMA UR QL; URINE NPTST536-URINALYSIS: NEGATIVE-UR WBC AUTO RESULT 28/HPE. UR RBC AUTO RESULT 15/HPE
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

Event #4: 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	20 / 167
Age at AE Onset	3
Laboratory Testing	20 (RX DAY -10): Chloride: 104 [102 - 112] MMOL/L; 20 (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; NPTST029-ANION GAP: 10.0 [3 - 11] MMOL/L; NPTST080-BUN/CREA RATIO: 15 [7 - 25] MG/DL; NPTST093-CA CORRECTED: 9.2 [8.7 - 10.7] MG/DL; NPTST197-EGFR AFRICAN AMERICAN: > 60 [60 - 60] UNIT NOT REPORTED; NPTST198-EGFR NON AFRICAN: >60 [60 - 60] UNIT NOT REPORTED; NPTST251-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	20 (RX DAY 113): OTHER TOXICOLOGY NPTST513-TOXICOLOGY: POSITIVE-MDS MDMA UR QL; URINE NPTST536-URINALYSIS: NEGATIVE-UR WBC AUTO RESULT 28/HPE. UR RBC AUTO RESULT 15/HPE
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: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 3 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, 2, 3 及び 4 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 (20 - 20)

Causality for UPADACITINIB (Blinded)

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

20 ALBUMIN: 4.5 G/DL (normal 3.0 to 4.5)

20 ALBUMIN GLOBULIN RATIO: 1.5 G/DL (normal 1.0 to 2.0)

20 ALKALINE PHOSPHATASE: 59 U/L (normal 37 to 47)

20	ALT: 11 U/L (normal 5 to 55)
20	ANION GAP: 10 MMOL/L (normal 3.0 to 11.0)
20	AST: 14 U/L (normal 8 to 42)
20	BILIRUBIN: 0.2 mg/dL (normal 0.3 to 1.2)
20	BLOOD UREA NITROGEN: 13 mg/dL (normal 5 to 25)
20	BUN CREATININE RATIO: 15 mg/dL (normal 7 to 25)
20	CA CORRECTED: 9.2 mg/dL (normal 8.7 to 10.7)
20	CALCIUM: 9.6 mg/dL (normal 8.7 to 10.7)
20	CHLORIDE: 104 MMOL/L (normal 102 to 112)
20	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
20	CREATININE: 0.87 mg/dL (normal 0.30 to 1.40)
20	EGFR (AFRICAN AMERICAN): > 60
20	EGFR (NON AFRICAN AMERICAN): 60
20	GLOBULIN: 3.1 G/DL (normal 2.2 to 4.0)
20	GLUCOSE: 104 mg/dL (normal 70 to 110)
20	POTASSIUM: 3.5 MMOL/L (normal 3.5 to 5.3)
20	SODIUM: 138 MMOL/L (normal 135 to 143)
20	PROTEIN: 7.6 G/DL (normal 6.0 to 8.0)
20	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"
20	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	21	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
ASTHMA	19[REDACTED]
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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 20[REDACTED] / 1	[REDACTED] 20[REDACTED] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	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██-██
ADALIMUMAB	80.000 mg	EVERY 2 WEEKS	Y-M: 20██-██ / -252
METRONIDAZOLE	500 mg	TID	Y-M: 20██-██ / -107
MACROGOL 3350	0.5 g	PRN	Y-M: 20██-██ / -39
BISACODYL	5 mg	OTHER: BID PRN	Y-M: 20██-██ / -43
SALBUTAMOL	2 OTHER: PUFF	PRN	Y: 19██
CETIRIZINE	10 mg	QD	Y: 20██ / -204
PREDNISONE	20 mg	QD	Y: 20██ / -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 / Stop Year-Month / RX Day	RX Day
ETONOGESTREL	68 mg	OTHER: Q 3 YEARS	Y-M: 20██-██	ONGOING
MACROGOL 3350	0.5 g	PRN	Y-M: 20██-██ / -39	ONGOING
BISACODYL	5 mg	OTHER: BID PRN	Y-M: 20██-██ / -43	ONGOING
LOPERAMIDE	2 mg	OTHER: QD PRN	Y-M: 20██-██ / 52	ONGOING
AZITHROMYCIN	250 mg	QD	Y-M: 20██-██ / 121	Y-M: 20██-██ / 126
FLUTICASONE;SALMETEROL	1 OTHER: PUFF	BID	Y-M: 20██-██ / 134	Y-M: 20██-██ / 192
LEVOFLOXACIN	500 mg	QD	Y-M: 20██-██ / 134	Y-M: 20██-██ / 141
PREDNISONE	40 mg	QD	Y-M: 20██-██ / 134	Y-M: 20██-██ / 135
SALBUTAMOL	2 OTHER: PUFF	PRN	Y: 19██	ONGOING
CETIRIZINE	10 mg	QD	Y: 20██ / -204	Y-M: 20██-██ / 131
PREDNISONE	20 mg	QD	Y: 20██ / -204	Y-M: 20██-██ / 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	███20██ / 186
Age at AE Onset	2█

Laboratory Testing

20 (RX DAY 131): Albumin: 27 [34 - 50] G/L; Alkaline Phosphatase: 79 [45 - 117] U/L; Basophils: 0.04 [0 - 0.1] 10⁹/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] 10⁹/L; Eosinophils/Leukocytes: 5.7 [1 - 4] %; Erythrocytes: 4.3 [3.7 - 5.17] 10¹²/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] 10⁹/L; Lymphocytes: 1.6 [1.1 - 3.8] 10⁹/L; Lymphocytes/Leukocytes: 17.9 [20 - 44] %; Monocytes: 0.95 [0.3 - 0.9] 10⁹/L; Monocytes/Leukocytes: 10.6 [2 - 9] %; NPTST019-ALT/SGPT: 15 [13 - 56] U/L; NPTST048-AST/SGOT: 12 [15 - 37] U/L; NPTST143-CO2: 29.0 [21 - 32] MMOL/L; NPTST330-MAGNESIUM: 2.0 [1.6 - 2.6] MG/DL; NPTST331-MCH: 25.1 [24.3 - 33.2] PG; NPTST332-MCHC: 32.0 [31.9 - 35.1] G/DL; NPTST334-MCV: 78.4 [75.6 - 97.8] FL; NPTST352-MPV: 10.9 [7 - 10.7] FL; NPTST440-RDW CV: 15.6 [12.1 - 16.8] %; NPTST540-URINE CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 5.83 [1.7 - 8] 10⁹/L; Neutrophils/Leukocytes: 65.2 [50 - 70] %; Platelets: 349 [156 - 380] 10⁹/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

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: 20 :11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 2 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cetirizine であった。

The patient's past medications include:

ADALIMUMAB for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

AZITHROMYCIN for BRONCHITIS (■■■■ 20■■ - ■■■■ 20■■)

Causality for UPADACITINIB (Blinded)

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

20	ALBUMIN: 2.7 G/DL (normal 3.4 to 5.0)
20	ALKALINE PHOSPHATASE: 79 U/L (normal 45 to 117)
20	ALT/SGPT: 15 U/L (normal 13 to 56)
20	AST/SGOT: 12 U/L (normal 15 to 37)
20	BILIRUBIN: 0.2 mg/dL (normal 0.0 to 1.0)
20	BLOOD UREA NITROGEN: 6 mg/dL (normal 7 to 18)
20	CHEST CT: Negative
20	CHEST X-RAY: Negative
20	CO2: 29.0 MMOL/L (normal 21.0 to 32.0)
20	HEMATOCRIT: 33.7 % (normal 30.4 to 44.6)
20	HEMOGLOBIN: 10.8 G/DL (normal 11.0 to 15.1)
20	LYMPHOCYTES %: 17.9 %
20	NEUTROPHILS %: 65.2 %
20	NEUTROPHILS ABS: 5.83 X10**3/MCL (normal 1.70 to 8.00)
20	PLATELET COUNT: 349 X10**3/MCL (normal 156 to 380)
20	URINE CULTURE: Negative
20	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	51	MALE	WHITE

Medical History	Onset Year
ASTHMA	19[REDACTED]
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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	ORAL	QD	20 / 1	20 / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20 / 1	20 / 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 / -
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20 / -
ENOXAPARIN	80 mg	BID	Y-M: 20 / -
PENTOXIFYLLINE	400 mg	TID	Y-M: 20 / -
AZATHIOPRINE	50 mg	BID	Y-M: 20 / -159
AZATHIOPRINE	50 mg	BID	Y: 19
BUDESONIDE;FORMOTEROL	160.45 uL	PRN	Y: 20
SALBUTAMOL	1-2 OTHER: PUFFS	PRN	Y: 20
PREDNISONE	40 mg	QD	Y: 20
APIXABAN	2.5 mg	QD	Y: 20
OMEPRAZOLE	40 mg	QD	Y: 20
MESALAZINE	.375 mg	QD	Y: 20

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
FOLIC ACID	5 mg	QD	Y-M: 19 / -	ONGOING
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20 / -	ONGOING
ENOXAPARIN	80 mg	BID	Y-M: 20 / -	ONGOING
PENTOXIFYLLINE	400 mg	TID	Y-M: 20 / -	ONGOING
CLINDAMYCIN	300 mg	BID	Y-M: 20 / 263	Y-M: 20 / 271
SULFAMETHOXAZOLE;TRIMETHOPRIM	800 mg	QD	Y-M: 20 / 282	Y-M: 20 / 285

VANCOMYCIN	500 mg	BID	Y-M: 20██-██ / 282	Y-M: 20██-██ / 285
BUDESONIDE;FORMOTEROL	160.45 uL	PRN	Y: 20██	ONGOING
SALBUTAMOL	1-2 OTHER: PUFFS	PRN	Y: 20██	ONGOING
APIXABAN	2.5 mg	QD	Y: 20██	ONGOING
OMEPRAZOLE	40 mg	QD	Y: 20██	ONGOING
MESALAZINE	.375 mg	QD	Y: 20██	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	███20██ / 275
Age at AE Onset	5█
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
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	███20██ / 318
Age at AE Onset	5█
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
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]:11:02

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■■ - ■■■■ 20■■, ■■■■ 20■■ - ■■■■ 20■■)

PREDNISON for ULCERATIVE COLITIS (20■■ - 20■■)

BACITRACIN for UNKNOWN INDICATION

PENICILLIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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

20 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	71	MALE	WHITE

Medical History	Onset Year
A. FIB	2011
ASTHMA	2011
ATRIAL FIBRILLATION	2011
BENIGN COLON POLYPS	2011
CHICKEN POX	1991
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	2011
CORONARY ARTERY DISEASE	2011
DEGENERATIVE DISC DISEASE	2011
DIVERTICULOSIS	2011
EXTENSIVE UC/PANCOLITIS	2011
HEART FAILURE	2011
HIGH CHOLESTEROL	2011
HYPERCHOLESTEROLEMIA	2011
HYPERTENSION	2011
OBESITY	1991
SLEEP APNEA	2011
TRIPLE BYPASS	2011

Prior Procedures	Procedure Year
PRIOR PROCEDURES: KYPHOPLASTY	1991
PRIOR PROCEDURES: QUADRICEP TENDON REPAIR	2011
PRIOR PROCEDURES: TRIPLE BYPASS	2011
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	2011

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	30	20██
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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	███20██ / 1	███20██ / 56	56
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	███20██ / 57	███20██ / 113	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	███20██ / 1	███20██ / 354	354

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██-██ / -211
METOPROLOL	12.5 mg	QD	Y-M: 20██-██ / -120
RIVAROXABAN	20 mg	QD	Y-M: 20██-██ / -107
PREDNISONE	10 mg	QD	Y-M: 20██-██ / -24
PREDNISONE	20 mg	QD	Y-M: 20██-██ / -27
OXYGEN	2 L	PRN	Y-M: 20██-██ / -34
ACETYLSALICYLIC ACID	81 mg	QD	Y: 20██
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y: 20██
ATORVASTATIN	40 mg	QD	Y: 20██
FUROSEMIDE	40 mg	QD	Y: 20██
IPRATROPIUM;SALBUTAMOL	0.5/2.5 mg	PRN	Y: 20██

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██-██ / -120	Y-M: 20██-██ / 43	

RIVAROXABAN	20 mg	QD	Y-M: 20██ / -107	ONGOING
PREDNISONE	10 mg	QD	Y-M: 20██ / -24	Y-M: 20██ / 42
PREDNISONE	20 mg	QD	Y-M: 20██ / -27	ONGOING
OXYGEN	2 L	PRN	Y-M: 20██ / -34	Y-M: 20██ / 41
OXYGEN	2 L	OTHER: CONTINUOUS	Y-M: 20██ / 42	Y-M: 20██ / 45
ENOXAPARIN	40 mg	QD	Y-M: 20██ / 43	Y-M: 20██ / 45
FAMOTIDINE	40 mg	QD	Y-M: 20██ / 43	Y-M: 20██ / 45
FUROSEMIDE	40 mg	QD	Y-M: 20██ / 43	Y-M: 20██ / 45
GUAIFENESIN	1200 mg	BID	Y-M: 20██ / 43	Y-M: 20██ / 45
LACTOBACILLUS ACIDOPHILUS	1 OTHER: CAP	QD	Y-M: 20██ / 43	Y-M: 20██ / 45
LEVOFLOXACIN	750 mg	OTHER: ONCE	Y-M: 20██ / 43	Y-M: 20██ / 43
METHYLPREDNISOLONE	40 mg	BID	Y-M: 20██ / 43	Y-M: 20██ / 45
METOPROLOL	25 mg	QD	Y-M: 20██ / 43	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: 20██ / 43	Y-M: 20██ / 44
PAROXETINE	40 mg	QD	Y-M: 20██ / 43	Y-M: 20██ / 45
PIPERACILLIN;TAZOBACTAM	3.375 g	QD	Y-M: 20██ / 43	Y-M: 20██ / 43
ACETYLSALICYLIC ACID	81 mg	QD	Y: 20██	ONGOING
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y: 20██	ONGOING
ATORVASTATIN	40 mg	QD	Y: 20██	ONGOING
FUROSEMIDE	40 mg	QD	Y: 20██	ONGOING
IPRATROPIUM;SALBUTAMOL	0.5/2.5 mg	PRN	Y: 20██	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	███20██ / 155
Age at AE Onset	7█
Laboratory Testing	███20██ (RX DAY 43): NPTST078-BNP: 150 [0 - 100] PG; NPTST522-TROPONIN I: <0.0010 [0 - 0.033] NG/ML
Microbiology	███20██ (RX DAY 42): BLOOD NPTST075-BLOOD CULTURE: NEGATIVE-NO GROWTH AFTER 5 DAYS
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: 2011:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 71 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、被験者はうつ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)

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

20 ■■■ **BLOOD CULTURE:** Negative (No growth after 5 days)

20 ■■■ **BNP:** 150 PG (normal 0 to 100)

20 ■■■ **CHEST X-RAY:** Abnormal: COPD and cardiomegaly NCS

20 ■■■ **CHEST X-RAY:** Negative

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

20 ■■■ **WEIGHT:** 16 ■■■ 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			
うつ血性心不全				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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 57	57
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20 / 1	20 / 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: 20 / -
SILDENAFIL	50 mg	PRN	Y-M: 20 / -
MESALAZINE	800 mg	QD	Y-M: 20 / -
PREDNISONE	5 mg	QD	Y-M: 20 / -
ATENOLOL	100 mg	BID	Y-M: 20 / -207
LISINOPRIL	20 mg	BID	Y-M: 20 / -207
CLONIDINE	5 mg	QD	Y-M: 20 / -214
MIRIKIZUMAB	300.000 mg	MONTHLY	Y-M: 20 / -167
WARFARIN	2.5 mg	QD	Y-M: 20 / -85
ACETYLSALICYLIC ACID	81 mg	QD	Y: 20
AMLODIPINE	10 mg	QD	Y: 20
OMEPRAZOLE	40 mg	QD	Y: 20

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
SILDENAFIL	50 mg	PRN	Y-M: 20 / -	ONGOING
PREDNISONE	5 mg	QD	Y-M: 20 / -	Y-M: 20 / 18
ATENOLOL	100 mg	BID	Y-M: 20 / -207	ONGOING
LISINOPRIL	20 mg	BID	Y-M: 20 / -207	ONGOING
CLONIDINE	5 mg	QD	Y-M: 20 / -214	ONGOING
WARFARIN	2.5 mg	QD	Y-M: 20 / -85	Y-M: 20 / 14
AZITHROMYCIN	250 mg	OTHER: ONCE	Y-M: 20 / 10	Y-M: 20 / 10
IPRATROPIUM	0.5 mg	TID	Y-M: 20 / 10	Y-M: 20 / 34
PANTOPRAZOLE	40 mg	QD	Y-M: 20 / 10	Y-M: 20 / 14

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

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

Event #1: Event of Interest - Adjudicated Other Cardiovascular event

Event Description	ACUTE CONGESTIVE HEART FAILURE
Preferred term	うつ血性心不全
AE Onset Date / Initial Rx Day	██ 20██ / 66
Age at AE Onset	6█
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
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	20 / 66
Age at AE Onset	6
Laboratory Testing	20 (RX DAY 9): Bicarbonate: 22 [21 - 28] MMOL/L; Leukocytes: 8.2 [4.5 - 11] 10 ⁹ /L; NPTST078-BNP: 400 [0 - 100] PG; NPTST307-INR: 3.7 [0.8 - 1.2] RATIO; NPTST426-PROTIME: 36.1 [9 - 11.8] SEC; Sodium: 125 [136 - 145] MMOL/L; pH: 7.489 [7.35 - 7.45] UNIT NOT REPORTED; 20 (RX DAY 10): Platelets: 105 [150 - 500] 10 ⁹ /L; 20 (RX DAY 16): NPTST283-HISTOPLASMA ANTIBODY TEST: POSITIVE AB [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED
Microbiology	20 (RX DAY 9): BLOOD NPTST075-BLOOD CULTURE: NEGATIVE-NO GROWTH AFTER 5 DAYS; 20 (RX DAY 16): OTHER LUNG TISSUE NPTST027-ANAEROBIC CULTURE: NEGATIVE-NO ANAEROBIC ORGANISMS ISOLATED; OTHER LUNG TISSUE NPTST171-CULTURE AFB W SMEAR: NEGATIVE-NO GROWTH, NO FUNGAL ELEMENTS; OTHER BODY FLUID OF LUNGS NPTST172-CULTURE LOWER RESPIRATORY: NEGATIVE-BILATERAL WASHING LUNGS- NORMAL FLORA; 20 (RX DAY 28): SPUTUM NPTST478-SMEAR GRAM STAIN: NEGATIVE-< 10 EPITHELIAL CELLS BARTLETT SCORE= 1-2
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	20 / 74 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6
Laboratory Testing	20 (RX DAY 17): NPTST158-CORTISOL: 5.78 [4.3 - 22.4] UG/DL; 20 (RX DAY 25): NPTST078-BNP: 1324 [0 - 100] PG/ML
Microbiology	NOT REPORTED
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	20 / 78 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6
Laboratory Testing	NOT APPLICABLE
Microbiology	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	20 / 79 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6
Laboratory Testing	20 (RX DAY 15): NPTST042-APTT: 44 [23 - 31] SEC; 20 (RX DAY 16): NPTST307-INR: 1.2 [0.8 - 1.2] RATIO; NPTST428-PT: 11.9 [9 - 11.8] SEC; 20 (RX DAY 17): NPTST042-APTT: 137 [23 - 31] SEC; 20 (RX DAY 20): NPTST042-APTT: 29 [23 - 31] SEC; 20 (RX DAY 22): NPTST307-INR: 3.4 [0.8 - 1.2] RATIO; NPTST428-PT: 33.8 [9 - 11.8] SEC; 20 (RX DAY 36): NPTST307-INR: 1.3 [2.5 - 3.5] RATIO; NPTST426-PROTIME: 13.5 [11 - 13.5] SEC
Microbiology	

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	UNCONTROLLED A. FIFTH 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: 2011:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6 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 年 月 日から 20 年 月 日まで盲検化された治験薬を投与された。20 年 月 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の腫瘍を認めた。腫瘍の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 (■■■■ 20■■ - ■■■■ 20■■)

MIRIKISUMAB for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

Causality for ABT-494 (Blinded)

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)

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

- 2012 LEAD EKG: Abnormal - findings of A. fib
- 2013 ANAEROBIC CULTURE: Negative, no anaerobic organisms isolated.
- 2014 AV NODE ABLATION: TOTAL rf TIME 529 seconds total number of RF applications 10. set lower rate to 80bpm
- 2015 BLOOD BICARB: 22 MMOL/L (normal 21 to 28)
- 2016 BLOOD CULTURE: Negative, no growth after 5 days.
- 2017 BNP: 400 PG (normal 0 to 100) 2018 BNP: 1324 pg/ml (normal 0 to 100)
- 2019 BODY TEMPERATURE: 102 degrees F
- 2020 BODY TEMPERATURE: 101 degrees F
- 2021 BRONCHOSCOPY: Negative for malignancy and histoplasmosis
- 2022 CHEST X-RAY: Acute congestive heart failure.
- 2023 CHEST X-RAY: S/P RLL LUNG Bx. No Pneumothorax.
- 2024 CHEST X-RAY: WORSENING INTERSTITIAL OPACITIES & CONSOLIDATED CHANGES IN THE RLL, POSSIBLE PULMONARY EDEMA
- 2025 CORTISOL: 5.78 ug/dl (normal 4.3 to 22.40)
- 2026 CT: ground glass opacities seen bilaterally to upper lobes - possible ARDS, sarcoidosis
- 2027 CT CHEST ANGIOGRAPHY: APICAL PULMONARY FIBROTIC 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.
- 2028 CT GUIDED RIGHT LOWER LOBE LUNG BIOPSY: Unspecified interstitial pneumonitis.
- 2029 CT OF CHEST WITHOUT CONTRAST: SIGNIFICANT IMPROVEMENT OF BILATERAL INFILTRATES, BILATERAL PLUERAL EFFUSIONS AND COMPRESSIVE ATELECTASIS SEEN GREATER IN THE LEFT .

20 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.

20 CULTURE AFB W SMEAR: Negative, no growth, no fungal elements.

20 CULTURE LOWER RESPIRATORY: Negative, bilateral washing lungs-normal flora.

20 EKG: Abnormal- findings of A. fib

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

20 INR: 3.7 ratio (normal 0.8 to 1.2)

20 INR: 2.0 ratio (normal 0.8 to 1.2)

20 INR: 1.3 ratio (normal 2.5 to 3.5)

20 PH: 7.489 no unit (normal 7.35 to 7.45)

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

20 PROTIME: 36.1 SEC (normal 9.0 to 11.8)

20 PROTIME: 13.5 sec (normal 11.0 to 13.5)

20 RIGHT UPPER QUADRANT ABDOMINAL ULTRASOUND: Negative findings.

20 SODIUM: 125 MMOL/L (normal 136 to 145)

20 SPO2: 86% on Room air at rest

20 SPO2: 86% on Room air with ambulation

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

20 TRANSTHORACIC ECHOCARDIOGRAM: left ventricle 50-55% EF with left atrium enlargement

20 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
貧血	X			X
末梢動脈閉塞性疾患				X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	5 [REDACTED]	MALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20 [REDACTED]
CORONARY ARTERY DISEASE	20 [REDACTED]
EXTENSIVE UC/PANCOLITIS	20 [REDACTED]
HIGH CHOLESTEROL	20 [REDACTED]
HYPERTENSION	20 [REDACTED]
HYPOKALEMIA	20 [REDACTED]
IRON DEFICIENCY ANEMIA	20 [REDACTED]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: CORONARY ARTERY BYPASS GRAFTING	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 64	64
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	20 / 1	20 / 378	378

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VEDOLIZUMAB	300.000 mg	ONCE EVERY 8 WEEKS	Y-M: 20 /
GLYCERYL TRINITRATE	0.4 mg	PRN	Y-M: 20 /
IPRATROPIUM;SALBUTA MOL	20/100 OTHER: MCG	PRN	Y-M: 20 /
ACETYLSALICYLIC ACID	325 mg	QD	Y-M: 20 /
FUROSEMIDE	40 mg	QD	Y-M: 20 /
MESALAZINE	4.8 g	QD	Y-M: 20 /
INFLIXIMAB	5.000 mg/kg	ONCE EVERY 8 WEEKS	Y-M: 20 /
RISANKIZUMAB	1800.000 mg	ONCE EVERY 4 WEEKS	Y-M: 20 / -351
PREDNISONE	40 mg	QD	Y: 20
ATORVASTATIN	40 mg	QD	Y: 20
CARVEDILOL	3.125 mg	QD	Y: 20
POTASSIUM	10 mEq	QD	Y: 20

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
GLYCERYL TRINITRATE	0.4 mg	PRN	Y-M: 20██-██	ONGOING
IPRATROPIUM;SALB UTAMOL	20/100 OTHER: MCG	PRN	Y-M: 20██-██	ONGOING
ACETYLSALICYLIC ACID	325 mg	QD	Y-M: 20██-██	Y-M: 20██-██ / 309
FUROSEMIDE	40 mg	QD	Y-M: 20██-██	ONGOING
MESALAZINE	4.8 g	QD	Y-M: 20██-██	Y-M: 20██-██ / 246
MESALAZINE	1.2 g	QD	Y-M: 20██-██ / 247	ONGOING
AMLODIPINE	5 mg	QD	Y-M: 20██-██ / 251	ONGOING
CARVEDILOL	6.25 mg	BID	Y-M: 20██-██ / 251	ONGOING
POTASSIUM	20 mEq	QD	Y-M: 20██-██ / 251	ONGOING
RED BLOOD CELLS	2 OTHER: UNITS	OTHER: ONCE	Y-M: 20██-██ / 258	Y-M: 20██-██ / 258
HYDROCODONE;PAR ACETAMOL	5/325 mg	PRN	Y-M: 20██-██ / 308	Y-M: 20██-██ / 310
RED BLOOD CELLS	2 OTHER: UNITS	OTHER: ONCE	Y-M: 20██-██ / 308	Y-M: 20██-██ / 309
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20██-██ / 309	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20██-██ / 309	ONGOING
BISACODYL	10 mg	BID	Y-M: 20██-██ / 364	Y-M: 20██-██ / 364
MACROGOL 3350	238 g	QD	Y-M: 20██-██ / 364	Y-M: 20██-██ / 364
PROPOFOL	UNK OTHER: UNK	OTHER: ONCE	Y-M: 20██-██ / 365	Y-M: 20██-██ / 365
ATORVASTATIN	40 mg	QD	Y: 20██	ONGOING
CARVEDILOL	3.125 mg	QD	Y: 20██	Y-M: 20██-██ / 250
POTASSIUM	10 mEq	QD	Y: 20██	Y-M: 20██-██ / 250

Event #1: Event of Interest - Anemia

Event Description	WORSENING ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	20 / 317
Age at AE Onset	6
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	322
Duration of AE	6 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 of Interest - Anemia

Event Description	WORSENING ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	20 / 372
Age at AE Onset	6
Laboratory Testing	
20 (RX DAY 307): Hemoglobin: 71 [116 - 156] G/L; 20 (RX DAY 309): Hemoglobin: 83 [116 - 156] G/L	

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day 373

Duration of AE 2 DAYS

Severity SEVERE

Relation to Study Drug by Investigator NO REASONABLE POSSIBILITY

Investigator Alternative Etiology PER DISCUSSION WITH PI, OTHER CAUSE IS LIKELY CHRONIC UC. SUBJECT'S LAST COLON IN [REDACTED] 20 [REDACTED] SHOWED ACTIVE UC. SUBJECT IS SCHEDULED TO BE EVALUATED [REDACTED] 20 [REDACTED].

Discontinued Study Drug Due to the Event NO

SAE Criteria HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Event of Interest - Adjudicated Arterial Thromboembolic Event

Event Description PERIPHRIAL ARTERIAL OCCLUSIVE DISEASE

Preferred term 末梢動脈閉塞性疾患

AE Onset Date / Initial Rx Day [REDACTED] 20 [REDACTED] / 372

Age at AE Onset 6 [REDACTED]

Laboratory Testing

NOT APPLICABLE

Microbiology

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]:11:02

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 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、貧血の悪化の事象を発現した。関連する病歴は、元喫煙者（1 日 1 箱を 25 年間）、潰瘍性大腸炎、コレステロール高値、高血圧、冠動脈バイパス移植、冠動脈閉塞、鉄欠乏性貧血及び非飲酒者であった。

Event 2 の臨床経過：

投与372日後＊，被験者は貧血の悪化を発現した。投与373日後＊，貧血の悪化は消失した。

本事象発現前、被験者は投与の約10ヵ月後＊に貧血の悪化（非重篤）及び投与の約12ヵ月後＊に末梢動脈閉塞性疾患（非重篤）を発現した。

投与372日後＊，被験者は右脚の血管インターベンションを受けた。被験者は血塊除去中にかなり失血し、更に経過観察を行うため入院となった。被験者は低ナトリウム食療法を受け、濃厚赤血球 2 単位を輸血された。投与373日後＊，被験者は状態が改善し、退院した。

治験責任医師によると、危険因子は潰瘍性大腸炎及び慢性貧血性疾患であった。

投与された薬剤は、プラビックス、赤血球、hydrocodone/APAP 及びアスピリンであった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS (20 - 20)

ENTYVIO for ULCERATIVE COLITIS (20 - 20)

REMICADE for ULCERATIVE COLITIS (20 - 20)

RISANKIZUMAB for ULCERATIVE COLITIS (20 - 20)

Causality for UPADACITINIB (Blinded)

1) Anemia aggravated (10054309) (Anaemia (10002034)) [v.24.0] [10054309]

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 ANEMIA

- **Investigator:** Per discussion with PI, other cause is likely chronic UC. subject's last colon in [REDACTED] 20 [REDACTED] showed active UC. Subject is scheduled to be evaluated [REDACTED] 20 [REDACTED]

- **AbbVie:** Event more likely related to losing "a fair amount of blood" during evacuation of peripheral clots in right leg as noted by PI. Additional risk factors include pre-existing ulcerative colitis and pre-existing iron deficiency anemia.

Relevant Laboratory & Other Diagnostic Tests

[REDACTED] 20 [REDACTED] **HEMOGLOBIN:** 8.3 G/DL (normal 11.6 to 15.6)

[REDACTED] 20 [REDACTED] **HEMOGLOBIN:** 7.1 G/DL (normal 11.6 to 15.6)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Anemia([REDACTED] 20 [REDACTED]): Study drug interrupted.

Peripheral arterial occlusive disease: Underlying reason is multi-factored, including history of high cholesterol, inflammation caused by UC, and a former history of smoking. Scheduled for a peripheral angiogram of the left leg, and admitted for a blood transfusion. Both the right and left common, external, and internal iliac arteries have mild disease. The right and left common femoral artery has mild disease. The right superficial femoral artery has total occlusion extending from the ostium to the adductor canal. The right profunda femoris and popliteal arteries has severe disease. The left superficial artery has severe disease. The left profunda femoris and popliteal has moderate to severe disease. Stud drug interrupted.

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 ARTHRALGIA	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██
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	19██
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	20██
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	20██
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	20██
PRIOR PROCEDURES: COLONOSCOPY WITH HOT BIOPSY OF POLYP	20██
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20██

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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	███-20██ / 1	███-20██ / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	███-20██ / 1	███-20██ / 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██-██
BALSALAZIDE	2250 mg	TID	Y-M: 20██-██
MESALAZINE	1000 mg	QD	Y-M: 20██-██
PREDNISONE	30 mg	QD	Y-M: 20██-██
MESALAZINE	1.2 g	QD	Y-M: 20██-██
BUDESONIDE	9 mg	QD	Y-M: 20██-██
METHYLPREDNISOLONE	8 mg	TID	Y-M: 20██-██
PREDNISONE	20 mg	QD	Y-M: 20██-██ / -121
TRAMADOL	50 mg	PRN	Y-M: 20██-██ / -121

DEXAMFETAMINE 10 mg TID Y: 19

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
BALSALAZIDE	2250 mg	TID	Y-M: 20 /	ONGOING
PREDNISON	20 mg	QD	Y-M: 20 / -121	Y-M: 20 / 28
TRAMADOL	50 mg	PRN	Y-M: 20 / -121	ONGOING
PREDNISON	15 mg	QD	Y-M: 20 / 29	Y-M: 20 / 36
PREDNISON	10 mg	QD	Y-M: 20 / 37	Y-M: 20 / 50
PREDNISON	7.5 mg	QD	Y-M: 20 / 51	Y-M: 20 / 57
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TAB	BID	Y-M: 20 / 55	Y-M: 20 / 62
PREDNISON	5.0 mg	QD	Y-M: 20 / 58	Y-M: 20 / 65
CEFALEXIN	500 mg	QD	Y-M: 20 / 62	Y-M: 20 / 72
CALCIUM ALGINATE	1 OTHER: APPLICATION	OTHER: WEEKLY	Y-M: 20 / 66	Y-M: 20 / 153
IODOFORM	1 OTHER: APPLICATION	OTHER: WEEKLY	Y-M: 20 / 66	Y-M: 20 / 139
PREDNISON	2.5 mg	QD	Y-M: 20 / 66	Y-M: 20 / 73
DEXAMFETAMINE	10 mg	TID	Y: 19	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	20 / 108
Age at AE Onset	6
Laboratory Testing	NOT REPORTED
Microbiology	20 (RX DAY 55): WOUND NPTST011-AEROBIC AND ANAEROBIC GRAM STAI: POSITIVE-RARE STAPH
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: 2011:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6 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 (20 - 20)

CANASA SUPPOSITORY for ULCERATIVE COLITIS (20 - 20)

LIALDA for ULCERATIVE COLITIS (20 - 20)

BUDESONIDE for ULCERATIVE COLITIS (20 - 20)

MEDROL DOSE PAK for ULCERATIVE COLITIS (20 - 20)

Causality for UPADACITINIB (Blinded)

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

20 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	71	MALE	WHITE

Medical History	Onset Year
ADRENAL INSUFFICIENCY	2001
ASBESTOSIS	2001
AZATHIOPINE INTOLERANCE	2001
BENIGN PROSTATIC HYPERTROPHY	2001
BILATERAL INGUINAL HERNIA	1998
BILATERAL PEDAL EDEMA	2001
BLURRED VISION	2001
CELLULITIS OF TOE	2001
CHRONIC ABDOMINAL PAIN	1998
CHRONIC ARTHRALGIA	2001
CHRONIC BACK PAIN	2001
CHRONIC DIARRHEA	1998
CHRONIC ECCHYMOSIS	2001
CHRONIC FATIGUE	2001
CHRONIC HAIR LOSS	2001
CHRONIC INDIGESTION	2001
CHRONIC INTERMITTENT ANEMIA	2001
CHRONIC INTERMITTENT APHTHOUS ULCERS	1998
CHRONIC INTERMITTENT CONSTIPATION	1998
CHRONIC NAUSEA	1998
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	2001
CHRONIC RIGHT LOWER EXTREMITY ERYTHEMA	2001
CHRONIC TACHYCARDIA	2001

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

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

Prior Procedures	Procedure Year
PRIOR PROCEDURES: BILATERAL INGUINAL HERNIA REPAIR	19
PRIOR PROCEDURES: BILATERAL LOWER EXTREMITY VENOUS DOPPLERS	20
PRIOR PROCEDURES: COLONOSCOPY	20
PRIOR PROCEDURES: COLONOSCOPY	20
PRIOR PROCEDURES: COLONOSCOPY	20
PRIOR PROCEDURES: COLONOSCOPY WITH ASPIRATE AND BIOPSIES	20
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSIES	20
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSY	20
PRIOR PROCEDURES: COLONOSCOPY WITH BIOPSY	20
PRIOR PROCEDURES: CT ANGIOGRAM OF THE CHEST	20
PRIOR PROCEDURES: CT SCAN OF THORAX	20
PRIOR PROCEDURES: CYSTOSCOPY	20
PRIOR PROCEDURES: CYSTOSCOPY WITH STENT PLACEMENT	20
PRIOR PROCEDURES: ESOPHAGEAL DILATATION	20
PRIOR PROCEDURES: ESOPHAGEAL DILATATION	20
PRIOR PROCEDURES: ESOPHAGODUODENOSCOPY WITH BIOPSY	20
PRIOR PROCEDURES: ESOPHAGODUODENOSCOPY WITH BIOPSY	20
PRIOR PROCEDURES: FINGER BIOPSY	20
PRIOR PROCEDURES: PERCUTANEOUS CORONARY INTERVENTION	20
PRIOR PROCEDURES: RIGHT KNEE ARTHROSCOPY	20
PRIOR PROCEDURES: RIGHT LOWER EXTREMITY VENOUS DOPPLER	20
PRIOR PROCEDURES: RIGHT TOTAL KNEE ARTHROPLASTY	20
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20

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

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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	20 / 1	20 / 57	57
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20 / 1	20 / 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 /
MESALAZINE	800 mg	QID	Y-M: 20 /
BUDESONIDE	9 mg	QD	Y-M: 20 /
BALSALAZIDE	2250 mg	TID	Y-M: 20 /
MESALAZINE	1000 mg	QD	Y-M: 20 /
AZATHIOPRINE	100 mg	QD	Y-M: 20 /
BUDESONIDE	9 mg	QD	Y-M: 20 /
MESALAZINE	2.4 g	QD	Y-M: 20 /
OMEPRazole	40 mg	QD	Y-M: 20 /
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20 /
MESALAZINE	800 mg	TID	Y-M: 20 /
MESALAZINE	2.4 g	QD	Y-M: 20 /
FENOFIBRATE	48 mg	QD	Y-M: 20 /
FOLIC ACID	1 mg	QD	Y-M: 20 /
MAGNESIUM OXIDE	400 mg	QD	Y-M: 20 /
METFORMIN	850 mg	TID	Y-M: 20 /
TAMSULOSIN	0.4 mg	QD	Y-M: 20 /
ERGOCALCIFEROL	1.25 mg	QD	Y-M: 20 /
PRAVASTATIN	80 mg	QD	Y-M: 20 /
FLUTICASONE;SALMETEROL	1 OTHER: PUFF	BID	Y-M: 20 /

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

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
OMEPRAZOLE	40 mg	QD	Y-M: 20■■■	Y-M: 20■■■ / 237
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20■■■	ONGOING
FENOFIBRATE	48 mg	QD	Y-M: 20■■■	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20■■■	ONGOING
MAGNESIUM OXIDE	400 mg	QD	Y-M: 20■■■	Y-M: 20■■■ / 34
METFORMIN	850 mg	TID	Y-M: 20■■■	ONGOING
TAMSULOSIN	0.4 mg	QD	Y-M: 20■■■	ONGOING
ERGOCALCIFEROL	1.25 mg	QD	Y-M: 20■■■	ONGOING
PRAVASTATIN	80 mg	QD	Y-M: 20■■■	ONGOING
FLUTICASONE;SALMETEROL	1 OTHER: PUFF	BID	Y-M: 20■■■	ONGOING
DIGOXIN	0.125 mg	QD	Y-M: 20■■■	ONGOING
GABAPENTIN	600 mg	BID	Y-M: 20■■■	ONGOING
BALSALAZIDE	2250 mg	TID	Y-M: 20■■■	ONGOING
NIFEDIPINE	30 mg	QD	Y-M: 20■■■	ONGOING
BUDESONIDE	9 mg	QD	Y-M: 20■■■	Y-M: 20■■■ / 95
PIOGLITAZONE	15 mg	QD	Y-M: 20■■■	ONGOING
LOSARTAN	100 mg	QD	Y-M: 20■■■ / -243	ONGOING
WARFARIN	5 mg	QD	Y-M: 20■■■ / 1	ONGOING
CEFTRIAZONE	1000 mg	QD	Y-M: 20■■■ / 35	Y-M: 20■■■ / 35
ENOXAPARIN	110 mg	QD	Y-M: 20■■■ / 35	Y-M: 20■■■ / 41
HYDROCODONE;PARACETAMOL	2 OTHER: TABS	PRN	Y-M: 20■■■ / 35	Y-M: 20■■■ / 95

INSULIN ASPART	2 OTHER: UNITS	PRN	Y-M: 20██ / 35	Y-M: 20██ / 41
PARACETAMOL	975 mg	PRN	Y-M: 20██ / 35	Y-M: 20██ / 41
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20██ / 35	Y-M: 20██ / 35
VANCOMYCIN	2000 mg	OTHER: ONCE	Y-M: 20██ / 35	Y-M: 20██ / 37
PIPERACILLIN;TAZOBACTAM	3.375 g	TID	Y-M: 20██ / 36	Y-M: 20██ / 37
CEFAZOLIN	2000 mg	OTHER: ONCE	Y-M: 20██ / 37	Y-M: 20██ / 37
HYDROMORPHONE	0.5 mg	PRN	Y-M: 20██ / 37	Y-M: 20██ / 41
CEFEPIME	2000 mg	TID	Y-M: 20██ / 38	Y-M: 20██ / 41
MORPHINE	4 mg	PRN	Y-M: 20██ / 38	Y-M: 20██ / 41
CEFEPIME	2000 mg	BID	Y-M: 20██ / 41	Y-M: 20██ / 78
POTASSIUM	20 mEq	OTHER: Q 4HRS	Y-M: 20██ / 45	Y-M: 20██ / 47
POTASSIUM	40 mEq	PRN	Y-M: 20██ / 45	Y-M: 20██ / 46
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20██ / 45	Y-M: 20██ / 45
PANTOPRAZOLE	40 mg	QD	Y-M: 20██ / 46	Y-M: 20██ / 48
POTASSIUM;SODIUM CHLORIDE	50 OTHER: ML/HR	OTHER: CONTINUOUS	Y-M: 20██ / 46	Y-M: 20██ / 49
POTASSIUM	20 mEq	BID	Y-M: 20██ / 47	ONGOING
MAGNESIUM OXIDE	400 mg	BID	Y-M: 20██ / 48	ONGOING
ALL OTHER NON-THERAPEUTIC PRODUCTS	30 %	OTHER: NIGHTLY	Y: 20██	ONGOING
METOPROLOL	100 mg	QD	Y: 20██	ONGOING
UMECLIDINIUM;VILANTEROL	1 OTHER: PUFF	QD	Y: 20██	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	███20██ / 91
Age at AE Onset	7█
Laboratory Testing	███20██ (RX DAY 35): Leukocytes: 10.9 [4 - 11] 10 ⁹ /L; NPTST084-C REACTIVE PROTEIN: 23.30 [0 - 0.9] MG/DL; ███20██ (RX DAY 41): NPTST268-HEMOGLOBIN A1C: 6.5 [0 - 6.5] UNIT NOT REPORTED
Microbiology	███20██ (RX DAY 36): OTHER JOINT FLUID NPTST255-GRAM STAIN AND CULTURE: POSITIVE-GRAM NEGATIVE RODS WITH 15-20 WBCS PER LPF; ███20██ (RX DAY 38): WOUND NPTST496-SURGICAL WOUND CULTURE W/ANAERO: POSITIVE-FEW SERRATIA MARCESCENS ISOLATED
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	20 / 91
Age at AE Onset	7
Laboratory Testing	20 (RX DAY 35): Leukocytes: 10.9 [4 - 11] 10 ⁹ /L; NPTST084-C REACTIVE PROTEIN: 23.30 [0 - 0.9] MG/DL; 20 (RX DAY 41): NPTST268-HEMOGLOBIN A1C: 6.5 [0 - 6.5] UNIT NOT REPORTED
Microbiology	20 (RX DAY 36): OTHER JOINT FLUID NPTST255-GRAM STAIN AND CULTURE: POSITIVE-GRAM NEGATIVE RODS WITH 15-20 WBCS PER LPF; 20 (RX DAY 38): WOUND NPTST496-SURGICAL WOUND CULTURE W/ANAERO: POSITIVE-FEW SERRATIA MARCESCENS ISOLATED
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	20 / 98
Age at AE Onset	7
Laboratory Testing	20 (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; NPTST126-CLOSTRIDIUM DIFFICILE ASSAY: NEGATIVE [NOT REPORTED -

NOT REPORTED] UNIT NOT REPORTED; NPTST248-GIARDIA BY EIA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST372-OCCULT BLOOD: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST376-OVA, CYSTS AND PARASITES: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 3.1 [3.5 - 5.1] MMOL/L; [REDACTED] 20 (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] 10⁹/L; NPTST330-MAGNESIUM: 1.8 [1.6 - 2.3] MG/DL; Potassium: 2.5 [3.5 - 5.1] MMOL/L; [REDACTED] 20 (RX DAY 47): Potassium: 2.8 [3.5 - 5.1] MMOL/L; [REDACTED] 20 (RX DAY 48): Potassium: 3.3 [3.5 - 5.1] MMOL/L; [REDACTED] 20 (RX DAY 49): NPTST330-MAGNESIUM: 1.2 [1.6 - 2.3] MG/DL; Potassium: 3.5 [3.5 - 5.1] MMOL/L

Microbiology

[REDACTED] 20 (RX DAY 45): STOOL NPTST491-STOOL CULTURE: POSITIVE-FECAL LEUKOCYTES PRESENT IN SMALL NUMBERS. NO ENTERIC PATHOGENS, RARE NORMAL FLORA

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 :11:02

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 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 **irrissept** 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 **irrissept** 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)

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

20 BODY TEMPERATURE: 103 Degrees F

20 CRP: 23.30 mg/dL (normal 0 to 0.90)

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

20 HBA1C: 6.5 % (normal 0 to 6.5)

20 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

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

20 WOUND CULTURE: Positive-FEW SERRATIA MARCESCENS ISOLATED

20 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.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 71 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、手動での排便を行った。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██ - ████ 20██)

PREDNISONE for ULCERATIVE COLITIS (████ 19██ - ████ 20██)

ASACOL for ULCERATIVE COLITIS (████ 20██ - ████ 20██, ████ 20██ - ████ 20██)

ENTOCORT for ULCERATIVE COLITIS (████ 20██ - ████ 20██, ████ 20██ - ████ 20██)

COLAZAL for ULCERATIVE COLITIS (████ 20██ - ████ 20██)

CANASA for ULCERATIVE COLITIS (████ 20██ - ████ 20██)

AZATHIOPRINE for ULCERATIVE COLITIS (████ 20██ - ████ 20██)

LIALDA for ULCERATIVE COLITIS (████ 20██ - ████ 20██, ████ 20██ - ████ 20██)

REMICADE for ULCERATIVE COLITIS (████ 20██ - ████ 20██)

ACETAMINOPHEN for RLE CELLULITIS (████ 20██ - ████ 20██)

INSULIN ASPART for DIABETES MELLITUS, TYPE 2 (████ 20██ - ████ 20██)

LOVENOX for DVT PROPHYLAXIS (████ 20██ - ████ 20██)

NORMAL SALINE for RLE CELLULITIS (████ 20██ - ████ 20██)

ROCEPHIN for RLE CELLULITIS (████ 20██ - ████ 20██)

VANCOMYCIN for RLE CELLULITIS (████ 20██ - ████ 20██)

ZOSYN for RLE CELLULITIS (████ 20██ - ████ 20██)

CEFAZOLIN for INFECTED RIGHT TOTAL ARTHROPLASTY (████ 20██ - ████ 20██)

DILAUDID for INFECTED TOTAL RIGHT KNEE ARTHROPLASTY (████ 20██ - ████ 20██)

MORPHINE for INFECTED RIGHT TOTAL KNEE ARTHROPLASTY (████ 20██ - ████ 20██)

Causality for UPADACITINIB (Blinded)

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 ulcerative colitis

Relevant Laboratory & Other Diagnostic Tests

20 ■ **ABDOMEN XRAY:** Continued distal colonic obstruction. Impaction resolved.

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

20 ■ **CLOSTRIDIUM DIFFICILE ASSAY:** Negative.

20 ■ **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.

20 ■ **GIARDIA BY EIA:** Negative.

20 ■ **HEMATOCRIT:** 36.0 % (normal 39.7 to 48.9)

20 ■ **HEMATOCRIT:** 29.9 % (normal 39.7 to 48.9)

20 ■ **HEMOGLOBIN:** 11.6 G/DL (normal 13.4 to 17.0)

20	HEMOGLOBIN: 9.9 G/DL (normal 13.4 to 17.0)
20	MAGNESIUM: 1.8 mg/dL (normal 1.6 to 2.3)
20	MAGNESIUM: 1.2 mg/dL (normal 1.6 to 2.3)
20	OCCULT BLOOD: Negative.
20	OVA, CYSTS AND PARASITES: Negative.
20	POTASSIUM: 3.1 MMOL/L (normal 3.5 to 5.1)
20	POTASSIUM: 2.5 MMOL/L (normal 3.5 to 5.1)
20	POTASSIUM: 2.8 MMOL/L (normal 3.5 to 5.1)
20	POTASSIUM: 3.3 MMOL/L (normal 3.5 to 5.1)
20	POTASSIUM: 3.5 MMOL/L (normal 3.5 to 5.1)
20	STOOL CULTURE: Positive; Fecal leukocytes present in small numbers. No enteric pathogens, rare normal flora.
20	WHITE BLOOD CELLS: 10.8 10 ³ /uL (normal 3.8 to 9.9)
20	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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20██ / 1	20██ / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	20██ / 1	20██ / 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██-██
MESALAZINE	1000 mg	QD	Y-M: 20██-██ / -256
MESALAZINE	1.2 g	QD	Y-M: 20██-██ / -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 / Stop Year-Month / RX Day
MESALAZINE	1.2 g	QD	Y-M: 20██-██ / -167 ONGOING
AZITHROMYCIN	1 OTHER: DOSE	OTHER: ONCE	Y-M: 20██-██ / 139 Y-M: 20██-██ / 169
CEFDINIR	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 148 Y-M: 20██-██ / 153
DOXYCYCLINE	100 mg	BID	Y-M: 20██-██ / 151 Y-M: 20██-██ / 155
BUMETANIDE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 155 ONGOING
CEFTRIAZONE	2 g	QD	Y-M: 20██-██ / 155 ONGOING
CHLORHEXIDINE	15 mL	BID	Y-M: 20██-██ / 155 ONGOING
CISATRACURIUM	0.5-10 OTHER: MCG/KG/MIN	OTHER: CONTINUOUS	Y-M: 20██-██ / 155 ONGOING
DOCUSATE;SENNA ALEXANDRINA	1 OTHER: TABLET	BID	Y-M: 20██-██ / 155 ONGOING
FAMOTIDINE	20 mg	BID	Y-M: 20██-██ / 155 ONGOING
HYDROXYCHLOROQUINE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20██-██ / 155 ONGOING
NOREPINEPHRINE	2-35 OTHER: MCG/MIN	OTHER: CONTINUOUS	Y-M: 20██-██ / 155 ONGOING
PARAFFIN	1 OTHER: APPLICATION	PRN	Y-M: 20██-██ / 155 ONGOING
PROPOFOL	5-100 OTHER: MCG/KG/MIN	OTHER: CONTINUOUS	Y-M: 20██-██ / 155 ONGOING

SODIUM CHLORIDE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20■■■■ / 155	ONGOING
APIXABAN	5 mg	BID	Y-M: 20■■■■ / 185	ONGOING
LEVOSALBUTAMOL	90 ug	OTHER: Q4H PRN	Y-M: 20■■■■ / 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	■■■■20■■ / 211 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6■
Laboratory Testing	■■■■20■■ (RX DAY 151): NPTST160-COVID-19: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; ■■■■20■■ (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; ■■■■20■■ (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] %; NPTST063-BASE EXC ART: 3.0 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST262-HCO3 ART: 28.0 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST330-MAGNESIUM: 2.5 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST370-O2 SAT ART: >99.0 [NOT REPORTED - NOT REPORTED] %; NPTST391-PCO2: 43 [NOT REPORTED - NOT REPORTED] mmHg; NPTST399-PH ART: 7.42 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST406-PHOSPHORUS: 3.9 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST410-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; ■■■■20■■ (RX DAY 185): Chloride: 103 [98 - 107] MMOL/L; Creatinine: 70.722608 [71 - 115] UMOL/L; NPTST145-CO2 TOTAL: 28 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST533-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	■■■■20■■ (RX DAY 151): BLOOD NPTST076-BLOOD CULTURES, 2 SETS: NEGATIVE-NO GROWTH TO DATE; ■■■■20■■ (RX DAY 156): SPUTUM NPTST482-SPUTUM GS: NEGATIVE-MODERATE WBC, NO ORGANISMS
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	20 / 233 (27 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
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: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6 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。被験者は COVID-19（非重篤）と診断され，この時点で治験薬は休薬された。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 (■■■■ 20■■ - ■■■■ 20■■)

Causality for UPADACITINIB (Blinded)

1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.24.0] [10084380]

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 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

20 ■ **ALANINE AMINO TRANSFERASE:** 50 U/L

20 ■ **ALKALINE PHOSPHATASE:** 99 U/L

20 ■ **ARTERIAL BASE EXCESS:** 3 MMOL/L

20 ■ **ARTERIAL O2 SATURATION:** 99 %

20 ■ **ARTERIAL PH:** 7.42 no units

20 ■ **ASPARTATE AMINO TRANSFERASE:** 89 U/L

20 ■ **BILATERAL VENOUS ULTRASOUND UPPER EXTREMITY:** EXAM POSITIVE FOR RIGHT UPPER EXTREMITY DEEP AND SUPERFICIAL VENOUS THROMBOSIS. THROMBOSIS DETECTED WITHIN THE RIGHT AXILLARY VEIN, RIGHT BASILIC VEIN, AND RIGHT CEPHALIC VEIN. NEGATIVE FOR LEFT UPPER EXTREMITY VENOUS THROMBOSIS.

20 ■ **BILIRUBIN:** 0.7 U/L

20 ■ **BLOOD CULTURES:** No growth to date

20 ■ **BMI:** 27.52096 kg/m2

20 ■ **BMI:** 23.9 kg/m2

20 ■ **BODY TEMPERATURE:** 101-102 F

20 ■ **CHEST XRAY:** Interstitial opacities and bronchitis.

20 ■ **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.

20 CHLORIDE: 103 no units

20 CO2: 28 no units

20 COVID 19 TEST: tested positive

20 COVID-19 NASOPHARYNGEAL SWAB: Positive

20 CREATININE: 1 mg/dL

20 CREATININE: 0.8 no units

20 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

20 ECHO 2D: ABNORMAL ECHOCARDIOGRAM STUDY. THE LEFT VENTRICULAR EJECTION FRACTION IS 60-65% BY VISUAL ESTIMATION. THE LEFT VENTRICULAR WALL MOTION IS NORMAL. THERE IS STE 1 IMPAIRED DIASTOLIC FILLING PATTERN. THERE IS NO PERICARDIAL EFFUSION.

20 GLUCOSE: 125 mg/dL

20 HCO3: 28 MMOL/L

20 HEMATOCRIT: 36.6 %

20 HEMOGLOBIN: 12.0 G/DL

20 INFLUENZA TEST: Negative

20 LYMPHOCYTES %: 6.2 %

20 NEUTROPHILS %: 90.4 %

20 PCO2: 43 mmHg

20 PLATELET COUNT: 351 X10**3/MCL

20 PO2: 180 mmHg

20 POTASSIUM: 3.6 MMOL/L

20 POTASSIUM: 3.7 no units

20 SODIUM: 133 MMOL/L

20 SODIUM: 134 no units

20 SPUTUM GS: Moderate WBC, no organisms

20 UREA NITROGEN: 12 no units

20 VASCULAR 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.

20 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.

20 WEIGHT (WEEK 12): 18 Pounds

20 WHITE BLOOD CELLS: 7.9 X10**3/MCL

20 WHITE BLOOD CELLS: 8.8 X10**3/MCL

20 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.

20 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

20 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.

20 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.

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

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Deep Vein thrombosis: Vein involved is Right axillary Vein of Upper limb. Risk factors include age >40years, Inflammatory Bowel disease, Congestive heart failure, Prolonged immobilization (i e., prolonged bed rest, lower extremity surgery/casting etc.), Recent surgical procedure or hospitalization. Confirmed by imaging (Echocardiogram).

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
血中クレアチンホスホキナーゼ増加				X
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	51	MALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
DEPRESSION	2011
DVT	2011
ELEVATED C- REACTIVE PROTEIN	2011
GASTROESOPHAGEAL REFLUX DISEASE	2011
HISTORY OF DRUG ABUSE (COCAINE)	2011
HYPERTENSION	2011
LEFT SIDED UC	2011
REVISE MEDIAN N/CARPAL TUNNEL	2011
RIGHT HIP PAIN	2011
SUICIDE ATTEMPT	2011

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	2011
PRIOR PROCEDURES: BUNIONECTOMY	2011
PRIOR PROCEDURES: COLONOSCOPY	2011
PRIOR PROCEDURES: INCISION OF WRIST CAPSULE	2011
PRIOR PROCEDURES: TONSILLECTOMY	1999
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	2011

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	20	2011
CIGARS	NEVER			

E-CIGARETTES	FORMER	12 SESSIONS	1	20
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 61	61
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	20 / 1	20 / 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: 20 /
MESALAZINE	1.2 g	QD	Y-M: 20 /
PREDNISONE	60 mg	QD	Y-M: 20 /
PREDNISONE	60 mg	QD	Y-M: 20 /
MESALAZINE	4.8 g	QD	Y-M: 20 /
VITAMINS NOS	1 OTHER: TAB	QD	Y: 20

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
PARACETAMOL	500 mg	PRN	Y-M: 20 /	ONGOING
MESALAZINE	4.8 g	QD	Y-M: 20 /	ONGOING
HYDROCHLOROTHIAZIDE; LISINAPRIL	20-12.5 mg	QD	Y-M: 20 / 62	ONGOING
HYDROMORPHONE	1 mg	OTHER: 1 TIME	Y-M: 20 / 268	Y-M: 20 / 268
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20 / 268	Y-M: 20 / 270
PREDNISONE	40 mg	QD	Y-M: 20 / 268	Y-M: 20 / 274
VANCOMYCIN	125 mg	QID	Y-M: 20 / 268	Y-M: 20 / 278
LACTOBACILLUS ACIDOPHILUS 2 OTHER: CAPSULES		QD	Y-M: 20 / 271	ONGOING
PREDNISONE	30 mg	QD	Y-M: 20 / 275	Y-M: 20 / 281
PREDNISONE	20 mg	QD	Y-M: 20 / 282	Y-M: 20 / 288
PREDNISONE	10 mg	QD	Y-M: 20 / 289	Y-M: 20 / 295

BISACODYL	5 mg	OTHER: 1 TIME	Y-M: 20██ / 369	Y-M: 20██ / 369
MACROGOL 3350	1 OTHER: BOTTLE	OTHER: 1 TIME	Y-M: 20██ / 369	Y-M: 20██ / 369
FENTANYL	50 ug	OTHER: 1 TIME	Y-M: 20██ / 370	Y-M: 20██ / 370
MIDAZOLAM	2 mg	OTHER: 1 TIME	Y-M: 20██ / 370	Y-M: 20██ / 370
PROPOFOL	20 mg	OTHER: 5 X 1 DOSE	Y-M: 20██ / 370	Y-M: 20██ / 370
PROPOFOL	30 mg	OTHER: 3 X 1 DOSE	Y-M: 20██ / 370	Y-M: 20██ / 370
VITAMINS NOS	1 OTHER: TAB	QD	Y: 20██	ONGOING

Event #1: Event of Interest - Creatine Phosphokinase (CPK) Elevation

Event Description	ELEVATED CREATININE PHOSPHOKINASE
Preferred term	血中クレアチンホスホキナーゼ増加
AE Onset Date / Initial Rx Day	███20██ / 19
Age at AE Onset	5█
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
AE Stopped Initial 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

Event #2: 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	███20██ / 329
Age at AE Onset	5█

Laboratory Testing

20 (RX DAY 268): Albumin: 40 [35 - 50] G/L; Alkaline Phosphatase: 64 [30 - 150] U/L; Basophils: 0 [0 - 0.2] 10⁹/L; Basophils/Leukocytes: 0.3 [0 - 2] %; Bilirubin: 10.262334 [3.420778 - 20.524668] UMOL/L; Blood Urea Nitrogen: 3.92667 [2.14182 - 7.85334] MMOL/L; Calcium: 2.320443 [2.120835 - 2.619855] MMOL/L; Chloride: 103 [99 - 110] MMOL/L; Creatinine: 86.635195 [70.722608 - 114.924238] UMOL/L; Eosinophils: 0.2 [0 - 0.7] 10⁹/L; Eosinophils/Leukocytes: 1.6 [1 - 4] %; Erythrocytes: 5.16 [4.4 - 5.8] 10¹²/L; Glucose: 5.939249 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.364 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 115 [135 - 175] G/L; Leukocytes: 10 [4 - 11] 10⁹/L; Lymphocytes: 1.9 [0.8 - 4.1] 10⁹/L; Lymphocytes/Leukocytes: 18.6 [20 - 44] %; Monocytes: 0.8 [0 - 1] 10⁹/L; Monocytes/Leukocytes: 8.3 [2 - 9] %; NPTST018-ALT-SGPT: 23 [0 - 55] U/L; NPTST030-ANION GAP WITH K: 10 [6 - 20] MEQ/L; NPTST046-AST-SGOT: 19 [0 - 35] U/L; NPTST082-BUN/CREATININE RATION: 11.2 [10 - 25] UNIT NOT REPORTED; NPTST143-CO2: 28 [20 - 29] MEQ/L; NPTST165-CRP: 63.0 [0 - 8] MG/L; NPTST197-EGFR AFRICAN AMERICAN: > 90 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST200-EGFR NON-AFRICAN AMERICAN: 80 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST300-IMMATURE GRANULOCYTE: 0.03 [0 - 0.06] K/UL; NPTST303-IMMATURE GRANULOCYTE PERCENT: 0.3 [NOT REPORTED - NOT REPORTED] %; NPTST331-MCH: 22.3 [25.5 - 34] PG; NPTST332-MCHC: 31.6 [31.5 - 36.5] G/DL; NPTST334-MCV: 70.5 [80 - 98] FL; NPTST352-MPV: 10.5 [8.5 - 12] FL; NPTST369-NUCLEATED RBC: 0 [NOT REPORTED - NOT REPORTED] /100WBC'S; NPTST441-RDW-CV: 14.9 [11.5 - 15.5] %; NPTST462-SARS-COV-2: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST465-SEG NEUT ABSOLUTE: 7.1 [1.8 - 8] K/UL; Neutrophils: 7,100 [2400 - 7560] /UL; Neutrophils/Leukocytes: 70.9 [50 - 70] %; Occult Blood: 37.1 [35.5 - 50] fL; Platelets: 308 [140 - 400] 10⁹/L; Potassium: 3.9 [3.5 - 5.3] MMOL/L; Protein: 73 [60 - 82] G/L; Sodium: 137 [135 - 145] MMOL/L; 20 (RX DAY 269): Albumin: 40 [35 - 50] G/L; Alkaline Phosphatase: 61 [30 - 150] U/L; Basophils: 0 [0 - 0.2] 10⁹/L; Basophils/Leukocytes: 0.1 [0 - 2] %; Blood Urea Nitrogen: 2.85576 [2.14182 - 7.85334] MMOL/L; Calcium: 2.295492 [2.120835 - 2.619855] MMOL/L; Chloride: 101 [99 - 110] MMOL/L; Creatinine: 72.490673 [70.722608 - 114.924238] UMOL/L; Eosinophils: 0 [0 - 0.7] 10⁹/L; Eosinophils/Leukocytes: 0.1 [1 - 4] %; Erythrocytes: 4.85 [4.4 - 5.8] 10¹²/L; Glucose: 6.716347 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.341 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 107 [135 - 175] G/L; Leukocytes: 12.7 [4 - 11] 10⁹/L; Lymphocytes: 1.5 [0.8 - 4.1] 10⁹/L; Lymphocytes/Leukocytes: 12 [20 - 44] %; Monocytes: 0.6 [0 - 1] 10⁹/L; Monocytes/Leukocytes: 4.4 [2 - 9] %; NPTST018-ALT-SGPT: 21 [0 - 55] U/L; NPTST030-ANION GAP WITH K: 12 [6 - 20] MEQ/L; NPTST046-AST-SGOT: 13 [0 - 35] U/L; NPTST068-BILIRUBIN DIRECT: 0.2 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST070-BILIRUBIN TOTAL: 0.4 [0.2 - 1.2] MG/DL; NPTST081-BUN/CREATININE RATIO: 9.8 [10 - 25] MG/DL; NPTST143-CO2: 29 [20 - 29] MEQ/L; NPTST165-CRP: 46.6 [0 - 8] MG/L; NPTST197-EGFR AFRICAN AMERICAN: >90 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST200-EGFR NON-AFRICAN AMERICAN: >90 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST300-IMMATURE GRANULOCYTE: 0.09 [NOT REPORTED - NOT REPORTED] %; NPTST303-IMMATURE GRANULOCYTE PERCENT: 0.7 [NOT REPORTED - NOT REPORTED] %; NPTST304-INDIRECT BILIRUBIN: 0.2 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST331-MCH: 22.1 [25.5 - 34] PG; NPTST332-MCHC: 31.4 [31.5 - 36.5] G/DL; NPTST334-MCV: 70.3 [80 - 98] FL; NPTST352-MPV: 9.9 [8.5 - 12] FL; NPTST369-NUCLEATED RBC: 0 [NOT REPORTED - NOT REPORTED] /100 WBC'S; NPTST419-PROTEIN TOTAL: 7.1 [6 - 8.2] G/DL; NPTST441-RDW-CV: 15.1 [11.5 - 15.5] %; NPTST442-RDW-SD: 37.2 [35.5 - 50] FL; NPTST465-SEG NEUT ABSOLUTE: 10.5 [1.8 - 8] K/UL; Neutrophils: 10,500 [2400 - 7560] /UL; Neutrophils/Leukocytes: 82.7 [50 - 70] %; Platelets: 304 [140 - 400] 10⁹/L; Potassium: 3.8 [3.5 - 5.3] MMOL/L; Sodium: 138 [135 - 145] MMOL/L; 20 (RX DAY 270): Albumin: 33 [35 - 50] G/L; Alkaline Phosphatase: 53 [30 - 150] U/L; Basophils: 0 [0 - 0.2] 10⁹/L; Basophils/Leukocytes: 0.2 [0 - 2] %; Blood Urea Nitrogen: 3.5697 [2.14182 - 7.85334] MMOL/L; Calcium: 2.120835 [2.120835 - 2.619855] MMOL/L; Chloride: 105 [99 - 110] MMOL/L; Creatinine: 79.562934 [70.722608 - 114.924238] UMOL/L; Eosinophils: 0 [0 - 0.7] 10⁹/L; Eosinophils/Leukocytes: 0.3 [1 - 4] %; Erythrocytes: 4.27 [4.4 - 5.8] 10¹²/L; Glucose: 5.328672 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.301 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 95 [135 - 175] G/L; Leukocytes: 10.5 [4 - 11] 10⁹/L; Lymphocytes: 3 [0.8 - 4.1] 10⁹/L; Lymphocytes/Leukocytes: 28.7 [20 - 44] %; Monocytes: 0.6 [0 - 1] 10⁹/L; Monocytes/Leukocytes: 5.6 [2 - 9] %; NPTST018-ALT-SGPT: 19 [0 - 55] U/L; NPTST030-ANION GAP WITH K: 14 [6 - 20] MEQ/L; NPTST046-AST-SGOT: 12 [0 - 35] U/L; NPTST069-BILIRUBIN INDIRECT: 0.1 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST070-BILIRUBIN TOTAL: 0.2 [0.2 - 1.2] MG/DL; NPTST082-BUN/CREATININE RATION: 11.1 [10 - 25] MG/DL; NPTST100-CAMPYLOBACTER: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST143-CO2: 26 [20 - 29] MEQ/L; NPTST186-

DIRECT BILIRUBIN: 0.1 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST197-EGFR AFRICAN AMERICAN: >90 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST199-EGFR NON AFRICAN AMERICAN: 89 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST300-IMMATURE GRANULOCYTE: 0.04 [NOT REPORTED - NOT REPORTED] %; NPTST303-IMMATURE GRANULOCYTE PERCENT: 0.4 [NOT REPORTED - NOT REPORTED] %; NPTST331-MCH: 22.2 [25.5 - 34] PG; NPTST332-MCHC: 31.6 [31.5 - 36.5] G/DL; NPTST334-MCV: 70.5 [80 - 98] FL; NPTST352-MPV: 10.7 [8.5 - 12] FL; NPTST365-NOROVIRUS: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST369-NUCLEATED RBC: 0 [NOT REPORTED - NOT REPORTED] /100WBC'S; NPTST419-PROTEIN TOTAL: 6.0 [6 - 8.2] G/DL; NPTST441-RDW-CV: 15.1 [11.5 - 15.5] %; NPTST442-RDW-SD: 37.2 [35.5 - 50] FL; NPTST453-ROTAVIRUS: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST458-SALMONELLA: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST465-SEG NEUT ABSOLUTE: 6.8 [1.8 - 8] K/UL; NPTST473-SHIGA-LIKE TOXIN 1: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST474-SHIGA-LIKE TOXIN 2: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST475-SHIGELLA: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST544-VIBRIO: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST555-YERSINIA ENTEROCOLITICA: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 6,800 [2400 - 7560] /UL; Neutrophils/Leukocytes: 64.8 [50 - 70] %; Platelets: 297 [140 - 400] 10⁹/L; Potassium: 3.7 [3.5 - 5.3] MMOL/L; Sodium: 141 [135 - 145] MMOL/L; ■■■■■ (RX DAY 271): Albumin: 37 [35 - 50] G/L; Alkaline Phosphatase: 62 [30 - 150] U/L; Basophils: 0 [0 - 0.2] 10⁹/L; Basophils/Leukocytes: 0.2 [0 - 2] %; Blood Urea Nitrogen: 4.64061 [2.14182 - 7.85334] MMOL/L; Calcium: 2.220639 [2.120835 - 2.619855] MMOL/L; Chloride: 104 [99 - 110] MMOL/L; Creatinine: 83.983097 [70.722608 - 114.924238] UMOL/L; Eosinophils: 0.1 [0 - 0.7] 10⁹/L; Eosinophils/Leukocytes: 0.4 [1 - 4] %; Erythrocytes: 4.58 [4.4 - 5.8] 10¹²/L; Glucose: 5.051137 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.328 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 101 [135 - 175] G/L; Leukocytes: 12.6 [4 - 11] 10⁹/L; Lymphocytes: 3.7 [0.8 - 4.1] 10⁹/L; Lymphocytes/Leukocytes: 29.3 [20 - 44] %; Monocytes: 0.9 [0 - 1] 10⁹/L; Monocytes/Leukocytes: 7.1 [2 - 9] %; NPTST018-ALT-SGPT: 23 [0 - 55] U/L; NPTST030-ANION GAP WITH K: 13 [6 - 20] MEQ/L; NPTST046-AST-SGOT: 17 [0 - 35] U/L; NPTST069-BILIRUBIN INDIRECT: 0.1 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST070-BILIRUBIN TOTAL: 0.2 [0.2 - 1.2] MG/DL; NPTST081-BUN/CREATININE RATIO: 13.7 [10 - 25] MG/DL; NPTST143-CO2: 28 [20 - 29] MEQ/L; NPTST165-CRP: 12.5 [0 - 8] MG/L; NPTST186-DIRECT BILIRUBIN: 0.1 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST197-EGFR AFRICAN AMERICAN: >90 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST199-EGFR NON AFRICAN AMERICAN: 83 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST300-IMMATURE GRANULOCYTE: 0.10 [NOT REPORTED - NOT REPORTED] %; NPTST303-IMMATURE GRANULOCYTE PERCENT: 0.8 [NOT REPORTED - NOT REPORTED] %; NPTST331-MCH: 22.1 [25.5 - 34] PG; NPTST332-MCHC: 30.8 [31.5 - 36.5] G/DL; NPTST334-MCV: 71.6 [80 - 98] FL; NPTST352-MPV: 10.6 [8.5 - 12] FL; NPTST369-NUCLEATED RBC: 0 [NOT REPORTED - NOT REPORTED] /100WBC'S; NPTST419-PROTEIN TOTAL: 6.5 [6 - 8.2] G/DL; NPTST441-RDW-CV: 15.3 [11.5 - 15.5] %; NPTST442-RDW-SD: 39.0 [35.5 - 50] FL; NPTST465-SEG NEUT ABSOLUTE: 7.8 [1.8 - 8] K/UL; Neutrophils: 7,800 [2400 - 7560] /UL; Neutrophils/Leukocytes: 62.2 [50 - 70] %; Platelets: 341 [140 - 400] 10⁹/L; Potassium: 3.5 [3.5 - 5.3] MMOL/L; Sodium: 141 [135 - 145] MMOL/L

Microbiology

20 (RX DAY 268): STOOL NPTST514-TOXIGENIC C. DIFFICILE: POSITIVE-C. DIFF DETECTED IN THE FECAL TESTING

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: 20 :11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 5 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 2 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332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を経験しているとのことであった。

投与された薬剤は、ソル・メドロール、バンコマイシン、prednisone 及び dilaudid 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)

1) Clostridium difficile infection (10054236) (Clostridium difficile infection (10054236)) [v.24.0]
[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

20 HEART RATE: 76 /min

20 NASOPHARYNGEAL SWAB: COVID-19: Negative

20 POTASSIUM: 3.9 No Unit

20 SODIUM: 137 No Unit

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Blood creatine phosphokinase increased: Asymptomatic. Related to starting a new Exercise program. Retest done.

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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 58	58
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	20 / 1	20 / 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: 20 /
VERAPAMIL	80 mg	TID	Y-M: 20 /
AZATHIOPRINE	50 mg	QD	Y-M: 20 / -210
FINASTERIDE	0.75 mg	QD	Y-M: 20 / -214
PREDNISONE	20 mg	QD	Y-M: 20 / -183
INFLIXIMAB	5.000 mg/kg	EVERY 8 WEEKS	Y: 20
ADALIMUMAB	40.000 mg	NOT REPORTED	Y: 20
TAMSULOSIN	0.4 mg	OTHER: EVERY OTHER DAY	Y: 20
VEDOLIZUMAB	300.000 mg	EVERY 4 WEEKS	Y: 20

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
ATORVASTATIN	20 mg	QD	Y-M: 20 / ONGOING
VERAPAMIL	80 mg	TID	Y-M: 20 / ONGOING
FINASTERIDE	0.75 mg	QD	Y-M: 20 / -214 ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20 / 31 Y-M: 20 / 336
ESOMEPRAZOLE	40 mg	QD	Y-M: 20 / 250 ONGOING
DEXAMETHASONE	10 mg	QD	Y-M: 20 / 317 Y-M: 20 / 317
PARACETAMOL	650 mg	PRN	Y-M: 20 / 317 ONGOING
REMDESIVIR	200 mg	QD	Y-M: 20 / 317 Y-M: 20 / 317
ENOXAPARIN	90 mg	OTHER: Q12H	Y-M: 20 / 318 ONGOING
REMDESIVIR	100 mg	OTHER: EVERY 24 HOUR	Y-M: 20 / 318 Y-M: 20 / 321
ALPRAZOLAM	0.25 mg	QD	Y-M: 20 / 319 Y-M: 20 / 319
LISINOPRIL	5.0 mg	QD	Y-M: 20 / 331 Y-M: 20 / 351

TAMSULOSIN 0.4 mg OTHER: EVERY Y: 20 ONGOING
OTHER DAY

Event #1: Serious Adverse Event

Event Description ACUTE RESPIRATORY FAILURE

Preferred term 急性呼吸不全

AE Onset Date / Initial Rx Day / 375

Age at AE Onset 6

Laboratory Testing

(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] 10¹²/L; Hemoglobin: 131 [135 - 180] G/L; Leukocytes: 14.9 [4.5 - 11] 10⁹/L

Microbiology

(RX DAY 317): OTHER NASOPHARYNX NPTST160-COVID-19: POSITIVE-COVID-19 VIRUS DETECTED AND SUBJECT PRESENTED WITH ACUTE HYPOXEMIC RESPIRATORY FAILURE

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: :11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6 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■■ - 20■■)

HUMIRA for ULCERATIVE COLITIS (20■■ - 20■■)

ENTYVIO for ULCERATIVE COLITIS (20■■ - ■■■■ 20■■)

AZATHIOPRINE for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

PREDNISONE for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

Causality for UPADACITINIB (Blinded)

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

20 ■ **ALT:** 41 U/L (normal 16 to 61)

20 ■ **AST:** 40 U/L (normal 15 to 37)

20 ■ **BMI:** 29.1 kg/m2

20 ■ **BUN:** 29 mg/dL (normal 7 to 18)

20 ■ **CALCIUM:** 8.3 mg/dL (normal 8.5 to 10.1)

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

20 ■ **CHEST X-RAY:** Stable bilateral Covid-19 pneumonitis.

20 ■ **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.

20 ■ **COVID-19 TEST:** Nasopharyngeal swab: Positive for COVID-19

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

20 ■ **CREATININE:** 1.13 mg/dL (normal 0.70 to 1.30)

20 ■ **HEMOGLOBIN:** 13.1 G/DL (normal 13.5 to 18)

20 ■ **RBC:** 4.38 M/uL (normal 4.5 to 6)

20 ■ **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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 55	55
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	20 / 1	20 / 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: 20 /		
PREDNISONE		60 mg	QD	Y-M: 20 /		
ADALIMUMAB		80.000 mg	ONCE ON DAY 1, THEN @ DAY 15	Y-M: 20 / -363		
PARACETAMOL		500 mg	PRN	Y-M: 20 / -42		
BUDESONIDE;FORMOTEROL		90 OTHER: MCG	QD	Y: 20		
FLUTICASONE		50 OTHER: MCG	PRN	Y: 20		
LORATADINE		10 mg	PRN	Y: 20		
MONTELUKAST		10 mg	QD	Y: 20		
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: 20 /	Y-M: 20 /	86
PARACETAMOL		500 mg	PRN	Y-M: 20 / -42	ONGOING	
EMOLLIENTS AND PROTECTIVES 1 OTHER: SOFT GEL			QID	Y-M: 20 / 29	ONGOING	
PREDNISONE		5 mg	QD	Y-M: 20 / 7	Y-M: 20 /	11
CEFTRIAXONE		2 g	OTHER: ONCE	Y-M: 20 / 41	Y-M: 20 /	41
GLYCOPYRRONIUM		0.2 mg	OTHER: ONE TIME	Y-M: 20 / 41	Y-M: 20 /	41
SODIUM CHLORIDE		1000 mL	OTHER: ONE TIME	Y-M: 20 / 41	Y-M: 20 /	41
PREDNISONE		40 mg	QD	Y-M: 20 / 43	Y-M: 20 /	78
HYDROCORTISONE		100 mg	OTHER: EVERY 6 HOURS	Y-M: 20 / 45	Y-M: 20 /	51

METRONIDAZOLE	500 mg	OTHER: EVERY 8 HOURS	Y-M: 20██ / 45	Y-M: 20██ / 51
ENOXAPARIN	40 mg	QD	Y-M: 20██ / 46	Y-M: 20██ / 51
INFLIXIMAB	5 mg/kg	OTHER: AS DIRECTED	Y-M: 20██ / 46	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20██ / 46	Y-M: 20██ / 51
PANTOPRAZOLE	40 mg	QD	Y-M: 20██ / 52	Y-M: 20██ / 86
PREDNISONE	35 mg	QD	Y-M: 20██ / 79	ONGOING
BUDESONIDE;FORMOTEROL	90 OTHER: MCG	QD	Y: 20██	ONGOING
FLUTICASONE	50 OTHER: MCG	PRN	Y: 20██	ONGOING
LORATADINE	10 mg	PRN	Y: 20██	ONGOING
MONTELUKAST	10 mg	QD	Y: 20██	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 20██ / 93

Age at AE Onset 5█

Laboratory Testing

20██ (RX DAY 45): Creatinine: 119.344401 [53.041956 - 106.083912] UMOL/L; Leukocytes: 12.52 [4.4 - 10.5] 10⁹/L; Lymphocytes/Leukocytes: 12.4 [20.5 - 45] %; Monocytes: 1.38 [0 - 0.8] 10⁹/L; NPTST166-CRP INFLAMMATORY: 20.7 [0 - 5] MG/L; NPTST307-INR: 1.17 [0.8 - 1.2] RATIO; NPTST428-PT: 14.5 [11.5 - 14.9] RATIO; Neutrophils: 9.43 [1.5 - 7.5] 10⁹/L; Neutrophils/Leukocytes: 76.1 [50 - 70] %; Platelets: 487 [139 - 361] 10⁹/L; 20██ (RX DAY 46): NPTST219-FECES C DIFFICILE AG: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST220-FECES C DIFFICILE TOXIN EIA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST222-FECES LACTOFERRIN: POSITIVE [0 - 0] UNIT NOT REPORTED; 20██ (RX DAY 47): NPTST221-FECES CAMPYLOBACTER GRP PCR: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST223-FECES SALMONELLA SPP PCR: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST224-FECES SHIGELLA SPP PCR: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST225-FECES VIBRIO PCR: NOT DETECTED [10 - 100] UNIT NOT REPORTED; 20██ (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] 10⁹/L; NPTST144-CO2 LVL: 23 [24 - 32] MMOL/L; NPTST165-CRP: 2.1 [0.3 - 5] MG/L; Platelets: 392 [139 - 361] 10⁹/L; Potassium: 3.3 [3.5 - 5] MMOL/L; Protein: 58 [65 - 80] G/L

Microbiology

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: 2011:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 51 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 (2011 - 2011)

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

20 ■ ABDOMINAL CT: Not reported

20 ■ CO2 LVL: 23 MMOL/L (normal 24 to 32)

20 ■ CREATININE: 1.35 mg/dL (normal 0.60 to 1.20)

20 ■ CRP: 2.1 MG/L (normal <5)

20 ■ CRP INFLAMMATORY: 20.7 MG/L (normal 0 to 5)

20 ■ FECES C DIFFICILE AG: Negative

20 ■ FECES C DIFFICILE TOXIN EIA: Negative

20 ■ FECES CAMPYLOBACTER GRP PCR: Not Detected

20 ■ FECES LACTOFERRIN: Positive

20 ■ FECES SALMONELLA SPP PCR: Not Detected

20 ■ FECES SHIGELLA SPP PCR: Not Detected

20 ■ FECES VIBRIO PCR: Not Detected

20	GLUCOSE: 114 mg/dL (normal 70 to 100)
20	HEMATOCRIT: 35.9 % (normal 36.9 to 48.5)
20	HEMOGLOBIN: 12.0 G/DL (normal 12.6 to 16.7)
20	INR: 1.17 RATIO (normal 0.8 to 1.2)
20	LYMPHOCYTES %: 12.4 % (normal 20.5 to 45.0)
20	MONOCYTES ABS: 1.38 X10**3/MCL (normal 0 to 0.80)
20	NEUTROPHILS %: 76.1 %(normal 50.0 to 70.0)
20	NEUTROPHILS ABS: 9.43 X10**3/MCL (normal 1.50 to 7.50)
20	PLATELET COUNT: 487 X10**9/L (normal 139 to 361)
20	PLATELET COUNT: 392 X10**9/L (normal 139 to 361)
20	POTASSIUM: 3.3 MEQ/L (normal 3.5 to 5.0)
20	PROTEIN: 5.8 G/DL (normal 6.5 to 8.0)
20	PT: 14.5 RATIO (normal 11.5 to 14.9)
20	WHITE BLOOD CELLS: 12.52 10^3/uL (normal 4.40 to 10.50)
20	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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 64	64
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[REDACTED] 20 [REDACTED] / 1	[REDACTED] 20 [REDACTED] / 366	366

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██-██
PREDNISONE	20 mg	QD	Y-M: 20██-██
AMFETAMINE;DEXAMFETAMINE	10 mg	BID	Y-M: 20██-██
AZATHIOPRINE	150 mg	QD	Y-M: 20██-██ / -199
DICYCLOVERINE	20 mg	OTHER: EVERY 6 HOURS AS NEEDED	Y-M: 20██-██ / -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 / Stop Year-Month / RX Day
DESVENLAFAXINE	100 mg	QD	Y-M: 20██-██ / ONGOING
AMFETAMINE;DEXAMFETAMINE	10 mg	BID	Y-M: 20██-██ / ONGOING
DICYCLOVERINE	20 mg	OTHER: EVERY 6 HOURS AS NEEDED	Y-M: 20██-██ / -109 / ONGOING
BREXPIPIRAZOLE	2 mg	QD	Y-M: 20██-██ / 102 Y-M: 20██-██ / 216
DULOXETINE	30 mg	QD	Y-M: 20██-██ / 102 Y-M: 20██-██ / 185
LAMOTRIGINE	25 mg	QD	Y-M: 20██-██ / 198 Y-M: 20██-██ / 231

Event #1: Serious Adverse Event

Event Description	WORSENING ANXIETY, WORSENING DEPRESSION
Preferred term	不安, うつ病
AE Onset Date / Initial Rx Day	██-██-20██ / 249
Age at AE Onset	4█
Laboratory Testing	NOT REPORTED
Microbiology	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
Event #2: Serious Adverse Event	
Event Description	WORSENING ANXIETY, WORSENING DEPRESSION
Preferred term	不安, うつ病
AE Onset Date / Initial Rx Day	20 / 249
Age at AE Onset	4
Laboratory Testing	
NOT REPORTED	
Microbiology	
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: 20:11:02

Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 4 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 及び 2 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 (■■■■ 20■■ - ■■■■ 20■■)

AZATHIOPRINE for ULCERATIVE COLITIS (■■■■ 20■■ - ■■■■ 20■■)

Causality for UPADACITINIB (Blinded)

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

20 BODY WEIGHT: 17 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	61	FEMALE	WHITE

Medical History	Onset Year
APPENDICITIS	2008
ASTIGMATISM	2008
BREAST CYST (LEFT)	2008
CIATALGIA (SCIATIC NEURITIS)	2008
LEFT SIDED UC	2008
MENOPAUSE	2008
MYOPIA	2008
OVARIAN CYST (RIGHT)	1998
ULCERATIVE COLITIS	2008

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	2008
PRIOR PROCEDURES: BOTH BREAST IMPLANT SURGERY	2008
PRIOR PROCEDURES: BOTH BREAST IMPLANT SURGERY	2008
PRIOR PROCEDURES: LEFT BREAST CYST REMOVALSURGERY	2008
PRIOR PROCEDURES: NECK PLASTIC SURGERY	2008
PRIOR PROCEDURES: NOSE PLASTIC SURGERY	2008
PRIOR PROCEDURES: OVARIAN CYST REMOVAL SURGERY	1998
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	2008

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	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	20 / 1	20 / 62	62
M14-234 SS3 Placebo (MAIN)		ORAL	QD	20 / 1	20 / 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
VEDOLIZUMAB	300.000 mg	EVERY 2 WEEKS (Q2W)	Y: 20
BOTULINUM TOXIN TYPE A	50 OTHER: UNITS	OTHER: EVERY 6 MONTHS	Y: 20
PYRIDOXINE	100 mg	OTHER: EVERY 6 MONTHS (Q6M)	Y: 20
THIAMINE	100 mg	OTHER: EVERY 6 MONTHS (Q6M)	Y: 20
VITAMIN B12 NOS	10000 OTHER: MCG	OTHER: EVERY 6 MONTHS	Y: 20

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
BOTULINUM TOXIN TYPE A	50 OTHER: UNITS	OTHER: EVERY 6 MONTHS	Y: 20	ONGOING
PYRIDOXINE	100 mg	OTHER: EVERY 6 MONTHS (Q6M)	Y: 20	ONGOING
THIAMINE	100 mg	OTHER: EVERY 6 MONTHS (Q6M)	Y: 20	ONGOING
VITAMIN B12 NOS	10000 OTHER: MCG	OTHER: EVERY 6 MONTHS	Y: 20	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	20 / 293
Age at AE Onset	6
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
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

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Program Source Code:

Investigator No.:

Subject Number:

Protocol Number: M14-234

治験責任医師からの報告。本被験者は米国の 6 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瘍を指摘された。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，腫瘍はステージ 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，腫瘍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██ - 20██)

VEDOLIZUMAB for ULCERATIVE COLITIS (20██ - █████ 20██)

Causality for UPADACITINIB (Blinded)

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

■ 20 ■ **BREAST PHYSICAL EXAMINATION:** ABNORMAL: MASS IN RIGHT BREAST

■ 20 ■ **MAMMOGRAPHY:** IRREGULAR MASS RIGHT BREAST, 3 O'CLOCK MIDDLE DEPTH 4 CM FROM THE NIPPLE

■ 20 ■ **RIGHT BREAST ULTRASOUND:** IRREGULAR MASS RIGHT BREAST, AT 3 O'CLOCK MIDDLE DEPTH 4 CM FORM THE NIPPLE

■ 20 ■ **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 NOTINHAM 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 (20 年 月 日データカットオフ)

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： 308 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、シンガポール、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 [プエルトリコを含む]）	
治験調整医師： MD	
公表文献（参考資料）： なし	
治験期間： 最初の被験者の初回来院日：20 年 月 日 データカットオフ日：20 年 月 日	開発のフェーズ： 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。 本報告書では、20 年 月 日のデータカットオフまでの更新した安全性データを示した。20 年 月 日のデータカットオフまでの有効性の結果は、前回の中間報告書（5.3.5.2-1 項）に示した。更新した有効性データは、最終報告書に示す予定である。	
被験者数（計画時と解析時）： 計画時：950 例、解析時：1088 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 574 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 514 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。

2.7.6 個々の試験のまとめ

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	
ウパダシチニブ	15 mg	経口	
ウパダシチニブ	30 mg	経口	

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], [REDACTED], [REDACTED], [REDACTED]

評估基準：

有効性：

20●●年●月●日のデータカットオフまでの有効性の結果は、前回の中間報告書（5.3.5.2-1 項）に示した。更新した有効性データは、最終報告書に示す予定である。

安全性：

臨床検査値及びバイタルサインの長期継続投与ベースラインからの平均変化量に関する解析では、長期継続投与ベースラインを、長期継続投与試験中の治験薬初回投与日又はそれ以前の最後の非欠測値と定義した。臨床的な意義があると判断した臨床検査値及びバイタルサインの解析でのベースラインは、第 IIb 相又は第 III 相導入療法試験でウパダシチニブを投与した被験者については、第 IIb 相又は第 III 相導入療法試験でウパダシチニブを投与前の最後の利用可能な測定値と定義し、第 IIb 相又は第 III 相導入療法試験でプラセボを投与した被験者については、第 IIb 相又は第 III 相導入療法試験でプラセボを投与前の最後の利用可能な測定値と定義した。

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：

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、長期継続投与ベースラインからの平均変化量を要約した。

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に、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、非重篤な膀胱炎及び重篤な尿路性敗血症が各 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。

本試験では、評価期間中の死亡が 4 例報告された（SA1 集団及び SA2 集団で各 2 例）。SA2 集団では、死亡に至った有害事象として、膵腺癌が 1 例、COVID-19 及び肺塞栓症が 1 例に認められ、いずれもウパダシチニブ 30 mg 1 日 1 回群（以下「30 mg 群」）の被験者であった。SA1 集団では、死亡に至った有害事象として、脳損傷がウパダシチニブ 15 mg 1 日 1 回群（以下「15 mg 群」）で 1 例、血管肉腫がウパダシチニブ 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 1 例に認められた。膵腺癌及び脳損傷は、前回の中間報告書（5.3.5.2-1 項、データカットオフ日：20 年 月 日、以下同様）で報告した事象であった。死亡に至った有害事象のうち、治験責任医師により治験薬との因果関係が「関連あり」と判断された事象は、血管肉腫のみであった。

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 COVID-19、潰瘍性大腸炎、上咽頭炎及び上気道感染であり、30 mg 群で COVID-19、潰瘍性大腸炎、血中クレアチンホスホキナーゼ増加、注射部位疼痛及び関節痛であった。重篤な有害事象の 100 人年あたりの発現件数は、15 mg 群と比較して 30 mg 群の方が多かった。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 群と 30 mg 群で同程度であった。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が、すべての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、プラセボ群と 15 mg 群及び 30 mg 群でおおむね同程度であった。また、重篤な有害事象の 100 人年あたりの発現件数は、プラセボ群と 15 mg 群で同程度であったが、プラセボ群と比較して 30 mg 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、血中クレアチンホスホキナーゼ増加、関節痛及び頭痛であり、15 mg/30 mg 群で潰瘍性大腸炎、上咽頭炎、血中クレアチンホスホキナーゼ増加、関節痛、COVID-19 及び注射部位疼痛であった。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 人年以上であった特に注目すべき有害事象は、重篤な感染症、好中球減少症、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、日和見感染が 2 件（サイトメガロウイルス感染及びサイトメガロウイルス性大腸炎）認められ、いずれも 30 mg 群の被験者であった。SA2 集団では、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 例に認められたが、いずれも前回の中間報告書で報告した事象であった。SA2 集団では、帯状疱疹の 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。SA2 集団では、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。SA2 集団では、眼帯状疱疹が 2 例に認められた。SA2 集団では、非重篤な神経合併症を伴う帯状疱疹感染が 15 mg 群の 1 例に認められたが、前回の中間報告書で報告した事象であった。

SA2 集団では、本試験のデータカットオフまでの悪性腫瘍の 100 人年あたりの発現件数は、15 mg 群と比較して 30 mg 群の方が数値的に多かった。非黒色腫皮膚癌（以下「NMSC」）を除く悪性腫瘍は、15 mg 群で 1 件（0.5 件/100 人年）、30 mg 群で 2 件（0.8 件/100 人年）認められた。NMSC は 4 件認められ、いずれも 30 mg 群であった。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 集団及び SA1 集団の投与群を通しておおむね同程度であった。

SA2 集団では、主要心血管事象は認められなかった。SA1 集団では、主要心血管事象が 3 例（非致死性心筋梗塞 2 例、非致死性脳卒中 1 例）に認められ、いずれも 15 mg 群の被験者であった。SA2 集団では、静脈血栓塞栓症として肺塞栓症が 15 mg 群及び 30 mg 群の各 1 例に認められた。SA1 集団では、静脈血栓塞栓症が 6 例に認められ、内訳は、15 mg 群で深部静脈血栓症が 3 例、肺塞栓症が 1 例、深部静脈血栓症と肺塞栓症の併発が 1 例、15 mg/30 mg 群で深部静脈血栓症が 1 例であった。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、消化管穿孔は 15 mg 群及び 15 mg/30 mg 群の各 1 例（15 mg 群では大腸穿孔、15 mg/30 mg 群では腹部膿瘍）に認められた。いずれもの事象も重篤であった。このうち、腹部膿瘍では治験薬の投与が中止され、治験薬との因果関係は治験責任医師により「関連あり」と判断された。

SA2 集団では、薬剤に関連する肝障害のほとんどの 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いずれも非重篤で、ほとんどの事象の重症度は軽度又は中等度であり、治験薬の投与中止に至った事象はなかった。SA1 集団では、横紋筋融解症が 2 件認められ、1 件は重篤で、もう 1 件は非重篤であった。重篤であった事象は、前回の中間報告書で報告した事象であった。

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、おおむね低かった。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。前回の中間報告書と同様に、新た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（40 例）で 187.1 件/100 人年、30 mg 群（49 例）で 275.9 件/100 人年、プラセボ群（10 例）で 222.2 件/100 人年であった。ウパダシチニブ群で 5 件/100 人年以上認められた有害事象は、15 mg 群で上咽頭炎、注射部位疼痛、発熱、潰瘍性大腸炎及び高脂血症、30 mg 群で口腔ヘルペス、注射部位疼痛、好中球数減少、上咽頭炎、発熱、帯状疱疹、血中クレアチンホスホキナーゼ増加、四肢痛及び皮脂欠乏性湿疹であった。

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 31.2 件/100 人年、30 mg 群で 54.2 件/100 人年、プラセボ群で 55.6 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 群で好中球数減少、帯状疱疹、リンパ球数減少及び白血球数減少であった。

高度の有害事象の 100 人年あたりの発現件数は、15 mg 群で 2.4 件/100 人年、30 mg 群で 17.2 件/100 人年、プラセボ群で 27.8 件/100 人年であった。15 mg 群及び 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、15 mg 群で 4.8 件/100 人年、30 mg 群で 14.8 件/100 人年、プラセボ群で 13.9 件/100 人年であった。15 mg 群及び 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 4.8 件/100 人年、30 mg 群で 7.4 件/100 人年、プラセボ群で 13.9 件/100 人年であった。15 mg 群及び 30 mg 群で 2 件以上認められた治験薬の投与中止に至った有害事象はなかった。

SA1 集団

有害事象の 100 人年あたりの発現件数は、15 mg 群（61 例）で 267.4 件/100 人年、15 mg/30 mg 群（19 例）で 344.4 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、口腔ヘルペス及び発熱、15 mg/30 mg 群で上咽頭炎、クロストリジウム・ディフィシレ感染、不眠症、腹部膨満、血中クレアチンホスホキナーゼ増加及びアレルギー性鼻炎であった。

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 57.8 件/100 人年、15 mg/30 mg 群で 85.2 件/100 人年であった。100 人年あたりの発現件数が 5 件/100 人以上であった治験薬と関連ありの有害事象は、15 mg 群で帯状疱疹及び口腔ヘルペス、15 mg/30 mg 群で血中クレアチンホスホキナーゼ増加、白血球減少症及び肺炎であった。

高度の有害事象の 100 人年あたりの発現件数は、15 mg 群で 2.5 件/100 人年、15 mg/30 mg 群で 3.7 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 13.4 件/100 人年、15 mg/30 mg 群で 14.8 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 2.5 件/100 人年、15 mg/30 mg 群で 11.1 件/100 人年であった。いずれの投与群でも、2 件以上認められた治験薬の投与中止に至った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

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 UPADACITINIB (ULCERATIVE COLITIS)
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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=574)	UPA 15 mg QD/ UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Subjects with:								
Any adverse event (AE)	419 (73.0)	185 (74.3)	497 (86.6)	30 (58.8)	1 (100)	119 (62.6)	170 (62.5)	787 (75.9)
Any AE with reasonable possibility of being related to study drug\$	193 (33.6)	104 (41.8)	264 (46.0)	13 (25.5)	0	36 (18.9)	71 (26.1)	371 (35.8)
Any severe AE	56 (9.8)	28 (11.2)	84 (14.6)	3 (5.9)	1 (100)	11 (5.8)	23 (8.5)	119 (11.5)
Any serious AE	61 (10.6)	38 (15.3)	94 (16.4)	4 (7.8)	1 (100)	15 (7.9)	29 (10.7)	139 (13.4)
Any AE leading to discontinuation of study drug	36 (6.3)	27 (10.8)	63 (11.0)	3 (5.9)	0	10 (5.3)	11 (4.0)	84 (8.1)
Any AE leading to death	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	2 (0.7)	4 (0.4)
Deaths#	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	2 (0.7)	4 (0.4)
Occurring <= 30 days after last dose	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	2 (0.7)	4 (0.4)
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:

表2

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 UPADACITINIB (ULCERATIVE COLITIS)
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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=574)	UPA 15 mg QD/ UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
Any treatment-emergent:								
Any adverse event (AE)	2302 (280.2)	958 (274.9)	3260 (278.6)	100 (218.3)	2 (71.4)	475 (236.8)	556 (233.5)	4293 (266.4)
Any AE with reasonable possibility of being related to study drug\$	520 (63.3)	249 (71.4)	769 (65.7)	34 (74.2)	0	90 (44.9)	167 (70.1)	1026 (63.7)
Any severe AE	71 (8.6)	44 (12.6)	115 (9.8)	3 (6.6)	1 (35.7)	15 (7.5)	28 (11.8)	159 (9.9)
Any serious AE	101 (12.3)	64 (18.4)	165 (14.1)	5 (10.9)	1 (35.7)	20 (10.0)	41 (17.2)	227 (14.1)
Any AE leading to discontinuation of study drug	41 (5.0)	33 (9.5)	74 (6.3)	3 (6.6)	0	11 (5.5)	16 (6.7)	101 (6.3)
Any AE leading to death	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	3 (1.3)	5 (0.3)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/100 PYs = 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.

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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/ UPA 15 mg QD UPA 30 mg QD Total			Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events	Events	Events	Events	Events	Events	Events	Events
	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
Deaths#	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	2 (0.8)	4 (0.2)
Occurring <= 30 days after last dose	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	2 (0.8)	4 (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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD/ UPA 30 mg QD			UPA 15 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	(N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
Any adverse event	419 (73.0)	185 (74.3)	497 (86.6)	30 (58.8)	1 (100)	119 (62.6)	170 (62.5)	787 (75.9)
血液およびリンパ系障害	49 (8.5)	19 (7.6)	67 (11.7)	4 (7.8)	0	12 (6.3)	15 (5.5)	94 (9.1)
貧血	24 (4.2)	4 (1.6)	28 (4.9)	1 (2.0)	0	5 (2.6)	5 (1.8)	38 (3.7)
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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
顆粒球減少症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
内出血発生の増加傾向	1 (0.2)	1 (0.4)	2 (0.3)	1 (2.0)	0	0	1 (0.4)	3 (0.3)
鉄欠乏性貧血	3 (0.5)	3 (1.2)	6 (1.0)	0	0	2 (1.1)	0	8 (0.8)
白血球増加症	1 (0.2)	1 (0.4)	2 (0.3)	0	0	1 (0.5)	0	3 (0.3)
白血球減少症	5 (0.9)	3 (1.2)	8 (1.4)	1 (2.0)	0	2 (1.1)	6 (2.2)	16 (1.5)
リンパ節症	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	0	3 (0.3)
リンパ球増加症	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
血液およびリンパ系障害 (Cont.)								
リンパ球減少症	10 (1.7)	4 (1.6)	13 (2.3)	0	0	1 (0.5)	1 (0.4)	15 (1.4)
小球性貧血	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
好中球減少症	9 (1.6)	4 (1.6)	13 (2.3)	1 (2.0)	0	1 (0.5)	6 (2.2)	20 (1.9)
好中球増加症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
汎血球減少症	0	0	0	0	0	0	1 (0.4)	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 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
心臓障害	12 (2.1)	5 (2.0)	17 (3.0)	1 (2.0)	0	3 (1.6)	6 (2.2)	26 (2.5)
急性心筋梗塞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
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 (0.4)	1 (<0.1)
心房細動	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
心臓障害 (Cont.)								
完全房室ブロック	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
第一度房室ブロック	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
徐脈性不整脈	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
徐脈	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
脚ブロック	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
左脚ブロック	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
心拡大	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
うつ血性心筋症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
冠動脈疾患	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
期外収縮	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
虚血性心筋症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
心筋梗塞	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
心臓障害 (Cont.)								
動悸	2 (0.3)	0	2 (0.3)	1 (2.0)	0	0	0	2 (0.2)
心嚢液貯留	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
心膜炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
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 (1.1)	0	2 (0.2)
頻脈	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	0	3 (0.3)
心室性期外収縮	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	2 (0.7)	4 (0.4)
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	4 (0.7)	0	4 (0.7)	0	0	2 (1.1)	1 (0.4)	7 (0.7)
先天性横隔膜ヘルニア	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
ジルベール症候群	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
陰嚢水腫	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
先天性、家族性および遺伝性障害 (Cont.)								
魚鱗癬	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
歯原性嚢胞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
包茎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
汗孔角化症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
耳および迷路障害	11 (1.9)	5 (2.0)	15 (2.6)	0	0	2 (1.1)	7 (2.6)	24 (2.3)
伝音難聴	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
耳痛	3 (0.5)	1 (0.4)	3 (0.5)	0	0	1 (0.5)	0	4 (0.4)
外耳の炎症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
聴力低下	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
内耳障害	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
メニエール病	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
耳漏	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
耳および迷路障害 (Cont.)								
突発性難聴	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
耳鳴	4 (0.7)	1 (0.4)	5 (0.9)	0	0	0	3 (1.1)	8 (0.8)
回転性めまい	4 (0.7)	1 (0.4)	5 (0.9)	0	0	1 (0.5)	2 (0.7)	8 (0.8)
内分泌障害	5 (0.9)	2 (0.8)	7 (1.2)	0	0	0	0	7 (0.7)
アジソン病	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
副腎機能不全	0	1 (0.4)	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)
甲状腺腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
甲状腺機能亢進症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
甲状腺腫瘍	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)					
眼障害	29 (5.1)	9 (3.6)	37 (6.4)	5 (9.8)	0	4 (2.1)	6 (2.2)	47 (4.5)
無水晶体眼	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
眼精疲労	0	0	0	1 (2.0)	0	0	0	0
眼瞼炎	4 (0.7)	1 (0.4)	5 (0.9)	0	0	0	0	5 (0.5)
眼瞼痙攣	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
白内障	7 (1.2)	0	7 (1.2)	0	0	2 (1.1)	1 (0.4)	10 (1.0)
霰粒腫	1 (0.2)	1 (0.4)	2 (0.3)	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)	1 (0.4)	2 (0.3)	1 (2.0)	0	0	1 (0.4)	3 (0.3)
結膜弛緩症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
角膜浮腫	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
眼障害 (Cont.)								
後天性涙道狭窄	1 (0.2)	0	1 (0.2)	1 (2.0)	0	0	0	1 (<0.1)
ドライアイ	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	1 (0.4)	5 (0.5)
上強膜炎	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
眼刺激	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
眼痛	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
眼瞼嚢胞	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
緑内障	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
角膜炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
黄斑浮腫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
近視	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
眼充血	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
開放隅角緑内障	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
眼障害 (Cont.)								
網膜静脈閉塞	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
ぶどう膜炎	1 (0.2)	0	1 (0.2)	1 (2.0)	0	0	1 (0.4)	2 (0.2)
霧視	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
視力低下	0	0	0	2 (3.9)	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	204 (35.5)	76 (30.5)	250 (43.6)	13 (25.5)	0	44 (23.2)	47 (17.3)	341 (32.9)
腹部不快感	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
腹部膨満	4 (0.7)	3 (1.2)	7 (1.2)	1 (2.0)	0	1 (0.5)	2 (0.7)	10 (1.0)
腹部ヘルニア	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
腹痛	20 (3.5)	3 (1.2)	23 (4.0)	0	0	4 (2.1)	4 (1.5)	31 (3.0)
下腹部痛	7 (1.2)	0	7 (1.2)	0	0	0	0	7 (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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)					
胃腸障害 (Cont.)								
上腹部痛	6 (1.0)	2 (0.8)	8 (1.4)	1 (2.0)	0	1 (0.5)	2 (0.7)	11 (1.1)
腹部圧痛	6 (1.0)	0	6 (1.0)	0	0	0	1 (0.4)	7 (0.7)
裂肛	4 (0.7)	1 (0.4)	5 (0.9)	0	0	0	0	5 (0.5)
痔瘻	3 (0.5)	0	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
肛門失禁	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
肛門ポリープ	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
肛門そう痒症	0	1 (0.4)	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)	3 (1.2)	7 (1.2)	0	0	1 (0.5)	0	8 (0.8)
口唇のひび割れ	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
大腸炎	1 (0.2)	3 (1.2)	4 (0.7)	1 (2.0)	0	0	0	4 (0.4)
潰瘍性大腸炎	99 (17.2)	36 (14.5)	126 (22.0)	4 (7.8)	0	11 (5.8)	14 (5.1)	151 (14.6)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
胃腸障害 (Cont.)								
結腸異形成	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
便秘	7 (1.2)	3 (1.2)	10 (1.7)	1 (2.0)	0	5 (2.6)	4 (1.5)	19 (1.8)
クローン病	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
便意切迫	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	0	4 (0.4)
齲齒	4 (0.7)	1 (0.4)	5 (0.9)	0	0	1 (0.5)	1 (0.4)	7 (0.7)
歯組織の壊死	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
下痢	21 (3.7)	5 (2.0)	26 (4.5)	1 (2.0)	0	2 (1.1)	2 (0.7)	30 (2.9)
血性下痢	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
腸憩室	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
十二指腸炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
消化不良	9 (1.6)	6 (2.4)	15 (2.6)	0	0	1 (0.5)	0	16 (1.5)
小腸炎	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	(N=1037) n (%)
胃腸障害 (Cont.)								
腸炎	1 (0.2)	0	1 (0.2)	0	0	0	2 (0.7)	3 (0.3)
おくび	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
軟便	0	1 (0.4)	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	8 (1.4)	2 (0.8)	10 (1.7)	0	0	2 (1.1)	0	12 (1.2)
食中毒	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
排便回数増加	1 (0.2)	1 (0.4)	2 (0.3)	0	0	1 (0.5)	0	3 (0.3)
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	5 (0.9)	1 (0.4)	6 (1.0)	1 (2.0)	0	0	0	6 (0.6)
胃腸障害	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
消化管運動障害	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)					
胃腸障害 (Cont.)								
消化器痛	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
胃食道逆流性疾患	11 (1.9)	1 (0.4)	12 (2.1)	2 (3.9)	0	4 (2.1)	1 (0.4)	17 (1.6)
血便排泄	2 (0.3)	0	2 (0.3)	1 (2.0)	0	0	0	2 (0.2)
痔出血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
痔核	9 (1.6)	3 (1.2)	12 (2.1)	0	0	4 (2.1)	3 (1.1)	19 (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	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
イレウス	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
炎症性腸疾患	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
単径ヘルニア	0	2 (0.8)	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
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)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)					
胃腸障害 (Cont.)								
過敏性腸症候群	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	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	6 (1.0)	2 (0.8)	8 (1.4)	2 (3.9)	0	1 (0.5)	3 (1.1)	12 (1.2)
口唇障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
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 (0.4)	5 (0.9)	0	0	1 (0.5)	0	6 (0.6)
悪心	26 (4.5)	10 (4.0)	34 (5.9)	1 (2.0)	0	6 (3.2)	4 (1.5)	44 (4.2)
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 (0.4)	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)
腭炎	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
胃腸障害 (Cont.)								
歯周病	1 (0.2)	0	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 (0.5)	0	4 (0.4)
直腸炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
偽性ポリポーシス	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
直腸異形成	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
直腸出血	4 (0.7)	1 (0.4)	5 (0.9)	0	0	0	0	5 (0.5)
直腸ポリープ	1 (0.2)	0	1 (0.2)	0	0	0	2 (0.7)	3 (0.3)
直腸しぶり	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
口内炎	5 (0.9)	1 (0.4)	6 (1.0)	0	0	0	0	6 (0.6)
舌障害	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
歯の障害	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
埋伏歯	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
胃腸障害 (Cont.)								
歯痛	3 (0.5)	5 (2.0)	8 (1.4)	0	0	1 (0.5)	3 (1.1)	12 (1.2)
臍ヘルニア	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
嘔吐	13 (2.3)	2 (0.8)	15 (2.6)	1 (2.0)	0	3 (1.6)	3 (1.1)	21 (2.0)
一般・全身障害および投与部位の状態	79 (13.8)	40 (16.1)	112 (19.5)	5 (9.8)	0	18 (9.5)	20 (7.4)	150 (14.5)
無力症	5 (0.9)	0	5 (0.9)	0	0	1 (0.5)	0	6 (0.6)
胸部不快感	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
胸痛	6 (1.0)	4 (1.6)	10 (1.7)	0	0	0	0	10 (1.0)
悪寒	6 (1.0)	2 (0.8)	8 (1.4)	1 (2.0)	0	1 (0.5)	2 (0.7)	11 (1.1)
異形成	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	1 (0.4)	4 (0.4)
疲労	26 (4.5)	11 (4.4)	36 (6.3)	1 (2.0)	0	6 (3.2)	4 (1.5)	46 (4.4)
異常感	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
体温変動感	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
一般・全身障害および投与部位の状態 (Cont.)								
高体温症	1 (0.2)	1 (0.4)	2 (0.3)	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)	4 (1.6)	11 (1.9)	0	0	0	1 (0.4)	12 (1.2)
注射部位疼痛	10 (1.7)	14 (5.6)	24 (4.2)	1 (2.0)	0	6 (3.2)	9 (3.3)	39 (3.8)
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	4 (0.7)	4 (1.6)	8 (1.4)	1 (2.0)	0	1 (0.5)	1 (0.4)	10 (1.0)
末梢性浮腫	5 (0.9)	2 (0.8)	7 (1.2)	0	0	0	0	7 (0.7)
疼痛	7 (1.2)	1 (0.4)	8 (1.4)	0	0	0	1 (0.4)	9 (0.9)
末梢腫脹	2 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
ポリープ	0	1 (0.4)	1 (0.2)	1 (2.0)	0	0	0	1 (<0.1)
偽ポリープ	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
発熱	26 (4.5)	10 (4.0)	35 (6.1)	3 (5.9)	0	6 (3.2)	7 (2.6)	48 (4.6)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
一般・全身障害および投与部位の状態 (Cont.)								
異物感	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
腫脹	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
顔面腫脹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
潰瘍	0	0	0	1 (2.0)	0	0	0	0
評価不能の事象	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
ワクチン接種部位疼痛	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
ワクチン接種部位反応	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
肝胆道系障害	16 (2.8)	4 (1.6)	20 (3.5)	0	0	4 (2.1)	2 (0.7)	26 (2.5)
胆道ジスキネジア	0	0	0	0	0	1 (0.5)	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 (0.4)
胆嚢炎	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
肝胆道系障害 (Cont.)								
胆石症	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
肝嚢胞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
肝機能異常	3 (0.5)	1 (0.4)	4 (0.7)	0	0	1 (0.5)	1 (0.4)	6 (0.6)
脂肪肝	3 (0.5)	2 (0.8)	5 (0.9)	0	0	2 (1.1)	0	7 (0.7)
肝細胞損傷	0	1 (0.4)	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	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
非アルコール性脂肪性肝疾患	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
免疫系障害	9 (1.6)	6 (2.4)	15 (2.6)	0	0	1 (0.5)	3 (1.1)	19 (1.8)
動物アレルギー	0	1 (0.4)	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 (0.4)	1 (<0.1)
薬物過敏症	0	2 (0.8)	2 (0.3)	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
免疫系障害 (Cont.)								
粉塵アレルギー	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
食物アレルギー	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
過敏症	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	0	3 (0.3)
ダニアレルギー	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
季節性アレルギー	6 (1.0)	2 (0.8)	8 (1.4)	0	0	1 (0.5)	1 (0.4)	10 (1.0)
感染症および寄生虫症	228 (39.7)	105 (42.2)	310 (54.0)	13 (25.5)	1 (100)	54 (28.4)	85 (31.3)	450 (43.4)
腹部膿瘍	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
腹壁膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
頸部膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
ダニ皮膚炎	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	0	3 (0.3)
急性副鼻腔炎	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
アデノウイルス感染	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.

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The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
歯槽骨炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
肛門膿瘍	1 (0.2)	3 (1.2)	4 (0.7)	0	0	1 (0.5)	3 (1.1)	8 (0.8)
虫垂炎	1 (0.2)	0	1 (0.2)	0	0	0	2 (0.7)	3 (0.3)
無症候性COVID-19	4 (0.7)	0	4 (0.7)	1 (2.0)	0	0	0	4 (0.4)
異型肺炎	0	1 (0.4)	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
細菌感染	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
細菌性膣症	0	1 (0.4)	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)
プ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	20 (3.5)	4 (1.6)	24 (4.2)	0	0	2 (1.1)	2 (0.7)	28 (2.7)
COVID-19	35 (6.1)	20 (8.0)	55 (9.6)	3 (5.9)	0	13 (6.8)	21 (7.7)	89 (8.6)
COVID-19肺炎	3 (0.5)	4 (1.6)	7 (1.2)	0	0	6 (3.2)	8 (2.9)	21 (2.0)

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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
カンピロバクター胃腸炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	1 (0.4)	3 (0.3)
カンピロバクター感染	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	0	3 (0.3)
カンジダ感染	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
蜂巣炎	5 (0.9)	0	5 (0.9)	0	0	2 (1.1)	2 (0.7)	9 (0.9)
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 (0.4)	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 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
クロストリジウム・ディフィシレ感染	5 (0.9)	4 (1.6)	9 (1.6)	0	0	0	2 (0.7)	11 (1.1)
結腸膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
結膜炎	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	1 (0.4)	5 (0.5)
ウイルス性結膜炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
コロナウイルス感染	1 (0.2)	1 (0.4)	2 (0.3)	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症 (Cont.)								
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	7 (1.2)	1 (0.4)	7 (1.2)	0	1 (100)	6 (3.2)	2 (0.7)	16 (1.5)
サイトメガロウイルス性大腸炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
サイトメガロウイルス感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
毛嚢虫症	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
感染性皮膚炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
爪の皮膚糸状菌症	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
医療機器関連敗血症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
感染性下痢	1 (0.2)	2 (0.8)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
憩室炎	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
耳感染	5 (0.9)	1 (0.4)	6 (1.0)	0	0	1 (0.5)	1 (0.4)	8 (0.8)
感染性腸炎	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症 (Cont.)								
丹毒	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
游走性紅斑	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
大腸菌感染	2 (0.3)	2 (0.8)	4 (0.7)	0	0	0	0	4 (0.4)
大腸菌性敗血症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
大腸菌性尿路感染	0	1 (0.4)	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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
毛包炎	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	1 (0.4)	5 (0.5)
皮膚真菌感染	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
せつ	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	2 (0.7)	4 (0.4)
胃腸炎	10 (1.7)	8 (3.2)	18 (3.1)	1 (2.0)	0	0	7 (2.6)	25 (2.4)
ウイルス性胃腸炎	7 (1.2)	1 (0.4)	8 (1.4)	0	0	0	1 (0.4)	9 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
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 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
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	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
陰部単純ヘルペス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
真菌性性器感染	0	1 (0.4)	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)
単径部膿瘍	1 (0.2)	0	1 (0.2)	1 (2.0)	0	0	0	1 (<0.1)
手足口病	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
ヘリコバクター性胃炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
ヘリコバクター感染	2 (0.3)	0	2 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
ヘルペス眼感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
単純ヘルペス	6 (1.0)	2 (0.8)	7 (1.2)	0	0	0	0	7 (0.7)
単純ヘルペス性咽頭炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
带状疱疹	32 (5.6)	16 (6.4)	47 (8.2)	1 (2.0)	0	6 (3.2)	9 (3.3)	62 (6.0)
神経合併症を伴う带状疱疹感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
耳带状疱疹	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
麦粒腫	4 (0.7)	3 (1.2)	7 (1.2)	0	0	1 (0.5)	0	8 (0.8)
膿痂疹	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
インフルエンザ	18 (3.1)	8 (3.2)	26 (4.5)	1 (2.0)	0	1 (0.5)	2 (0.7)	29 (2.8)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
クレブシエラ感染	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
大腸感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
喉頭炎	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	0	4 (0.4)
潜伏結核	7 (1.2)	1 (0.4)	8 (1.4)	0	0	2 (1.1)	2 (0.7)	12 (1.2)
限局性感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
下気道感染	4 (0.7)	0	4 (0.7)	0	0	0	0	4 (0.4)
ライム病	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
上咽頭炎	54 (9.4)	25 (10.0)	76 (13.2)	2 (3.9)	0	11 (5.8)	11 (4.0)	98 (9.5)
爪真菌症	4 (0.7)	1 (0.4)	5 (0.9)	0	0	3 (1.6)	0	8 (0.8)
口腔カンジダ症	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
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 (2.4)	14 (2.4)	1 (2.0)	0	1 (0.5)	6 (2.2)	21 (2.0)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症 (Cont.)								
精巣炎	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
骨髄炎	0	1 (0.4)	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)
中耳炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
爪囲炎	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
歯冠周囲炎	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
歯周炎	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	2 (0.7)	5 (0.5)
直腸周囲膿瘍	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
扁桃周囲炎	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
咽頭炎	2 (0.3)	2 (0.8)	4 (0.7)	1 (2.0)	0	1 (0.5)	2 (0.7)	7 (0.7)
毛巣嚢胞	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症 (Cont.)								
肺炎	6 (1.0)	6 (2.4)	12 (2.1)	0	0	0	0	12 (1.2)
細菌性肺炎	0	1 (0.4)	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)
術後創感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
歯髄炎	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
膿疱	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
腎盂腎炎	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
膿尿	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
膿疱性皮疹	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
直腸膿瘍	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
気道感染	4 (0.7)	2 (0.8)	6 (1.0)	0	0	1 (0.5)	0	7 (0.7)
ウイルス性気道感染	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	1 (0.4)	4 (0.4)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)					
感染症および寄生虫症 (Cont.)								
鼻炎	2 (0.3)	0	2 (0.3)	1 (2.0)	0	2 (1.1)	0	4 (0.4)
根管感染	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
敗血症	0	2 (0.8)	2 (0.3)	0	0	0	0	2 (0.2)
副鼻腔炎	13 (2.3)	6 (2.4)	19 (3.3)	1 (2.0)	0	2 (1.1)	4 (1.5)	25 (2.4)
皮膚感染	1 (0.2)	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
ブドウ球菌感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
レンサ球菌性尿路感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
皮下組織膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
細菌重複感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
股部白癬	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 (0.4)	1 (<0.1)
足部白癬	4 (0.7)	0	4 (0.7)	0	0	1 (0.5)	1 (0.4)	6 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症 (Cont.)								
扁桃炎	1 (0.2)	1 (0.4)	2 (0.3)	0	0	1 (0.5)	1 (0.4)	4 (0.4)
細菌性扁桃炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
歯膿瘍	3 (0.5)	2 (0.8)	5 (0.9)	0	0	0	2 (0.7)	7 (0.7)
歯感染	2 (0.3)	3 (1.2)	5 (0.9)	0	0	0	0	5 (0.5)
気管気管支炎	1 (0.2)	0	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	40 (7.0)	12 (4.8)	51 (8.9)	1 (2.0)	0	3 (1.6)	4 (1.5)	58 (5.6)
尿路感染	24 (4.2)	6 (2.4)	29 (5.1)	2 (3.9)	0	7 (3.7)	6 (2.2)	42 (4.1)
尿路性敗血症	0	0	0	0	1 (100)	0	0	1 (<0.1)
膣感染	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
ガードネレラ菌性膣炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
水痘	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
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 (0.3)	2 (0.8)	4 (0.7)	0	0	0	1 (0.4)	5 (0.5)
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 (1.2)	4 (0.7)	0	0	0	2 (0.7)	6 (0.6)
外陰部腔カンジダ症	3 (0.5)	0	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
外陰腔真菌感染	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
外陰腔炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
創傷感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
傷害、中毒および処置合併症	56 (9.8)	26 (10.4)	81 (14.1)	2 (3.9)	0	12 (6.3)	9 (3.3)	102 (9.8)
動物咬傷	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
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	2 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症 (Cont.)								
節足動物咬傷	1 (0.2)	2 (0.8)	3 (0.5)	0	0	1 (0.5)	1 (0.4)	5 (0.5)
骨挫傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
第2度熱傷	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
胸部損傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
挫傷	7 (1.2)	1 (0.4)	8 (1.4)	0	0	2 (1.1)	0	10 (1.0)
角膜擦過傷	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
上顎炎	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
眼外傷	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
転倒	8 (1.4)	4 (1.6)	12 (2.1)	0	0	0	0	12 (1.2)
腓骨骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
足骨折	5 (0.9)	2 (0.8)	7 (1.2)	0	0	2 (1.1)	1 (0.4)	10 (1.0)
骨折	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
傷害、中毒および処置合併症 (Cont.)								
仙骨骨折	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
手骨折	1 (0.2)	2 (0.8)	3 (0.5)	0	0	0	0	3 (0.3)
頭部損傷	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
熱射病	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
瘢痕ヘルニア	0	1 (0.4)	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)
企図の過量投与	0	0	0	0	0	1 (0.5)	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 (0.3)	0	2 (0.3)	0	0	1 (0.5)	0	3 (0.3)
靱帯断裂	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
靱帯捻挫	2 (0.3)	1 (0.4)	3 (0.5)	1 (2.0)	0	1 (0.5)	1 (0.4)	5 (0.5)
四肢損傷	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD/							
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症 (Cont.)								
つち指	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
半月板損傷	0	0	0	1 (2.0)	0	0	0	0
筋断裂	0	3 (1.2)	3 (0.5)	0	0	0	0	3 (0.3)
肉離れ	7 (1.2)	1 (0.4)	8 (1.4)	0	0	0	1 (0.4)	9 (0.9)
筋骨格内異物	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
過量投与	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
処置後血尿	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
処置後出血	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
外傷後頸部症候群	0	1 (0.4)	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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
傷害、中毒および処置合併症 (Cont.)								
術後イレウス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
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)	2 (0.8)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
肺挫傷	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
橈骨骨折	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
肋骨骨折	5 (0.9)	2 (0.8)	7 (1.2)	0	0	0	1 (0.4)	8 (0.8)
交通事故	2 (0.3)	1 (0.4)	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)
陰囊血腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
皮膚擦過傷	3 (0.5)	0	3 (0.5)	0	0	1 (0.5)	0	4 (0.4)
皮膚裂傷	4 (0.7)	2 (0.8)	6 (1.0)	0	0	0	0	6 (0.6)
軟部組織損傷	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
傷害、中毒および処置合併症 (Cont.)								
ストレス骨折	3 (0.5)	1 (0.4)	4 (0.7)	0	0	1 (0.5)	1 (0.4)	6 (0.6)
皮下血腫	2 (0.3)	0	2 (0.3)	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 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
脛骨骨折	1 (0.2)	1 (0.4)	2 (0.3)	0	0	1 (0.5)	0	3 (0.3)
歯牙破折	2 (0.3)	2 (0.8)	4 (0.7)	0	0	0	0	4 (0.4)
上肢骨折	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
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 (0.5)	0	1 (<0.1)
創合併症	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
傷害、中毒および処置合併症 (Cont.)								
手首関節骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
臨床検査	101 (17.6)	43 (17.3)	138 (24.0)	4 (7.8)	0	23 (12.1)	45 (16.5)	206 (19.9)
アラニンアミノトランスフェラーゼ増加	13 (2.3)	2 (0.8)	15 (2.6)	0	0	2 (1.1)	3 (1.1)	20 (1.9)
抗好中球細胞質抗体陽性	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
関節鏡検査	0	1 (0.4)	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	11 (1.9)	5 (2.0)	16 (2.8)	0	0	0	4 (1.5)	20 (1.9)
細菌検査陽性	1 (0.2)	0	1 (0.2)	1 (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	2 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
血中重炭酸塩減少	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
血中ビリルビン増加	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	2 (0.7)	4 (0.4)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査 (Cont.)								
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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
血中コレステロール増加	6 (1.0)	2 (0.8)	8 (1.4)	0	0	1 (0.5)	2 (0.7)	11 (1.1)
血中クレアチン増加	1 (0.2)	1 (0.4)	2 (0.3)	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	40 (7.0)	24 (9.6)	62 (10.8)	2 (3.9)	0	3 (1.6)	20 (7.4)	85 (8.2)
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 (0.4)	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)
血中铁減少	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
血中リン減少	1 (0.2)	0	1 (0.2)	0	0	0	2 (0.7)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査 (Cont.)								
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)
血圧上昇	3 (0.5)	0	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
血中トリグリセリド減少	0	1 (0.4)	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 (0.4)	5 (0.5)
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 (0.4)	2 (0.3)	0	0	0	2 (0.7)	4 (0.4)
骨密度減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
炭水化物耐性低下	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
心雑音	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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
臨床検査 (Cont.)								
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 (0.4)	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 (0.4)
γ-グルタミルトランスフェラーゼ増加	8 (1.4)	1 (0.4)	9 (1.6)	0	0	4 (2.1)	2 (0.7)	15 (1.4)
尿中ブドウ糖陽性	0	0	0	0	0	1 (0.5)	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 (0.8)	5 (0.9)	0	0	1 (0.5)	2 (0.7)	8 (0.8)
肝酵素上昇	5 (0.9)	2 (0.8)	7 (1.2)	0	0	2 (1.1)	2 (0.7)	11 (1.1)
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 (0.3)	1 (0.4)	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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
眼圧上昇	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査 (Cont.)								
臨床検査異常	0	1 (0.4)	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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
肝機能検査値上昇	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	1 (0.4)	4 (0.4)
低比重リボ蛋白減少	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
低比重リボ蛋白増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
リンパ球数減少	6 (1.0)	3 (1.2)	9 (1.6)	0	0	3 (1.6)	4 (1.5)	16 (1.5)
リンパ球百分率減少	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
平均赤血球容積増加	0	0	0	0	0	1 (0.5)	1 (0.4)	2 (0.2)
単球数増加	3 (0.5)	0	3 (0.5)	0	0	1 (0.5)	0	4 (0.4)
結核菌群検査陽性	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
好中球数減少	7 (1.2)	1 (0.4)	8 (1.4)	0	0	6 (3.2)	7 (2.6)	21 (2.0)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
臨床検査 (Cont.)								
好中球数増加	5 (0.9)	0	5 (0.9)	0	0	2 (1.1)	1 (0.4)	8 (0.8)
尿中亜硝酸塩陽性	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
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 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
尿蛋白	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
尿中蛋白陽性	2 (0.3)	0	2 (0.3)	0	0	2 (1.1)	1 (0.4)	5 (0.5)
赤血球数減少	4 (0.7)	0	4 (0.7)	0	0	0	2 (0.7)	6 (0.6)
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 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
血清フェリチン減少	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
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	3 (0.5)	0	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)

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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	(N=1037) n (%)
臨床検査 (Cont.)								
トランスフェリン増加	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
尿検査異常	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
尿中ケトン体陽性	2 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
尿中白血球エステラーゼ陽性	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	0	4 (0.4)
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)
ビタミンD増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
体重減少	0	2 (0.8)	2 (0.3)	0	0	1 (0.5)	0	3 (0.3)
体重増加	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
白血球数減少	9 (1.6)	1 (0.4)	10 (1.7)	1 (2.0)	0	4 (2.1)	7 (2.6)	21 (2.0)
白血球数増加	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
尿中白血球陽性	2 (0.3)	2 (0.8)	4 (0.7)	0	0	1 (0.5)	1 (0.4)	6 (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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	(N=1037) n (%)
代謝および栄養障害	50 (8.7)	15 (6.0)	65 (11.3)	2 (3.9)	0	17 (8.9)	15 (5.5)	97 (9.4)
食欲障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
乳製品不耐症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
食欲減退	3 (0.5)	0	3 (0.5)	0	0	1 (0.5)	1 (0.4)	5 (0.5)
脱水	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
糖尿病	0	0	0	1 (2.0)	0	0	2 (0.7)	2 (0.2)
脂質異常症	2 (0.3)	0	2 (0.3)	0	0	2 (1.1)	0	4 (0.4)
葉酸欠乏	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	0	3 (0.3)
耐糖能障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
痛風	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
ヒスタミン不耐性	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
高コレステロール血症	11 (1.9)	3 (1.2)	14 (2.4)	0	0	3 (1.6)	6 (2.2)	23 (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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	(N=1037) n (%)
代謝および栄養障害 (Cont.)								
高血糖	7 (1.2)	0	7 (1.2)	1 (2.0)	0	2 (1.1)	0	9 (0.9)
高ホモシステイン血症	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
高脂血症	7 (1.2)	1 (0.4)	8 (1.4)	0	0	5 (2.6)	4 (1.5)	17 (1.6)
高ナトリウム血症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
高トリグリセリド血症	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
高尿酸血症	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
低アルブミン血症	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
低カリウム血症	3 (0.5)	0	3 (0.5)	0	0	1 (0.5)	0	4 (0.4)
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 (1.2)	6 (1.0)	0	0	0	0	6 (0.6)
低蛋白血症	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
代謝および栄養障害 (Cont.)								
鉄欠乏	4 (0.7)	2 (0.8)	6 (1.0)	0	0	0	0	6 (0.6)
ラクトース不耐性	1 (0.2)	1 (0.4)	2 (0.3)	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	1 (0.5)	0	2 (0.2)
肥満	0	0	0	0	0	0	2 (0.7)	2 (0.2)
テタニー	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
2型糖尿病	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
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	6 (1.0)	1 (0.4)	7 (1.2)	0	0	1 (0.5)	2 (0.7)	10 (1.0)
筋骨格系および結合組織障害	109 (19.0)	53 (21.3)	153 (26.7)	9 (17.6)	0	31 (16.3)	24 (8.8)	208 (20.1)
関節痛	33 (5.7)	24 (9.6)	57 (9.9)	3 (5.9)	0	7 (3.7)	8 (2.9)	72 (6.9)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
筋骨格系および結合組織障害 (Cont.)								
関節炎	4 (0.7)	2 (0.8)	6 (1.0)	0	0	0	0	6 (0.6)
関節障害	8 (1.4)	1 (0.4)	9 (1.6)	0	0	5 (2.6)	2 (0.7)	16 (1.5)
腋窩腫瘍	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
背部痛	20 (3.5)	10 (4.0)	30 (5.2)	3 (5.9)	0	2 (1.1)	2 (0.7)	34 (3.3)
滑液包炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	1 (0.4)	3 (0.3)
軟骨萎縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
頸部脊柱管狭窄症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
ばち状指	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 (0.4)	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 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
筋骨格系および結合組織障害 (Cont.)								
外骨腫	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
四肢拘縮	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
側腹部痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
肱径部痛	2 (0.3)	0	2 (0.3)	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	7 (1.2)	2 (0.8)	9 (1.6)	1 (2.0)	0	3 (1.6)	2 (0.7)	14 (1.4)
関節滲出液	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
関節硬直	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
関節腫脹	2 (0.3)	0	2 (0.3)	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 (0.4)	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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
筋骨格系および結合組織障害 (Cont.)								
筋拘縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
筋痙縮	6 (1.0)	3 (1.2)	9 (1.6)	1 (2.0)	0	3 (1.6)	1 (0.4)	13 (1.3)
筋攣縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
筋骨格系胸痛	1 (0.2)	1 (0.4)	2 (0.3)	0	0	2 (1.1)	0	4 (0.4)
筋骨格痛	5 (0.9)	4 (1.6)	9 (1.6)	0	0	0	0	9 (0.9)
筋骨格硬直	4 (0.7)	1 (0.4)	5 (0.9)	1 (2.0)	0	0	0	5 (0.5)
筋肉痛	18 (3.1)	7 (2.8)	25 (4.4)	0	0	4 (2.1)	4 (1.5)	33 (3.2)
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)
頸部痛	2 (0.3)	5 (2.0)	7 (1.2)	0	0	1 (0.5)	0	8 (0.8)
変形性関節症	3 (0.5)	1 (0.4)	4 (0.7)	0	0	2 (1.1)	0	6 (0.6)
骨端症	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
筋骨格系および結合組織障害 (Cont.)								
骨壊死	2 (0.3)	1 (0.4)	3 (0.5)	0	0	1 (0.5)	0	4 (0.4)
骨減少症	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
骨粗鬆症	1 (0.2)	3 (1.2)	4 (0.7)	0	0	0	0	4 (0.4)
四肢痛	10 (1.7)	10 (4.0)	19 (3.3)	2 (3.9)	0	3 (1.6)	5 (1.8)	27 (2.6)
顎痛	2 (0.3)	0	2 (0.3)	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 (0.5)	0	1 (<0.1)
足底筋膜炎	5 (0.9)	2 (0.8)	7 (1.2)	0	0	1 (0.5)	1 (0.4)	9 (0.9)
横紋筋融解症	1 (0.2)	1 (0.4)	2 (0.3)	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	1 (0.4)	2 (0.2)
軟部組織腫瘍	0	1 (0.4)	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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
筋骨格系および結合組織障害 (Cont.)								
変形性脊椎症	2 (0.3)	2 (0.8)	4 (0.7)	0	0	0	0	4 (0.4)
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	1 (0.5)	1 (0.4)	3 (0.3)
軟骨下機能不全骨折	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
滑膜炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
顎関節症候群	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
腱炎	3 (0.5)	0	3 (0.5)	0	0	1 (0.5)	1 (0.4)	5 (0.5)
狭窄性腱鞘炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
弾発指	0	1 (0.4)	1 (0.2)	0	0	1 (0.5)	0	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)	22 (3.8)	14 (5.6)	35 (6.1)	3 (5.9)	0	7 (3.7)	9 (3.3)	51 (4.9)
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 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む）（Cont.）								
膵腺癌	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
エナメル上皮腫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
血管肉腫	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
肛門性器疣贅	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
基底細胞癌	2 (0.3)	3 (1.2)	5 (0.9)	0	0	0	2 (0.7)	7 (0.7)
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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
ボーエン病	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
乳癌	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
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)	2 (3.9)	0	0	1 (0.4)	5 (0.5)
線維腫	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) 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.）								
線維性組織球腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
血管腫	0	0	0	0	0	1 (0.5)	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 (0.4)	1 (<0.1)
メラノサイト性母斑	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
髄膜腫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
皮膚骨腫	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
前立腺癌	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
直腸腺腫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
脂漏性角化症	1 (0.2)	1 (0.4)	2 (0.3)	1 (2.0)	0	0	1 (0.4)	3 (0.3)
皮膚乳頭腫	5 (0.9)	3 (1.2)	8 (1.4)	0	0	1 (0.5)	1 (0.4)	10 (1.0)
扁平上皮癌	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む） (Cont.)								
皮膚有棘細胞癌	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
子宮頸部扁平上皮癌	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
舌扁平上皮癌	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
精巣（純粹）セミノーマ	0	1 (0.4)	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	2 (0.3)	0	2 (0.3)	0	0	2 (1.1)	0	4 (0.4)
神経系障害	68 (11.8)	35 (14.1)	100 (17.4)	2 (3.9)	0	13 (6.8)	17 (6.3)	130 (12.5)
健忘	0	1 (0.4)	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)
頸動脈硬化症	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
神経系障害 (Cont.)								
手根管症候群	1 (0.2)	2 (0.8)	3 (0.5)	0	0	1 (0.5)	0	4 (0.4)
大脳障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
頸髄圧迫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
頸髄神経根障害	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
注意力障害	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
浮動性めまい	7 (1.2)	4 (1.6)	11 (1.9)	0	0	4 (2.1)	1 (0.4)	16 (1.5)
異常感覚	0	1 (0.4)	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	35 (6.1)	14 (5.6)	48 (8.4)	2 (3.9)	0	7 (3.7)	7 (2.6)	62 (6.0)
知覚過敏	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
感覚鈍麻	3 (0.5)	3 (1.2)	6 (1.0)	0	0	0	1 (0.4)	7 (0.7)
ラクナ梗塞	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	(N=1037) n (%)
神経系障害 (Cont.)								
記憶障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
片頭痛	8 (1.4)	3 (1.2)	11 (1.9)	0	0	3 (1.6)	0	14 (1.4)
前兆を伴う片頭痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
脊髄症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
神経痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
神経炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
末梢性ニューロパチー	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
後頭神経痛	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
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)	3 (1.2)	6 (1.0)	0	0	0	0	6 (0.6)
睡眠の質低下	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
失神寸前の状態	0	1 (0.4)	1 (0.2)	0	0	0	2 (0.7)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
神経系障害 (Cont.)								
回内筋症候群	0	1 (0.4)	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 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
坐骨神経痛	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	3 (1.1)	7 (0.7)
発作様現象	0	1 (0.4)	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)
傾眠	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
会話障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
失神	3 (0.5)	3 (1.2)	6 (1.0)	0	0	0	1 (0.4)	7 (0.7)
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 (0.4)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
妊娠、産褥および周産期の状態	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
自然流産	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
精神障害	33 (5.7)	11 (4.4)	43 (7.5)	3 (5.9)	0	7 (3.7)	7 (2.6)	57 (5.5)
急性ストレス反応	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
不安	11 (1.9)	2 (0.8)	13 (2.3)	1 (2.0)	0	5 (2.6)	2 (0.7)	20 (1.9)
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)
双極1型障害	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
双極性障害	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
抑うつ気分	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
うつ病	10 (1.7)	1 (0.4)	11 (1.9)	0	0	2 (1.1)	3 (1.1)	16 (1.5)
薬物依存	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
全般性不安障害	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	(N=1037) n (%)
精神障害 (Cont.)								
不眠症	12 (2.1)	5 (2.0)	16 (2.8)	1 (2.0)	0	3 (1.6)	2 (0.7)	21 (2.0)
故意の自傷行為	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
気分変化	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
心的外傷後ストレス障害	0	1 (0.4)	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 (2.0)	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 (0.5)	0	1 (<0.1)
自殺企図	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
腎および尿路障害	31 (5.4)	18 (7.2)	48 (8.4)	2 (3.9)	0	2 (1.1)	5 (1.8)	55 (5.3)
急性腎障害	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
腎および尿路障害 (Cont.)								
膀胱タンポナーデ	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
膀胱結石	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
尿路結石	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
非感染性膀胱炎	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
排尿困難	8 (1.4)	4 (1.6)	11 (1.9)	0	0	1 (0.5)	0	12 (1.2)
血尿	2 (0.3)	4 (1.6)	6 (1.0)	0	0	0	0	6 (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 (2.0)	0	0	0	0
尿意切迫	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
腎炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
腎結石症	4 (0.7)	5 (2.0)	9 (1.6)	0	0	0	0	9 (0.9)
夜間頻尿	3 (0.5)	0	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
腎および尿路障害 (Cont.)								
頻尿	0	0	0	1 (2.0)	0	0	0	0
多尿	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
蛋白尿	6 (1.0)	1 (0.4)	7 (1.2)	1 (2.0)	0	1 (0.5)	3 (1.1)	11 (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)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
腎嚢胞	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
腎機能障害	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	0	3 (0.3)
腎尿細管機能障害	0	1 (0.4)	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 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
生殖系および乳房障害	17 (3.0)	7 (2.8)	24 (4.2)	0	0	7 (3.7)	4 (1.5)	35 (3.4)
無月経	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)					
生殖系および乳房障害 (Cont.)								
萎縮性外陰陰炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
良性前立腺肥大症	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	1 (0.4)	4 (0.4)
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)
子宮頸部上皮異形成	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
子宮頸部障害	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
子宮頸部の炎症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
性交出血	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
月経困難症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
性交困難	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
子宮内膜症	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
生殖系および乳房障害 (Cont.)								
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 (0.4)	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)
月経過多	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
不規則月経	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
不正子宮出血	0	0	0	0	0	1 (0.5)	1 (0.4)	2 (0.2)
卵巣嚢胞	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
閉経後出血	0	0	0	0	0	0	1 (0.4)	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 (0.8)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
精液変色	0	1 (0.4)	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.

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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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) 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)
膣出血	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
外陰膣不快感	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
外陰膣の炎症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
外陰膣そう痒症	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	70 (12.2)	25 (10.0)	94 (16.4)	0	0	14 (7.4)	11 (4.0)	119 (11.5)
喘息	4 (0.7)	1 (0.4)	5 (0.9)	0	0	0	0	5 (0.5)
無気肺	1 (0.2)	1 (0.4)	2 (0.3)	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	21 (3.7)	4 (1.6)	25 (4.4)	0	0	6 (3.2)	1 (0.4)	32 (3.1)
発声障害	2 (0.3)	0	2 (0.3)	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 SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害 (Cont.)								
呼吸困難	9 (1.6)	1 (0.4)	10 (1.7)	0	0	1 (0.5)	0	11 (1.1)
鼻出血	2 (0.3)	3 (1.2)	5 (0.9)	0	0	3 (1.6)	2 (0.7)	10 (1.0)
過換気	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
鼻閉	2 (0.3)	4 (1.6)	6 (1.0)	0	0	0	0	6 (0.6)
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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
鼻中隔穿孔	1 (0.2)	0	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 (0.5)	0	1 (<0.1)
口腔咽頭不快感	0	1 (0.4)	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
口腔咽頭痛	20 (3.5)	3 (1.2)	23 (4.0)	0	0	3 (1.6)	1 (0.4)	27 (2.6)
呼吸時疼痛	0	1 (0.4)	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 SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)								
胸水	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	0	4 (0.4)
胸膜痛	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
湿性咳嗽	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
肺塞栓症	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	4 (1.5)	7 (0.7)
肺腫瘍	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
逆流性咽喉炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
アレルギー性鼻炎	2 (0.3)	3 (1.2)	5 (0.9)	0	0	1 (0.5)	0	6 (0.6)
鼻漏	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
副鼻腔うっ血	2 (0.3)	1 (0.4)	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	6 (1.0)	1 (0.4)	7 (1.2)	0	0	1 (0.5)	0	8 (0.8)
咽喉刺激感	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)								
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 (0.4)	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 (0.8)	3 (0.5)	0	0	0	0	3 (0.3)
喘鳴	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
皮膚および皮下組織障害	94 (16.4)	41 (16.5)	130 (22.6)	5 (9.8)	0	23 (12.1)	25 (9.2)	178 (17.2)
ざ瘡	15 (2.6)	7 (2.8)	22 (3.8)	0	0	6 (3.2)	6 (2.2)	34 (3.3)
嚢胞性ざ瘡	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
光線性弾性線維症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
光線角化症	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	2 (0.7)	6 (0.6)
脱毛症	9 (1.6)	2 (0.8)	11 (1.9)	0	0	1 (0.5)	1 (0.4)	13 (1.3)
円形脱毛症	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
皮膚および皮下組織障害 (Cont.)								
水疱	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
皮膚囊腫	2 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
皮膚炎	3 (0.5)	1 (0.4)	4 (0.7)	1 (2.0)	0	0	0	4 (0.4)
ざ瘡様皮膚炎	3 (0.5)	1 (0.4)	4 (0.7)	0	0	1 (0.5)	1 (0.4)	6 (0.6)
アレルギー性皮膚炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
アトピー性皮膚炎	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
接触皮膚炎	4 (0.7)	0	4 (0.7)	0	0	1 (0.5)	0	5 (0.5)
剥脱性皮膚炎	0	1 (0.4)	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 (0.3)	3 (1.2)	5 (0.9)	0	0	0	0	5 (0.5)
異汗性湿疹	1 (0.2)	0	1 (0.2)	0	0	0	2 (0.7)	3 (0.3)
斑状出血	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
皮膚および皮下組織障害 (Cont.)								
湿疹	9 (1.6)	5 (2.0)	14 (2.4)	0	0	3 (1.6)	1 (0.4)	18 (1.7)
皮脂欠乏性湿疹	1 (0.2)	0	1 (0.2)	0	0	0	2 (0.7)	3 (0.3)
紅斑	5 (0.9)	0	5 (0.9)	0	0	0	2 (0.7)	7 (0.7)
環状紅斑	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
多汗症	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
過角化	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
嵌入爪	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
間擦疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
毛孔性角化症	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
黒子	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
扁平苔癬	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
汗疹	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
皮膚および皮下組織障害 (Cont.)								
爪床の炎症	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
爪肥厚	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
神経皮膚炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
寝汗	3 (0.5)	1 (0.4)	4 (0.7)	0	0	2 (1.1)	1 (0.4)	7 (0.7)
爪破損	0	1 (0.4)	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 (0.4)	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 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
点状出血	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
光線過敏性反応	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
そう痒症	7 (1.2)	5 (2.0)	12 (2.1)	1 (2.0)	0	1 (0.5)	2 (0.7)	15 (1.4)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
皮膚および皮下組織障害 (Cont.)								
乾癬	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
発疹	19 (3.3)	10 (4.0)	28 (4.9)	1 (2.0)	0	4 (2.1)	4 (1.5)	36 (3.5)
紅斑性皮疹	1 (0.2)	2 (0.8)	3 (0.5)	0	0	1 (0.5)	0	4 (0.4)
毛孔性皮疹	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
斑状皮疹	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
斑状丘疹状皮疹	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
丘疹性皮疹	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
そう痒性皮疹	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
酒さ	5 (0.9)	2 (0.8)	7 (1.2)	0	0	1 (0.5)	0	8 (0.8)
脂腺過形成	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
脂漏性皮膚炎	0	2 (0.8)	2 (0.3)	0	0	0	0	2 (0.2)
皮膚変色	1 (0.2)	1 (0.4)	2 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
皮膚および皮下組織障害 (Cont.)								
皮膚不快感	0	0	0	0	0	1 (0.5)	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)	2 (0.8)	6 (1.0)	0	0	0	2 (0.7)	8 (0.8)
皮膚腫瘍	0	0	0	1 (2.0)	0	0	0	0
皮膚潰瘍	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
蕁麻疹	1 (0.2)	1 (0.4)	2 (0.3)	1 (2.0)	0	2 (1.1)	1 (0.4)	5 (0.5)
乾皮症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
社会環境	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
閉経	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
閉経後	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
外科および内科処置	3 (0.5)	2 (0.8)	5 (0.9)	0	0	2 (1.1)	3 (1.1)	10 (1.0)
歯科インプラント埋込み	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
外科および内科処置 (Cont.)								
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	2 (0.3)	1 (0.4)	3 (0.5)	0	0	1 (0.5)	1 (0.4)	5 (0.5)
智歯抜歯	1 (0.2)	1 (0.4)	2 (0.3)	0	0	1 (0.5)	1 (0.4)	4 (0.4)
血管障害	30 (5.2)	11 (4.4)	41 (7.1)	4 (7.8)	0	7 (3.7)	5 (1.8)	53 (5.1)
大動脈硬化症	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
動脈硬化症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
コントロール不良の血圧	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
深部静脈血栓症	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	1 (0.4)	5 (0.5)
本態性高血圧症	2 (0.3)	0	2 (0.3)	1 (2.0)	0	0	0	2 (0.2)
出血	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
ほてり	4 (0.7)	0	4 (0.7)	0	0	0	0	4 (0.4)
高血圧	18 (3.1)	10 (4.0)	28 (4.9)	1 (2.0)	0	4 (2.1)	2 (0.7)	34 (3.3)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
血管障害 (Cont.)								
高血圧クリーゼ	1 (0.2)	0	1 (0.2)	1 (2.0)	0	0	0	1 (<0.1)
末梢静脈疾患	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
静脈炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
レイノー現象	1 (0.2)	0	1 (0.2)	1 (2.0)	0	1 (0.5)	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 (0.4)	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.

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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-----			-----SA 2 Population-----				--SA UPA--	
	UPA 15 mg QD/ UPA 15 mg QD			UPA 15 mg QD				All UPA	
	(N=574) (PYs=821.6) Events (E/100 PYs)	(N=249) (PYs=348.5) Events (E/100 PYs)	(N=574) (PYs=1170.1) Events (E/100 PYs)	(N=51) (PYs=45.8) Events (E/100 PYs)	(N=1) (PYs=2.8) Events (E/100 PYs)	(N=190) (PYs=200.6) Events (E/100 PYs)	(N=272) (PYs=238.1) Events (E/100 PYs)	(N=1037) (PYs=1611.6) Events (E/100 PYs)	
Any adverse event	2302 (280.2)	958 (274.9)	3260 (278.6)	100 (218.3)	2 (71.4)	475 (236.8)	556 (233.5)	4293 (266.4)	
血液およびリンパ系障害	66 (8.0)	25 (7.2)	91 (7.8)	5 (10.9)	0	14 (7.0)	26 (10.9)	131 (8.1)	
貧血	26 (3.2)	5 (1.4)	31 (2.6)	1 (2.2)	0	5 (2.5)	5 (2.1)	41 (2.5)	
大球性貧血	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)	
周期性好中球減少症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)	
顆粒球減少症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)	
内出血発生の増加傾向	1 (0.1)	1 (0.3)	2 (0.2)	1 (2.2)	0	0	1 (0.4)	3 (0.2)	
鉄欠乏性貧血	3 (0.4)	3 (0.9)	6 (0.5)	0	0	2 (1.0)	0	8 (0.5)	
白血球増加症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)	

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
MedDRA 23.0 System Organ Class Preferred Term								
血液およびリンパ系障害 (Cont.)								
白血球減少症	5 (0.6)	3 (0.9)	8 (0.7)	1 (2.2)	0	3 (1.5)	8 (3.4)	19 (1.2)
リンパ節症	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)
リンパ球増加症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
リンパ球減少症	10 (1.2)	5 (1.4)	15 (1.3)	0	0	1 (0.5)	2 (0.8)	18 (1.1)
小球性貧血	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
好中球減少症	11 (1.3)	5 (1.4)	16 (1.4)	2 (4.4)	0	1 (0.5)	7 (2.9)	24 (1.5)
好中球増加症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
汎血球減少症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
網状赤血球増加症	1 (0.1)	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.

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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---
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)								
血小板増加症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
心臓障害	17 (2.1)	8 (2.3)	25 (2.1)	1 (2.2)	0	4 (2.0)	7 (2.9)	36 (2.2)
急性心筋梗塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
不安定狭心症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
不整脈	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
心房細動	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
完全房室ブロック	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
第一度房室ブロック	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
徐脈性不整脈	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
心臓障害 (Cont.)								
徐脈	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
脚ブロック	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
左脚ブロック	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
心拡大	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
うっ血性心筋症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
冠動脈疾患	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
期外収縮	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
虚血性心筋症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
心筋梗塞	1 (0.1)	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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
心臟障害 (Cont.)								
動悸	3 (0.4)	0	3 (0.3)	1 (2.2)	0	0	0	3 (0.2)
心囊液貯留	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
心膜炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
上室性期外收縮	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
上室性頻脈	0	0	0	0	0	2 (1.0)	0	2 (0.1)
頻脈	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
心室性期外收縮	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	2 (0.8)	4 (0.2)
心室性頻脈	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
	UPA 15 mg QD	UPA 30 mg QD	Total	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
先天性、家族性および遺伝性障害	4 (0.5)	0	4 (0.3)	0	0	2 (1.0)	1 (0.4)	7 (0.4)
先天性横隔膜ヘルニア	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ジルベール症候群	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
陰嚢水腫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
魚鱗癬	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
歯原性嚢胞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
包茎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
汗孔角化症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
耳および迷路障害	13 (1.6)	5 (1.4)	18 (1.5)	0	0	3 (1.5)	8 (3.4)	29 (1.8)
伝音難聴	1 (0.1)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
耳および迷路障害 (Cont.)								
耳痛	3 (0.4)	1 (0.3)	4 (0.3)	0	0	1 (0.5)	0	5 (0.3)
外耳の炎症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
聴力低下	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
内耳障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
メニエール病	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
耳漏	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
突発性難聴	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
耳鳴	4 (0.5)	1 (0.3)	5 (0.4)	0	0	0	3 (1.3)	8 (0.5)
回転性めまい	4 (0.5)	1 (0.3)	5 (0.4)	0	0	2 (1.0)	2 (0.8)	9 (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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
内分泌障害	5 (0.6)	2 (0.6)	7 (0.6)	0	0	0	0	7 (0.4)
アジソン病	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
副腎機能不全	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
急性副腎皮質機能不全	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
クッシング様症状	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
甲状腺腫	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
甲状腺機能亢進症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
甲状腺腫瘍	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
眼障害	30 (3.7)	10 (2.9)	40 (3.4)	6 (13.1)	0	5 (2.5)	9 (3.8)	54 (3.4)
無水晶体眼	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
眼精疲労	0	0	0	1 (2.2)	0	0	0	0
眼瞼炎	4 (0.5)	1 (0.3)	5 (0.4)	0	0	0	0	5 (0.3)
眼瞼痙攣	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
白内障	7 (0.9)	0	7 (0.6)	0	0	2 (1.0)	1 (0.4)	10 (0.6)
霰粒腫	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
結膜嚢胞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
結膜出血	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
結膜充血	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
眼障害 (Cont.)								
アレルギー性結膜炎	1 (0.1)	1 (0.3)	2 (0.2)	1 (2.2)	0	0	1 (0.4)	3 (0.2)
結膜弛緩症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
角膜浮腫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
後天性涙道狭窄	1 (0.1)	0	1 (<0.1)	1 (2.2)	0	0	0	1 (<0.1)
ドライアイ	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	1 (0.4)	5 (0.3)
上強膜炎	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
眼刺激	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
眼痛	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
眼瞼嚢胞	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
眼障害 (Cont.)								
緑内障	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
角膜炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
黄斑浮腫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
近視	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
眼充血	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
開放隅角緑内障	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
網膜静脈閉塞	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
ぶどう膜炎	1 (0.1)	0	1 (<0.1)	1 (2.2)	0	0	1 (0.4)	2 (0.1)
霧視	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
眼障害 (Cont.)								
視力低下	0	0	0	2 (4.4)	0	0	0	0
視力障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
硝子体浮遊物	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
胃腸障害	378 (46.0)	139 (39.9)	517 (44.2)	18 (39.3)	0	64 (31.9)	60 (25.2)	641 (39.8)
腹部不快感	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
腹部膨満	4 (0.5)	5 (1.4)	9 (0.8)	1 (2.2)	0	1 (0.5)	2 (0.8)	12 (0.7)
腹部ヘルニア	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
腹痛	21 (2.6)	3 (0.9)	24 (2.1)	0	0	5 (2.5)	4 (1.7)	33 (2.0)
下腹部痛	7 (0.9)	0	7 (0.6)	0	0	0	0	7 (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.

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The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
上腹部痛	7 (0.9)	2 (0.6)	9 (0.8)	1 (2.2)	0	1 (0.5)	2 (0.8)	12 (0.7)
腹部圧痛	7 (0.9)	0	7 (0.6)	0	0	0	1 (0.4)	8 (0.5)
裂肛	5 (0.6)	1 (0.3)	6 (0.5)	0	0	0	0	6 (0.4)
痔瘻	3 (0.4)	0	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
肛門失禁	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肛門ポリープ	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
肛門そう痒症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
口角口唇炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
アフタ性潰瘍	5 (0.6)	3 (0.9)	8 (0.7)	0	0	1 (0.5)	0	9 (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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
口唇のひび割れ	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸炎	1 (0.1)	3 (0.9)	4 (0.3)	1 (2.2)	0	0	0	4 (0.2)
潰瘍性大腸炎	121 (14.7)	50 (14.3)	171 (14.6)	5 (10.9)	0	14 (7.0)	17 (7.1)	202 (12.5)
結腸異形成	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
便秘	10 (1.2)	3 (0.9)	13 (1.1)	1 (2.2)	0	6 (3.0)	4 (1.7)	23 (1.4)
クローン病	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
便意切迫	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	0	4 (0.2)
齲齒	4 (0.5)	2 (0.6)	6 (0.5)	0	0	1 (0.5)	1 (0.4)	8 (0.5)
歯組織の壊死	1 (0.1)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
下痢	21 (2.6)	5 (1.4)	26 (2.2)	1 (2.2)	0	2 (1.0)	2 (0.8)	30 (1.9)
血性下痢	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
腸憩室	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
十二指腸炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
消化不良	11 (1.3)	7 (2.0)	18 (1.5)	0	0	1 (0.5)	0	19 (1.2)
小腸炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
腸炎	1 (0.1)	0	1 (<0.1)	0	0	0	2 (0.8)	3 (0.2)
おくび	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
軟便	0	1 (0.3)	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.

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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---
	UPA 15 mg QD/ (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
大腿ヘルニア	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
鼓腸	8 (1.0)	2 (0.6)	10 (0.9)	0	0	2 (1.0)	0	12 (0.7)
食中毒	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
排便回数増加	1 (0.1)	2 (0.6)	3 (0.3)	0	0	2 (1.0)	0	5 (0.3)
胃障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
胃ポリープ	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
胃炎	6 (0.7)	1 (0.3)	7 (0.6)	1 (2.2)	0	0	0	7 (0.4)
胃腸障害	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
消化管運動障害	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
消化器痛	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
胃食道逆流性疾患	11 (1.3)	1 (0.3)	12 (1.0)	2 (4.4)	0	4 (2.0)	1 (0.4)	17 (1.1)
血便排泄	2 (0.2)	0	2 (0.2)	1 (2.2)	0	0	0	2 (0.1)
痔出血	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
痔核	9 (1.1)	3 (0.9)	12 (1.0)	0	0	4 (2.0)	3 (1.3)	19 (1.2)
血栓性痔核	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
裂孔ヘルニア	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
イレウス	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
炎症性腸疾患	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
単径ヘルニア	0	2 (0.6)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
腸閉塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腸管ポリープ	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
過敏性腸症候群	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
大腸穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	10 (1.2)	2 (0.6)	12 (1.0)	2 (4.4)	0	1 (0.5)	3 (1.3)	16 (1.0)
口唇障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
口唇潰瘍	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
口腔内潰瘍形成	4 (0.5)	1 (0.3)	5 (0.4)	0	0	1 (0.5)	0	6 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
悪心	29 (3.5)	12 (3.4)	41 (3.5)	1 (2.2)	0	6 (3.0)	4 (1.7)	51 (3.2)
食道運動低下	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
食道痛	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
口腔知覚不全	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
口腔扁平苔癬	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
膵炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
歯周病	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肛門周囲痛	3 (0.4)	0	3 (0.3)	0	0	1 (0.5)	0	4 (0.2)
直腸炎	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
偽性ポリポーシス	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
直腸異形成	0	0	0	0	0	2 (1.0)	0	2 (0.1)
直腸出血	4 (0.5)	2 (0.6)	6 (0.5)	0	0	0	0	6 (0.4)
直腸ポリープ	1 (0.1)	0	1 (<0.1)	0	0	0	2 (0.8)	3 (0.2)
直腸しぶり	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
口内炎	5 (0.6)	1 (0.3)	6 (0.5)	0	0	0	0	6 (0.4)
舌障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
歯の障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
埋伏歯	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
歯痛	3 (0.4)	5 (1.4)	8 (0.7)	0	0	1 (0.5)	3 (1.3)	12 (0.7)
臍ヘルニア	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
嘔吐	15 (1.8)	2 (0.6)	17 (1.5)	1 (2.2)	0	3 (1.5)	3 (1.3)	23 (1.4)
一般・全身障害および投与部位の状態	148 (18.0)	74 (21.2)	222 (19.0)	10 (21.8)	0	32 (16.0)	39 (16.4)	293 (18.2)
無力症	5 (0.6)	0	5 (0.4)	0	0	1 (0.5)	0	6 (0.4)
胸部不快感	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
胸痛	7 (0.9)	4 (1.1)	11 (0.9)	0	0	0	0	11 (0.7)
悪寒	8 (1.0)	2 (0.6)	10 (0.9)	1 (2.2)	0	2 (1.0)	2 (0.8)	14 (0.9)
異形成	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	1 (0.4)	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
疲労	34 (4.1)	14 (4.0)	48 (4.1)	1 (2.2)	0	6 (3.0)	7 (2.9)	61 (3.8)
異常感	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
体温変動感	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
高体温症	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)
治癒不良	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
インフルエンザ様疾患	9 (1.1)	4 (1.1)	13 (1.1)	0	0	0	1 (0.4)	14 (0.9)
注射部位疼痛	17 (2.1)	24 (6.9)	41 (3.5)	2 (4.4)	0	9 (4.5)	13 (5.5)	63 (3.9)
医療機器関連損傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
倦怠感	5 (0.6)	5 (1.4)	10 (0.9)	1 (2.2)	0	2 (1.0)	1 (0.4)	13 (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.

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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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
末梢性浮腫	5 (0.6)	2 (0.6)	7 (0.6)	0	0	0	0	7 (0.4)
疼痛	9 (1.1)	1 (0.3)	10 (0.9)	0	0	0	1 (0.4)	11 (0.7)
末梢腫脹	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
ポリープ	0	1 (0.3)	1 (<0.1)	1 (2.2)	0	0	0	1 (<0.1)
偽ポリープ	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
発熱	36 (4.4)	12 (3.4)	48 (4.1)	3 (6.6)	0	7 (3.5)	11 (4.6)	66 (4.1)
異物感	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腫脹	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
顔面腫脹	1 (0.1)	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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
潰瘍	0	0	0	1 (2.2)	0	0	0	0
評価不能の事象	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
ワクチン接種部位疼痛	0	2 (0.6)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
ワクチン接種部位反応	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
肝胆道系障害	21 (2.6)	5 (1.4)	26 (2.2)	0	0	4 (2.0)	3 (1.3)	33 (2.0)
胆道ジスキネジア	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
胆汁性嚢胞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
硬化性胆管炎	4 (0.5)	0	4 (0.3)	0	0	0	0	4 (0.2)
胆嚢炎	0	0	0	0	0	0	1 (0.4)	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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
肝胆道系障害 (Cont.)								
胆石症	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
肝嚢胞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肝機能異常	4 (0.5)	1 (0.3)	5 (0.4)	0	0	1 (0.5)	1 (0.4)	7 (0.4)
脂肪肝	3 (0.4)	3 (0.9)	6 (0.5)	0	0	2 (1.0)	0	8 (0.5)
肝細胞損傷	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肝腫大	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肝障害	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
非アルコール性脂肪性肝疾患	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
免疫系障害	9 (1.1)	9 (2.6)	18 (1.5)	0	0	1 (0.5)	3 (1.3)	22 (1.4)
動物アレルギー	0	1 (0.3)	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 (0.4)	1 (<0.1)
薬物過敏症	0	2 (0.6)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
粉塵アレルギー	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
食物アレルギー	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
過敏症	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
ダニアレルギー	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
季節性アレルギー	6 (0.7)	3 (0.9)	9 (0.8)	0	0	1 (0.5)	1 (0.4)	11 (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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
感染症および寄生虫症	549 (66.8)	223 (64.0)	772 (66.0)	19 (41.5)	2 (71.4)	104 (51.8)	142 (59.6)	1020 (63.3)
腹部膿瘍	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
腹壁膿瘍	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頸部膿瘍	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ダニ皮膚炎	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
急性副鼻腔炎	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
アデノウイルス感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
歯槽骨炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肛門膿瘍	1 (0.1)	3 (0.9)	4 (0.3)	0	0	1 (0.5)	3 (1.3)	8 (0.5)
虫垂炎	1 (0.1)	0	1 (<0.1)	0	0	0	2 (0.8)	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
無症候性COVID-19	4 (0.5)	0	4 (0.3)	1 (2.2)	0	0	0	4 (0.2)
異型肺炎	0	1 (0.3)	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
細菌感染	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
細菌性陰症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
バルトリン腺炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ブラストシスティス感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
気管支炎	26 (3.2)	5 (1.4)	31 (2.6)	0	0	2 (1.0)	2 (0.8)	35 (2.2)
COVID-19	36 (4.4)	20 (5.7)	56 (4.8)	3 (6.6)	0	13 (6.5)	24 (10.1)	93 (5.8)
COVID-19肺炎	3 (0.4)	4 (1.1)	7 (0.6)	0	0	6 (3.0)	8 (3.4)	21 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
カンピロバクター胃腸炎	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	1 (0.4)	3 (0.2)
カンピロバクター感染	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
カンジダ感染	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
蜂巣炎	5 (0.6)	0	5 (0.4)	0	0	4 (2.0)	2 (0.8)	11 (0.7)
感染性胆嚢炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
慢性副鼻腔炎	0	1 (0.3)	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 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
クロストリジウム・ディフィシレ感染	6 (0.7)	8 (2.3)	14 (1.2)	0	0	0	2 (0.8)	16 (1.0)
結腸膿瘍	1 (0.1)	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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
MedDRA 23.0 System Organ Class Preferred Term								
感染症および寄生虫症 (Cont.)								
結膜炎	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	1 (0.4)	5 (0.3)
ウイルス性結膜炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
コロナウイルス感染	1 (0.1)	1 (0.3)	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)
サイクロスポリジウム感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
膀胱炎	14 (1.7)	3 (0.9)	17 (1.5)	0	1 (35.7)	6 (3.0)	3 (1.3)	27 (1.7)
サイトメガロウイルス性大腸炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
サイトメガロウイルス感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
毛嚢虫症	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
感染性皮膚炎	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
爪の皮膚糸状菌症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
医療機器関連敗血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
感染性下痢	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
憩室炎	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
耳感染	5 (0.6)	2 (0.6)	7 (0.6)	0	0	1 (0.5)	1 (0.4)	9 (0.6)
感染性腸炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
丹毒	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
游走性紅斑	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸菌感染	2 (0.2)	2 (0.6)	4 (0.3)	0	0	0	0	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
大腸菌性敗血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸菌性尿路感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
眼感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
眼瞼感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
毛包炎	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	1 (0.4)	5 (0.3)
皮膚真菌感染	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
せつ	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	2 (0.8)	4 (0.2)
胃腸炎	10 (1.2)	8 (2.3)	18 (1.5)	1 (2.2)	0	0	8 (3.4)	26 (1.6)
ウイルス性胃腸炎	7 (0.9)	1 (0.3)	8 (0.7)	0	0	0	1 (0.4)	9 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
消化管内細菌過剰増殖	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
消化管感染	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
性器カンジダ症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
陰部ヘルペス	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
陰部単純ヘルペス	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
真菌性生殖器感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
歯肉膿瘍	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
歯肉炎	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
単径部膿瘍	1 (0.1)	0	1 (<0.1)	1 (2.2)	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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
手足口病	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
ヘリコバクター性胃炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ヘリコバクター感染	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
ヘルペス眼感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
単純ヘルペス	10 (1.2)	2 (0.6)	12 (1.0)	0	0	0	0	12 (0.7)
単純ヘルペス性咽頭炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
帯状疱疹	35 (4.3)	16 (4.6)	51 (4.4)	2 (4.4)	0	6 (3.0)	9 (3.8)	66 (4.1)
神経合併症を伴う帯状疱疹感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
耳帯状疱疹	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
麦粒腫	4 (0.5)	4 (1.1)	8 (0.7)	0	0	1 (0.5)	0	9 (0.6)
膿痂疹	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
感染性嚢腫	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
伝染性単核症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
インフルエンザ	21 (2.6)	9 (2.6)	30 (2.6)	1 (2.2)	0	1 (0.5)	2 (0.8)	33 (2.0)
クレブシエラ感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
喉頭炎	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	0	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
MedDRA 23.0 System Organ Class Preferred Term								
感染症および寄生虫症 (Cont.)								
潜伏結核	7 (0.9)	1 (0.3)	8 (0.7)	0	0	2 (1.0)	2 (0.8)	12 (0.7)
限局性感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
下気道感染	4 (0.5)	0	4 (0.3)	0	0	0	0	4 (0.2)
ライム病	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
上咽頭炎	71 (8.6)	31 (8.9)	102 (8.7)	2 (4.4)	0	13 (6.5)	11 (4.6)	126 (7.8)
爪真菌症	4 (0.5)	1 (0.3)	5 (0.4)	0	0	3 (1.5)	0	8 (0.5)
口腔カンジダ症	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
口腔真菌感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
口腔ヘルペス	37 (4.5)	9 (2.6)	46 (3.9)	1 (2.2)	0	1 (0.5)	10 (4.2)	57 (3.5)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
精巣炎	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
骨髓炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
外耳炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
中耳炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
爪囲炎	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
歯冠周囲炎	0	0	0	0	0	2 (1.0)	0	2 (0.1)
歯周炎	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	2 (0.8)	5 (0.3)
直腸周囲膿瘍	0	0	0	0	0	2 (1.0)	0	2 (0.1)
扁桃周囲炎	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
咽頭炎	3 (0.4)	2 (0.6)	5 (0.4)	1 (2.2)	0	1 (0.5)	2 (0.8)	8 (0.5)
毛巣嚢胞	0	4 (1.1)	4 (0.3)	0	0	0	0	4 (0.2)
ニューモシスチス・イロベチイ感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肺炎	8 (1.0)	6 (1.7)	14 (1.2)	0	0	0	0	14 (0.9)
細菌性肺炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ウイルス性肺炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
術後創感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
歯髄炎	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
膿疱	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD (N=574) (N=249) Total (PYs=821.6) (PYs=348.5) (PYs=1170.1)			Placebo (N=51) (PYs=45.8)	UPA 7.5 mg QD (N=1) (PYs=2.8)	UPA 15 mg QD (N=190) (PYs=200.6)	UPA 30 mg QD (N=272) (PYs=238.1)	All UPA (N=1037) (PYs=1611.6)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
腎盂腎炎	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
膿尿	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
膿疱性皮疹	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
直腸膿瘍	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
気道感染	5 (0.6)	2 (0.6)	7 (0.6)	0	0	1 (0.5)	0	8 (0.5)
ウイルス性気道感染	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	1 (0.4)	4 (0.2)
鼻炎	2 (0.2)	0	2 (0.2)	1 (2.2)	0	2 (1.0)	0	4 (0.2)
根管感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
敗血症	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
副鼻腔炎	16 (1.9)	6 (1.7)	22 (1.9)	1 (2.2)	0	2 (1.0)	4 (1.7)	28 (1.7)
皮膚感染	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
ブドウ球菌感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
レンサ球菌性尿路感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
皮下組織膿瘍	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
細菌重複感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
股部白癬	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
白癬感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
足部白癬	4 (0.5)	0	4 (0.3)	0	0	1 (0.5)	1 (0.4)	6 (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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD (N=574) (N=249) (PYs=821.6) (PYs=348.5) Events (E/100 PYs)			Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
MedDRA 23.0 System Organ Class Preferred Term			Total (N=574) (PYs=1170.1) Events (E/100 PYs)					
感染症および寄生虫症 (Cont.)								
扁桃炎	1 (0.1)	1 (0.3)	2 (0.2)	0	0	1 (0.5)	1 (0.4)	4 (0.2)
細菌性扁桃炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
歯膿瘍	3 (0.4)	2 (0.6)	5 (0.4)	0	0	0	2 (0.8)	7 (0.4)
歯感染	2 (0.2)	3 (0.9)	5 (0.4)	0	0	0	0	5 (0.3)
気管気管支炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
結核	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
上気道感染	62 (7.5)	15 (4.3)	77 (6.6)	1 (2.2)	0	13 (6.5)	4 (1.7)	94 (5.8)
尿路感染	27 (3.3)	6 (1.7)	33 (2.8)	3 (6.6)	0	7 (3.5)	6 (2.5)	46 (2.9)
尿路性敗血症	0	0	0	0	1 (35.7)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
膣感染	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
ガードネレラ菌性膣炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
水痘	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ウイルス性下痢	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ウイルス感染	2 (0.2)	2 (0.6)	4 (0.3)	0	0	0	1 (0.4)	5 (0.3)
ウイルス性咽頭炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ウイルス性上気道感染	1 (0.1)	3 (0.9)	4 (0.3)	0	0	0	2 (0.8)	6 (0.4)
外陰部膣カンジダ症	4 (0.5)	0	4 (0.3)	0	0	0	3 (1.3)	7 (0.4)
外陰膣真菌感染	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
外陰膺炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
創傷感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
傷害、中毒および処置合併症	92 (11.2)	44 (12.6)	136 (11.6)	2 (4.4)	0	18 (9.0)	12 (5.0)	166 (10.3)
動物咬傷	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
動物による引っかき傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
足関節部骨折	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
節足動物咬傷	1 (0.1)	2 (0.6)	3 (0.3)	0	0	1 (0.5)	1 (0.4)	5 (0.3)
骨挫傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
第2度熱傷	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
胸部損傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
挫傷	7 (0.9)	1 (0.3)	8 (0.7)	0	0	3 (1.5)	0	11 (0.7)
角膜擦過傷	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
上顎炎	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
眼外傷	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
転倒	9 (1.1)	6 (1.7)	15 (1.3)	0	0	0	0	15 (0.9)
腓骨骨折	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
足骨折	6 (0.7)	2 (0.6)	8 (0.7)	0	0	2 (1.0)	1 (0.4)	11 (0.7)
骨折	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)			--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)	
傷害、中毒および処置合併症 (Cont.)								
仙骨骨折	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
手骨折	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)
頭部損傷	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
熱射病	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
癰疽ヘルニア	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
損傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
企図の過量投与	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
関節脱臼	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
関節損傷	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)			--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)	
傷害、中毒および処置合併症 (Cont.)								
靱帯断裂	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
靱帯捻挫	2 (0.2)	1 (0.3)	3 (0.3)	1 (2.2)	0	1 (0.5)	1 (0.4)	5 (0.3)
四肢損傷	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
つち指	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
半月板損傷	0	0	0	1 (2.2)	0	0	0	0
筋断裂	0	4 (1.1)	4 (0.3)	0	0	0	0	4 (0.2)
肉離れ	7 (0.9)	1 (0.3)	8 (0.7)	0	0	0	1 (0.4)	9 (0.6)
筋骨格内異物	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
過量投与	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
膝蓋骨骨折	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
骨盤骨折	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
処置後血尿	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
処置後出血	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
外傷後頸部症候群	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
外傷後疼痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
術後イレウス	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
処置による腸管穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
処置による疼痛	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
肺挫傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
橈骨骨折	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
肋骨骨折	5 (0.6)	2 (0.6)	7 (0.6)	0	0	0	1 (0.4)	8 (0.5)
交通事故	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
癰疽	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
陰囊血腫	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
皮膚擦過傷	4 (0.5)	0	4 (0.3)	0	0	2 (1.0)	0	6 (0.4)
皮膚裂傷	4 (0.5)	2 (0.6)	6 (0.5)	0	0	0	0	6 (0.4)
軟部組織損傷	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
ストレス骨折	3 (0.4)	1 (0.3)	4 (0.3)	0	0	1 (0.5)	1 (0.4)	6 (0.4)
皮下血腫	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
腱損傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腱断裂	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
熱傷	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
脛骨骨折	1 (0.1)	1 (0.3)	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)
歯牙破折	2 (0.2)	2 (0.6)	4 (0.3)	0	0	0	0	4 (0.2)
上肢骨折	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮穿孔	1 (0.1)	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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
MedDRA 23.0 System Organ Class Preferred Term								
傷害、中毒および処置合併症 (Cont.)								
ワクチン接種合併症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
創傷	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
創合併症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
手首関節骨折	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
臨床検査	215 (26.2)	71 (20.4)	286 (24.4)	4 (8.7)	0	43 (21.4)	84 (35.3)	413 (25.6)
アラニンアミノトランスフェラーゼ増 加	16 (1.9)	2 (0.6)	18 (1.5)	0	0	2 (1.0)	3 (1.3)	23 (1.4)
抗好中球細胞質抗体陽性	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
関節鏡検査	0	1 (0.3)	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	13 (1.6)	5 (1.4)	18 (1.5)	0	0	0	4 (1.7)	22 (1.4)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD (N=574) (N=249) Total (PYs=821.6) (PYs=348.5) (PYs=1170.1)			Placebo (N=51) (PYs=45.8)	UPA 7.5 mg QD (N=1) (PYs=2.8)	UPA 15 mg QD (N=190) (PYs=200.6)	UPA 30 mg QD (N=272) (PYs=238.1)	All UPA (N=1037) (PYs=1611.6)
MedDRA 23.0 System Organ Class Preferred Term	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
臨床検査 (Cont.)								
細菌検査陽性	1 (0.1)	0	1 (<0.1)	1 (2.2)	0	0	0	1 (<0.1)
好塩基球数増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血中アルブミン増加	1 (0.1)	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	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
血中重炭酸塩減少	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
血中ビリルビン増加	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	5 (2.1)	7 (0.4)
血中カルシウム増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血中コレステロール減少	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
血中コレステロール増加	6 (0.7)	2 (0.6)	8 (0.7)	0	0	1 (0.5)	2 (0.8)	11 (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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
血中クレアチン増加	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
血中クレアチンホスホキナーゼMB増加	1 (0.1)	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	47 (5.7)	28 (8.0)	75 (6.4)	2 (4.4)	0	3 (1.5)	21 (8.8)	99 (6.1)
血中クレアチニン増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血中葉酸減少	1 (0.1)	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 (0.4)	1 (<0.1)
血中ブドウ糖増加	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
血中铁減少	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
血中リン減少	1 (0.1)	0	1 (<0.1)	0	0	0	2 (0.8)	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
血中カリウム減少	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血中カリウム増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血圧上昇	3 (0.4)	0	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
血中トリグリセリド減少	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
血中トリグリセリド増加	4 (0.5)	0	4 (0.3)	0	0	0	1 (0.4)	5 (0.3)
血中尿素増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
尿中血陽性	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	2 (0.8)	4 (0.2)
骨密度減少	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
炭水化物耐性低下	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
心雑音	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
クロストリジウム検査陽性	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
凝固時間延長	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
尿中結晶陽性	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
心電図QT延長	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
便中カルプロテクチン増加	4 (0.5)	0	4 (0.3)	0	0	0	0	4 (0.2)
γ-グルタミルトランスフェラーゼ増加	10 (1.2)	1 (0.3)	11 (0.9)	0	0	6 (3.0)	2 (0.8)	19 (1.2)
尿中ブドウ糖陽性	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
ヘマトクリット減少	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
ヘモグロビン減少	3 (0.4)	2 (0.6)	5 (0.4)	0	0	1 (0.5)	2 (0.8)	8 (0.5)
肝酵素上昇	6 (0.7)	2 (0.6)	8 (0.7)	0	0	2 (1.0)	3 (1.3)	13 (0.8)
B型肝炎DNA測定陽性	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
高比重リボ蛋白増加	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
ヒト乳頭腫ウイルス検査陽性	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
眼圧上昇	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
臨床検査異常	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
リパーゼ増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肝機能検査異常	0	1 (0.3)	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.

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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--
	UPA 15 mg QD/ (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
肝機能検査値上昇	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	1 (0.4)	4 (0.2)
低比重リボ蛋白減少	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
低比重リボ蛋白増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
リンパ球数減少	7 (0.9)	3 (0.9)	10 (0.9)	0	0	3 (1.5)	4 (1.7)	17 (1.1)
リンパ球百分率減少	0	0	0	0	0	0	2 (0.8)	2 (0.1)
平均赤血球容積増加	0	0	0	0	0	1 (0.5)	1 (0.4)	2 (0.1)
単球数増加	3 (0.4)	0	3 (0.3)	0	0	1 (0.5)	0	4 (0.2)
結核菌群検査陽性	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
好中球数減少	8 (1.0)	1 (0.3)	9 (0.8)	0	0	7 (3.5)	9 (3.8)	25 (1.6)

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.

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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--
	UPA 15 mg QD/ (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
好中球数増加	5 (0.6)	0	5 (0.4)	0	0	2 (1.0)	1 (0.4)	8 (0.5)
尿中亜硝酸塩陽性	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
血小板数減少	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血小板数増加	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
尿蛋白	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
尿中蛋白陽性	3 (0.4)	0	3 (0.3)	0	0	2 (1.0)	1 (0.4)	6 (0.4)
赤血球数減少	4 (0.5)	0	4 (0.3)	0	0	0	2 (0.8)	6 (0.4)
赤血球数増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
網状赤血球数増加	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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--
	UPA 15 mg QD/ (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
血清フェリチン減少	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
尿比重増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
トランスアミナーゼ上昇	3 (0.4)	0	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
トランスフェリン増加	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
尿検査異常	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
尿中ケトン体陽性	3 (0.4)	0	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
尿中白血球エステラーゼ陽性	4 (0.5)	1 (0.3)	5 (0.4)	0	0	0	0	5 (0.3)
尿量減少	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ビタミンB12減少	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
ビタミンD増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
体重減少	0	2 (0.6)	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)
体重増加	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
白血球数減少	9 (1.1)	1 (0.3)	10 (0.9)	1 (2.2)	0	5 (2.5)	7 (2.9)	22 (1.4)
白血球数増加	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
尿中白血球陽性	2 (0.2)	3 (0.9)	5 (0.4)	0	0	1 (0.5)	1 (0.4)	7 (0.4)
代謝および栄養障害	66 (8.0)	19 (5.5)	85 (7.3)	2 (4.4)	0	20 (10.0)	20 (8.4)	125 (7.8)
食欲障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
乳製品不耐症	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
食欲減退	3 (0.4)	0	3 (0.3)	0	0	1 (0.5)	1 (0.4)	5 (0.3)
脱水	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
糖尿病	0	0	0	1 (2.2)	0	0	2 (0.8)	2 (0.1)
脂質異常症	2 (0.2)	0	2 (0.2)	0	0	2 (1.0)	0	4 (0.2)
葉酸欠乏	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
耐糖能障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
痛風	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
ヒスタミン不耐性	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
高コレステロール血症	11 (1.3)	3 (0.9)	14 (1.2)	0	0	3 (1.5)	6 (2.5)	23 (1.4)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
高血糖	7 (0.9)	0	7 (0.6)	1 (2.2)	0	4 (2.0)	0	11 (0.7)
高ホモシステイン血症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
高脂血症	7 (0.9)	1 (0.3)	8 (0.7)	0	0	5 (2.5)	5 (2.1)	18 (1.1)
高ナトリウム血症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
高トリグリセリド血症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
高尿酸血症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
低アルブミン血症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
低カリウム血症	3 (0.4)	0	3 (0.3)	0	0	1 (0.5)	0	4 (0.2)
低マグネシウム血症	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
低ナトリウム血症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
低リン酸血症	3 (0.4)	4 (1.1)	7 (0.6)	0	0	0	0	7 (0.4)
低蛋白血症	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
鉄欠乏	4 (0.5)	2 (0.6)	6 (0.5)	0	0	0	0	6 (0.4)
ラクトース不耐性	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
代謝性アシドーシス	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
肥満	0	0	0	0	0	0	2 (0.8)	2 (0.1)
テタニー	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
2型糖尿病	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
過少体重	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ビタミンB群欠乏	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ビタミンB12欠乏	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ビタミンD欠乏	6 (0.7)	1 (0.3)	7 (0.6)	0	0	1 (0.5)	2 (0.8)	10 (0.6)
筋骨格系および結合組織障害	188 (22.9)	93 (26.7)	281 (24.0)	11 (24.0)	0	46 (22.9)	36 (15.1)	363 (22.5)
関節痛	42 (5.1)	27 (7.7)	69 (5.9)	3 (6.6)	0	7 (3.5)	13 (5.5)	89 (5.5)
関節炎	4 (0.5)	2 (0.6)	6 (0.5)	0	0	0	0	6 (0.4)
関節障害	8 (1.0)	1 (0.3)	9 (0.8)	0	0	5 (2.5)	2 (0.8)	16 (1.0)
腋窩腫瘍	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
背部痛	23 (2.8)	11 (3.2)	34 (2.9)	3 (6.6)	0	2 (1.0)	2 (0.8)	38 (2.4)
滑液包炎	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	1 (0.4)	4 (0.2)
軟骨萎縮	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頸部脊柱管狭窄症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ばち状指	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
尾骨痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
コンパートメント症候群	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
指炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腱付着部症	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
外骨腫	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
四肢拘縮	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
側腹部痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肱径部痛	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
椎間板変性症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
椎間板障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
椎間板突出	7 (0.9)	2 (0.6)	9 (0.8)	1 (2.2)	0	3 (1.5)	2 (0.8)	14 (0.9)
関節滲出液	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
関節硬直	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
関節腫脹	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
腰部脊柱管狭窄症	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
脛骨内側過労性症候群	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
筋拘縮	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
筋痙縮	7 (0.9)	3 (0.9)	10 (0.9)	1 (2.2)	0	3 (1.5)	1 (0.4)	14 (0.9)
筋攣縮	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
筋骨格系胸痛	1 (0.1)	1 (0.3)	2 (0.2)	0	0	3 (1.5)	0	5 (0.3)
筋骨格痛	5 (0.6)	4 (1.1)	9 (0.8)	0	0	0	0	9 (0.6)
筋骨格硬直	4 (0.5)	1 (0.3)	5 (0.4)	1 (2.2)	0	0	0	5 (0.3)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD (N=574) (N=249) (PYs=821.6) (PYs=348.5) Events (E/100 PYs)			Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
MedDRA 23.0 System Organ Class Preferred Term			Total (N=574) (PYs=1170.1) Events (E/100 PYs)					
筋骨格系および結合組織障害 (Cont.)								
筋肉痛	20 (2.4)	8 (2.3)	28 (2.4)	0	0	6 (3.0)	4 (1.7)	38 (2.4)
筋膜疼痛症候群	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ミオパチー	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頸部痛	2 (0.2)	5 (1.4)	7 (0.6)	0	0	1 (0.5)	0	8 (0.5)
変形性関節症	4 (0.5)	1 (0.3)	5 (0.4)	0	0	2 (1.0)	0	7 (0.4)
骨端症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
骨壊死	2 (0.2)	1 (0.3)	3 (0.3)	0	0	1 (0.5)	0	4 (0.2)
骨減少症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
骨粗鬆症	1 (0.1)	3 (0.9)	4 (0.3)	0	0	0	0	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
四肢痛	11 (1.3)	11 (3.2)	22 (1.9)	2 (4.4)	0	4 (2.0)	6 (2.5)	32 (2.0)
顎痛	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
膝蓋大腿関節痛症候群	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
関節周囲炎	0	0	0	0	0	2 (1.0)	0	2 (0.1)
足底筋膜炎	5 (0.6)	2 (0.6)	7 (0.6)	0	0	1 (0.5)	1 (0.4)	9 (0.6)
横紋筋融解症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
肩回旋筋腱板症候群	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
軟部組織腫瘍	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
脊柱変形	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
変形性脊椎症	2 (0.2)	2 (0.6)	4 (0.3)	0	0	0	0	4 (0.2)
脊椎炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脊椎関節障害	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	1 (0.4)	3 (0.2)
軟骨下機能不全骨折	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
滑膜炎	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
顎関節症候群	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
腱炎	3 (0.4)	0	3 (0.3)	0	0	1 (0.5)	1 (0.4)	5 (0.3)
狭窄性腱鞘炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
弾発指	0	1 (0.3)	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/							
	UPA 15 mg QD	UPA 30 mg QD	Total	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
Events	Events	Events	Events	Events	Events	Events	Events	
(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(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）	27 (3.3)	21 (6.0)	48 (4.1)	3 (6.6)	0	7 (3.5)	12 (5.0)	67 (4.2)
アクロコルドン	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
結腸腺癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
膵腺癌	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
エナメル上皮腫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
血管肉腫	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肛門性器疣贅	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
基底細胞癌	2 (0.2)	4 (1.1)	6 (0.5)	0	0	0	2 (0.8)	8 (0.5)
肺の良性新生物	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む） (Cont.)								
精巣の良性新生物	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ボーエン病	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
乳癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
気管支の良性新生物	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸腺腫	4 (0.5)	0	4 (0.3)	2 (4.4)	0	0	1 (0.4)	5 (0.3)
線維腫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
線維性組織球腫	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血管腫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
喉頭扁平上皮癌	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む） (Cont.)								
脂肪腫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
メラノサイト性母斑	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
髄膜腫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
皮膚骨腫	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
前立腺癌	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
直腸腺腫	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脂漏性角化症	1 (0.1)	1 (0.3)	2 (0.2)	1 (2.2)	0	0	1 (0.4)	3 (0.2)
皮膚乳頭腫	5 (0.6)	5 (1.4)	10 (0.9)	0	0	1 (0.5)	1 (0.4)	12 (0.7)
扁平上皮癌	1 (0.1)	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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む） (Cont.)								
皮膚有棘細胞癌	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
子宮頸部扁平上皮癌	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
舌扁平上皮癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精巣（純粹）セミノーマ	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精巣癌	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
甲状腺腺腫	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
子宮平滑筋腫	2 (0.2)	0	2 (0.2)	0	0	2 (1.0)	0	4 (0.2)
神経系障害	91 (11.1)	47 (13.5)	138 (11.8)	3 (6.6)	0	21 (10.5)	21 (8.8)	180 (11.2)
健忘	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
神経系障害 (Cont.)								
脳損傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
灼熱感	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頸動脈硬化症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
手根管症候群	1 (0.1)	3 (0.9)	4 (0.3)	0	0	1 (0.5)	0	5 (0.3)
大脳障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頸髄圧迫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
頸髄神経根障害	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
注意力障害	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
浮動性めまい	8 (1.0)	4 (1.1)	12 (1.0)	0	0	5 (2.5)	1 (0.4)	18 (1.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
神経系障害 (Cont.)								
異常感覚	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
構語障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頭痛	42 (5.1)	16 (4.6)	58 (5.0)	3 (6.6)	0	9 (4.5)	7 (2.9)	74 (4.6)
知覚過敏	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
感覚鈍麻	3 (0.4)	3 (0.9)	6 (0.5)	0	0	0	1 (0.4)	7 (0.4)
ラクナ梗塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
記憶障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
片頭痛	8 (1.0)	3 (0.9)	11 (0.9)	0	0	4 (2.0)	0	15 (0.9)
前兆を伴う片頭痛	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
神経系障害 (Cont.)								
脊髄症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
神経痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
神経炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
末梢性ニューロパチー	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
後頭神経痛	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
起立不耐性	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
錯感覚	3 (0.4)	3 (0.9)	6 (0.5)	0	0	0	0	6 (0.4)
睡眠の質低下	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
失神寸前の状態	0	1 (0.3)	1 (<0.1)	0	0	0	2 (0.8)	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
神経系障害 (Cont.)								
回内筋症候群	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
神経根痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
下肢静止不能症候群	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
坐骨神経痛	5 (0.6)	1 (0.3)	6 (0.5)	0	0	0	3 (1.3)	9 (0.6)
発作様現象	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
副鼻腔炎に伴う頭痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
傾眠	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
会話障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
失神	3 (0.4)	3 (0.9)	6 (0.5)	0	0	0	1 (0.4)	7 (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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
神経系障害 (Cont.)								
緊張性頭痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
視野欠損	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
妊娠、産褥および周産期の状態	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
自然流産	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精神障害	49 (6.0)	16 (4.6)	65 (5.6)	3 (6.6)	0	12 (6.0)	9 (3.8)	86 (5.3)
急性ストレス反応	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
不安	11 (1.3)	2 (0.6)	13 (1.1)	1 (2.2)	0	5 (2.5)	2 (0.8)	20 (1.2)
注意欠如・多動性障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
自閉症スペクトラム障害	1 (0.1)	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.

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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--
	UPA 15 mg QD/							
	UPA 15 mg QD	UPA 30 mg QD	Total	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
MedDRA 23.0 System Organ Class	Events	Events	Events	Events	Events	Events	Events	Events
Preferred Term	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
精神障害 (Cont.)								
双極1型障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
双極性障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
抑うつ気分	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
うつ病	17 (2.1)	1 (0.3)	18 (1.5)	0	0	2 (1.0)	3 (1.3)	23 (1.4)
薬物依存	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
全般性不安障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
不眠症	12 (1.5)	7 (2.0)	19 (1.6)	1 (2.2)	0	3 (1.5)	2 (0.8)	24 (1.5)
故意の自傷行為	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
気分変化	1 (0.1)	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.

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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.

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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--
	UPA 15 mg QD/ (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
精神障害 (Cont.)								
心的外傷後ストレス障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
落ち着きのなさ	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
睡眠障害	2 (0.2)	0	2 (0.2)	1 (2.2)	0	0	0	2 (0.1)
社交不安障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ストレス	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
自殺念慮	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
自殺企図	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
腎および尿路障害	37 (4.5)	24 (6.9)	61 (5.2)	3 (6.6)	0	4 (2.0)	5 (2.1)	70 (4.3)
急性腎障害	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/100PYs = Number of events per 100 patient-years.

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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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
腎および尿路障害 (Cont.)								
膀胱タンポナーデ	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
膀胱結石	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
尿路結石	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
非感染性膀胱炎	0	0	0	0	0	2 (1.0)	0	2 (0.1)
排尿困難	9 (1.1)	5 (1.4)	14 (1.2)	0	0	1 (0.5)	0	15 (0.9)
血尿	2 (0.2)	5 (1.4)	7 (0.6)	0	0	0	0	7 (0.4)
緊張性膀胱	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ケトン尿	0	0	0	1 (2.2)	0	0	0	0
尿意切迫	1 (0.1)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
腎および尿路障害 (Cont.)								
腎炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腎結石症	5 (0.6)	6 (1.7)	11 (0.9)	0	0	0	0	11 (0.7)
夜間頻尿	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
頻尿	0	0	0	1 (2.2)	0	0	0	0
多尿	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
蛋白尿	6 (0.7)	1 (0.3)	7 (0.6)	1 (2.2)	0	1 (0.5)	3 (1.3)	11 (0.7)
腎萎縮	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腎仙痛	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
腎嚢胞	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
腎および尿路障害 (Cont.)								
腎機能障害	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
腎尿細管機能障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
尿管閉塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
尿管結石症	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)
生殖系および乳房障害	21 (2.6)	10 (2.9)	31 (2.6)	0	0	8 (4.0)	4 (1.7)	43 (2.7)
無月経	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
萎縮性外陰膺炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
良性前立腺肥大症	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	1 (0.4)	4 (0.2)
乳房障害	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)								
乳房腫大	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
乳房腫瘍	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮頸部上皮異形成	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮頸部障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮頸部の炎症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
性交出血	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
月経困難症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
性交困難	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
子宮内膜症	0	0	0	0	0	1 (0.5)	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.

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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--
	UPA 15 mg QD/ (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)								
勃起不全	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
性器びらん	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
閉経期症状	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
月経過多	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
不規則月経	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
不正子宮出血	0	0	0	0	0	1 (0.5)	1 (0.4)	2 (0.1)
卵巣嚢胞	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
閉経後出血	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
月経前症候群	1 (0.1)	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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)								
前立腺炎	1 (0.1)	5 (1.4)	6 (0.5)	0	0	0	1 (0.4)	7 (0.4)
精液変色	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮ポリープ	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮脱	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
膣出血	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
外陰膣不快感	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
外陰膣の炎症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
外陰膣そう痒症	1 (0.1)	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.

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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.

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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/ UPA 15 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害	103 (12.5)	34 (9.8)	137 (11.7)	0	0	21 (10.5)	11 (4.6)	169 (10.5)
喘息	6 (0.7)	1 (0.3)	7 (0.6)	0	0	0	0	7 (0.4)
無気肺	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
気管支反応性亢進	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
慢性閉塞性肺疾患	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
咳嗽	23 (2.8)	5 (1.4)	28 (2.4)	0	0	6 (3.0)	1 (0.4)	35 (2.2)
発声障害	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
呼吸困難	10 (1.2)	1 (0.3)	11 (0.9)	0	0	1 (0.5)	0	12 (0.7)
鼻出血	2 (0.2)	3 (0.9)	5 (0.4)	0	0	3 (1.5)	2 (0.8)	10 (0.6)
過換気	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
鼻閉	2 (0.2)	5 (1.4)	7 (0.6)	0	0	0	0	7 (0.4)
鼻中隔弯曲	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
鼻中隔障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
鼻中隔穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
鼻甲介肥大	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
鼻潰瘍	0	0	0	0	0	2 (1.0)	0	2 (0.1)
口腔咽頭不快感	0	1 (0.3)	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
口腔咽頭痛	24 (2.9)	3 (0.9)	27 (2.3)	0	0	3 (1.5)	1 (0.4)	31 (1.9)
呼吸時疼痛	0	1 (0.3)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
胸水	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	0	4 (0.2)
胸膜痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
湿性咳嗽	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
肺塞栓症	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	4 (1.7)	7 (0.4)
肺腫瘍	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
逆流性喉頭炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
アレルギー性鼻炎	2 (0.2)	3 (0.9)	5 (0.4)	0	0	1 (0.5)	0	6 (0.4)
鼻漏	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
副鼻腔うっ血	2 (0.2)	3 (0.9)	5 (0.4)	0	0	0	0	5 (0.3)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
副鼻腔痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
睡眠時無呼吸症候群	6 (0.7)	1 (0.3)	7 (0.6)	0	0	1 (0.5)	0	8 (0.5)
咽喉刺激感	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
扁桃肥大	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
上気道うっ血	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
上気道の炎症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
上気道咳症候群	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)
喘鳴	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害	132 (16.1)	63 (18.1)	195 (16.7)	6 (13.1)	0	33 (16.5)	34 (14.3)	262 (16.3)
ざ瘡	16 (1.9)	7 (2.0)	23 (2.0)	0	0	6 (3.0)	6 (2.5)	35 (2.2)
嚢胞性ざ瘡	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
光線性弾性線維症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
光線角化症	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	2 (0.8)	6 (0.4)
脱毛症	10 (1.2)	2 (0.6)	12 (1.0)	0	0	1 (0.5)	2 (0.8)	15 (0.9)
円形脱毛症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
水疱	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
皮膚嚢腫	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
皮膚炎	3 (0.4)	1 (0.3)	4 (0.3)	1 (2.2)	0	0	0	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
ざ瘡様皮膚炎	3 (0.4)	1 (0.3)	4 (0.3)	0	0	1 (0.5)	1 (0.4)	6 (0.4)
アレルギー性皮膚炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
アトピー性皮膚炎	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
接触皮膚炎	4 (0.5)	0	4 (0.3)	0	0	1 (0.5)	0	5 (0.3)
剥脱性皮膚炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
薬疹	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
皮膚乾燥	2 (0.2)	3 (0.9)	5 (0.4)	0	0	0	0	5 (0.3)
異汗性湿疹	1 (0.1)	0	1 (<0.1)	0	0	0	2 (0.8)	3 (0.2)
斑状出血	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
湿疹	10 (1.2)	5 (1.4)	15 (1.3)	0	0	3 (1.5)	1 (0.4)	19 (1.2)
皮脂欠乏性湿疹	1 (0.1)	0	1 (<0.1)	0	0	0	3 (1.3)	4 (0.2)
紅斑	5 (0.6)	0	5 (0.4)	0	0	0	2 (0.8)	7 (0.4)
環状紅斑	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
多汗症	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
過角化	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
嵌入爪	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
間擦疹	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
毛孔性角化症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
黒子	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
扁平苔癬	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
汗疹	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)
爪床の炎症	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
爪肥厚	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
神経皮膚炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
寝汗	4 (0.5)	1 (0.3)	5 (0.4)	0	0	2 (1.0)	1 (0.4)	8 (0.5)
爪破損	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
爪甲剥離症	1 (0.1)	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.

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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--
	UPA 15 mg QD/ (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
脂肪織炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
丘疹	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
口囲皮膚炎	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
点状出血	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
光線過敏性反応	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
そう痒症	9 (1.1)	5 (1.4)	14 (1.2)	1 (2.2)	0	2 (1.0)	2 (0.8)	18 (1.1)
乾癬	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
発疹	20 (2.4)	12 (3.4)	32 (2.7)	2 (4.4)	0	5 (2.5)	4 (1.7)	41 (2.5)
紅斑性皮疹	1 (0.1)	3 (0.9)	4 (0.3)	0	0	1 (0.5)	0	5 (0.3)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
毛孔性皮疹	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
斑状皮疹	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
斑状丘疹状皮疹	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
丘疹性皮疹	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
そう痒性皮疹	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
酒さ	5 (0.6)	2 (0.6)	7 (0.6)	0	0	1 (0.5)	0	8 (0.5)
脂腺過形成	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
脂漏性皮膚炎	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)
皮膚変色	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
皮膚不快感	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
皮膚剥脱	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
皮膚病変	4 (0.5)	2 (0.6)	6 (0.5)	0	0	0	2 (0.8)	8 (0.5)
皮膚腫瘍	0	0	0	1 (2.2)	0	0	0	0
皮膚潰瘍	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
蕁麻疹	1 (0.1)	1 (0.3)	2 (0.2)	1 (2.2)	0	2 (1.0)	1 (0.4)	5 (0.3)
乾皮症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
社会環境	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
閉経	0	1 (0.3)	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.

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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--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
社会環境 (Cont.)								
閉経後	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
外科および内科処置	4 (0.5)	2 (0.6)	6 (0.5)	0	0	2 (1.0)	3 (1.3)	11 (0.7)
歯科インプラント埋込み	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
植込み型除細動器挿入	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
拔牙	2 (0.2)	1 (0.3)	3 (0.3)	0	0	1 (0.5)	1 (0.4)	5 (0.3)
智歯拔牙	1 (0.1)	1 (0.3)	2 (0.2)	0	0	1 (0.5)	1 (0.4)	4 (0.2)
血管障害	37 (4.5)	12 (3.4)	49 (4.2)	4 (8.7)	0	7 (3.5)	6 (2.5)	62 (3.8)
大動脈硬化症	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
動脈硬化症	1 (0.1)	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.

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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---
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
血管障害 (Cont.)								
コントロール不良の血圧	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
深部静脈血栓症	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	1 (0.4)	5 (0.3)
本態性高血圧症	2 (0.2)	0	2 (0.2)	1 (2.2)	0	0	0	2 (0.1)
出血	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ほてり	4 (0.5)	0	4 (0.3)	0	0	0	0	4 (0.2)
高血圧	20 (2.4)	11 (3.2)	31 (2.6)	1 (2.2)	0	4 (2.0)	3 (1.3)	38 (2.4)
高血圧クリーゼ	1 (0.1)	0	1 (<0.1)	1 (2.2)	0	0	0	1 (<0.1)
末梢静脈疾患	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
静脈炎	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
血管障害 (Cont.)								
レイノー現象	1 (0.1)	0	1 (<0.1)	1 (2.2)	0	1 (0.5)	0	2 (0.1)
静脈瘤	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
静脈血栓症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
白衣性高血圧	0	0	0	0	0	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All_UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
Any adverse event	193 (33.6)	104 (41.8)	264 (46.0)	13 (25.5)	0	36 (18.9)	71 (26.1)	371 (35.8)
血液およびリンパ系障害	20 (3.5)	13 (5.2)	32 (5.6)	3 (5.9)	0	6 (3.2)	9 (3.3)	47 (4.5)
貧血	6 (1.0)	0	6 (1.0)	1 (2.0)	0	1 (0.5)	2 (0.7)	9 (0.9)
周期性好中球減少症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
内出血発生の増加傾向	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
鉄欠乏性貧血	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
白血球増加症	0	1 (0.4)	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
白血球減少症	5 (0.9)	3 (1.2)	8 (1.4)	1 (2.0)	0	2 (1.1)	6 (2.2)	16 (1.5)
リンパ球増加症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
リンパ球減少症	9 (1.6)	4 (1.6)	12 (2.1)	0	0	1 (0.5)	1 (0.4)	14 (1.4)
好中球減少症	8 (1.4)	4 (1.6)	12 (2.1)	1 (2.0)	0	1 (0.5)	5 (1.8)	18 (1.7)
好中球増加症	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
血液およびリンパ系障害 (Cont.)								
汎血球減少症	0	0	0	0	0	0	1 (0.4)	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)
心臓障害	2 (0.3)	3 (1.2)	5 (0.9)	0	0	0	1 (0.4)	6 (0.6)
急性心筋梗塞	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 (0.4)	1 (<0.1)
期外収縮	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
動悸	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
心嚢液貯留	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
心膜炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
頻脈	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
耳および迷路障害	3 (0.5)	2 (0.8)	5 (0.9)	0	0	0	1 (0.4)	6 (0.6)
耳痛	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
耳および迷路障害 (Cont.)								
外耳の炎症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
内耳障害	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
メニエール病	0	0	0	0	0	0	1 (0.4)	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)
眼障害	0	2 (0.8)	2 (0.3)	2 (3.9)	0	0	0	2 (0.2)
眼精疲労	0	0	0	1 (2.0)	0	0	0	0
眼瞼炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
角膜炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
ぶどう膜炎	0	0	0	1 (2.0)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸障害	36 (6.3)	16 (6.4)	50 (8.7)	6 (11.8)	0	6 (3.2)	11 (4.0)	67 (6.5)
腹部膨満	1 (0.2)	0	1 (0.2)	1 (2.0)	0	0	0	1 (<0.1)
腹痛	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	0	3 (0.3)
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 (0.4)	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)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
大腸炎	1 (0.2)	2 (0.8)	3 (0.5)	0	0	0	0	3 (0.3)
潰瘍性大腸炎	13 (2.3)	7 (2.8)	19 (3.3)	2 (3.9)	0	1 (0.5)	5 (1.8)	25 (2.4)
結腸異形成	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
便秘	1 (0.2)	1 (0.4)	2 (0.3)	0	0	3 (1.6)	1 (0.4)	6 (0.6)
便意切迫	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸障害 (Cont.)								
下痢	3 (0.5)	1 (0.4)	4 (0.7)	1 (2.0)	0	0	0	4 (0.4)
大腿ヘルニア	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
鼓腸	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
胃炎	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
胃食道逆流性疾患	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
血便排泄	0	0	0	1 (2.0)	0	0	0	0
痔核	2 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
悪心	3 (0.5)	0	3 (0.5)	1 (2.0)	0	1 (0.5)	1 (0.4)	5 (0.5)
肺炎	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
胃腸障害 (Cont.)								
直腸出血	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
口内炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
歯痛	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
嘔吐	2 (0.3)	0	2 (0.3)	1 (2.0)	0	1 (0.5)	2 (0.7)	5 (0.5)
一般・全身障害および投与部位の状態	16 (2.8)	9 (3.6)	25 (4.4)	1 (2.0)	0	1 (0.5)	3 (1.1)	29 (2.8)
無力症	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
悪寒	1 (0.2)	1 (0.4)	2 (0.3)	1 (2.0)	0	1 (0.5)	1 (0.4)	4 (0.4)
疲労	4 (0.7)	1 (0.4)	5 (0.9)	0	0	0	1 (0.4)	6 (0.6)
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)	2 (0.8)	5 (0.9)	0	0	0	1 (0.4)	6 (0.6)
注射部位疼痛	0	1 (0.4)	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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
一般・全身障害および投与部位の状態 (Cont.)								
疼痛	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
末梢腫脹	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
発熱	4 (0.7)	4 (1.6)	8 (1.4)	1 (2.0)	0	0	0	8 (0.8)
評価不能の事象	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
肝胆道系障害	3 (0.5)	1 (0.4)	4 (0.7)	0	0	0	0	4 (0.4)
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 (0.4)	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	2 (0.8)	2 (0.3)	0	0	0	0	2 (0.2)
薬物過敏症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
過敏症	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症	101 (17.6)	44 (17.7)	137 (23.9)	5 (9.8)	0	15 (7.9)	28 (10.3)	180 (17.4)
腹部膿瘍	0	1 (0.4)	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)
急性副鼻腔炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
肛門膿瘍	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
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 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
細菌性腔症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
気管支炎	6 (1.0)	2 (0.8)	8 (1.4)	0	0	1 (0.5)	0	9 (0.9)
COVID-19	2 (0.3)	2 (0.8)	4 (0.7)	0	0	0	3 (1.1)	7 (0.7)
COVID-19肺炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	1 (0.4)	3 (0.3)
カンジダ感染	2 (0.3)	0	2 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
蜂巣炎	2 (0.3)	0	2 (0.3)	0	0	2 (1.1)	0	4 (0.4)
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 (0.4)	4 (0.7)	0	0	0	1 (0.4)	5 (0.5)
結膜炎	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
ウイルス性結膜炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
サイトメガロウイルス感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
毛嚢虫症	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
爪の皮膚糸状菌症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
感染性下痢	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
耳感染	2 (0.3)	0	2 (0.3)	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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症 (Cont.)								
毛包炎	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	1 (0.4)	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	1 (0.4)	1 (<0.1)
胃腸炎	0	2 (0.8)	2 (0.3)	1 (2.0)	0	0	0	2 (0.2)
ウイルス性胃腸炎	0	1 (0.4)	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)
陰部単純ヘルペス	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
真菌性生殖器感染	0	1 (0.4)	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)
単径部膿瘍	1 (0.2)	0	1 (0.2)	1 (2.0)	0	0	0	1 (<0.1)
手足口病	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
ヘルペス眼感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
単純ヘルペス	2 (0.3)	1 (0.4)	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)
带状疱疹	28 (4.9)	12 (4.8)	40 (7.0)	1 (2.0)	0	5 (2.6)	8 (2.9)	53 (5.1)
耳带状疱疹	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
麦粒腫	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
伝染性単核症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
インフルエンザ	5 (0.9)	1 (0.4)	6 (1.0)	1 (2.0)	0	0	0	6 (0.6)
潜伏結核	5 (0.9)	0	5 (0.9)	0	0	1 (0.5)	1 (0.4)	7 (0.7)
限局性感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
下気道感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
上咽頭炎	11 (1.9)	9 (3.6)	20 (3.5)	0	0	1 (0.5)	2 (0.7)	23 (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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
爪真菌症	2 (0.3)	0	2 (0.3)	0	0	2 (1.1)	0	4 (0.4)
口腔カンジダ症	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
口腔ヘルペス	3 (0.5)	3 (1.2)	6 (1.0)	1 (2.0)	0	0	1 (0.4)	7 (0.7)
精巣炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
中耳炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
爪囲炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
直腸周囲膿瘍	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
咽頭炎	0	2 (0.8)	2 (0.3)	1 (2.0)	0	0	0	2 (0.2)
肺炎	4 (0.7)	3 (1.2)	7 (1.2)	0	0	0	0	7 (0.7)
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)
直腸膿瘍	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD							
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
感染症および寄生虫症 (Cont.)								
気道感染	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
ウイルス性気道感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
鼻炎	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
根管感染	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
敗血症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
副鼻腔炎	6 (1.0)	1 (0.4)	7 (1.2)	0	0	0	0	7 (0.7)
皮膚感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
皮下組織膿瘍	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
股部白癬	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 (0.4)	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
歯膿瘍	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
感染症および寄生虫症 (Cont.)								
菌感染	0	1 (0.4)	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	26 (4.5)	6 (2.4)	32 (5.6)	1 (2.0)	0	1 (0.5)	2 (0.7)	35 (3.4)
尿路感染	8 (1.4)	2 (0.8)	9 (1.6)	1 (2.0)	0	2 (1.1)	0	11 (1.1)
膣感染	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
水痘	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
ウイルス感染	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
ウイルス性上気道感染	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
外陰部膣カンジダ症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
外陰膣真菌感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
傷害、中毒および処置合併症	2 (0.3)	2 (0.8)	4 (0.7)	0	0	0	0	4 (0.4)
筋断裂	0	2 (0.8)	2 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
傷害、中毒および処置合併症 (Cont.)								
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	63 (11.0)	29 (11.6)	89 (15.5)	3 (5.9)	0	6 (3.2)	29 (10.7)	124 (12.0)
アラニンアミノトランスフェラーゼ増加	9 (1.6)	2 (0.8)	11 (1.9)	0	0	0	2 (0.7)	13 (1.3)
アスパラギン酸アミノトランスフェラーゼ増加	8 (1.4)	4 (1.6)	12 (2.1)	0	0	0	3 (1.1)	15 (1.4)
細菌検査陽性	0	0	0	1 (2.0)	0	0	0	0
血中アルカリホスファターゼ増加	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
血中ビリルビン増加	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
血中コレステロール増加	4 (0.7)	1 (0.4)	5 (0.9)	0	0	0	1 (0.4)	6 (0.6)
血中クレアチンホスホキナーゼ増加	30 (5.2)	19 (7.6)	47 (8.2)	1 (2.0)	0	1 (0.5)	12 (4.4)	60 (5.8)
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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査 (Cont.)								
血圧上昇	2 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
血中トリグリセリド増加	3 (0.5)	0	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
尿中血陽性	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
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	3 (0.5)	0	3 (0.5)	0	0	0	2 (0.7)	5 (0.5)
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 (0.3)	1 (0.4)	3 (0.5)	0	0	0	1 (0.4)	4 (0.4)
肝酵素上昇	2 (0.3)	2 (0.8)	4 (0.7)	0	0	0	1 (0.4)	5 (0.5)
高比重リポ蛋白増加	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
臨床検査異常	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
肝機能検査異常	0	1 (0.4)	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 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査 (Cont.)								
低比重リボ蛋白増加	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
リンパ球数減少	4 (0.7)	3 (1.2)	7 (1.2)	0	0	2 (1.1)	4 (1.5)	13 (1.3)
リンパ球百分率減少	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
平均赤血球容積増加	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
好中球数減少	6 (1.0)	0	6 (1.0)	0	0	4 (2.1)	5 (1.8)	15 (1.4)
好中球数増加	2 (0.3)	0	2 (0.3)	0	0	2 (1.1)	1 (0.4)	5 (0.5)
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 (0.4)	1 (<0.1)
尿蛋白	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
尿中蛋白陽性	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
赤血球数減少	2 (0.3)	0	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
網状赤血球数増加	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査 (Cont.)								
トランスアミナーゼ上昇	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
尿中ケトン体陽性	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
尿中白血球エステラーゼ陽性	2 (0.3)	0	2 (0.3)	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	7 (1.2)	0	7 (1.2)	1 (2.0)	0	3 (1.6)	4 (1.5)	14 (1.4)
尿中白血球陽性	1 (0.2)	1 (0.4)	2 (0.3)	0	0	1 (0.5)	1 (0.4)	4 (0.4)
代謝および栄養障害	12 (2.1)	2 (0.8)	14 (2.4)	0	0	4 (2.1)	3 (1.1)	21 (2.0)
脂質異常症	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
痛風	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
高コレステロール血症	5 (0.9)	1 (0.4)	6 (1.0)	0	0	1 (0.5)	2 (0.7)	9 (0.9)
高血糖	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
高脂血症	2 (0.3)	0	2 (0.3)	0	0	2 (1.1)	0	4 (0.4)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
代謝および栄養障害 (Cont.)								
低リン酸血症	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
低蛋白血症	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
肥満	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
筋骨格系および結合組織障害	18 (3.1)	6 (2.4)	24 (4.2)	2 (3.9)	0	5 (2.6)	5 (1.8)	34 (3.3)
関節痛	5 (0.9)	3 (1.2)	8 (1.4)	2 (3.9)	0	2 (1.1)	3 (1.1)	13 (1.3)
関節障害	2 (0.3)	0	2 (0.3)	0	0	1 (0.5)	0	3 (0.3)
背部痛	2 (0.3)	1 (0.4)	3 (0.5)	0	0	1 (0.5)	0	4 (0.4)
指炎	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
四肢拘縮	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
筋拘縮	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
筋痙縮	1 (0.2)	0	1 (0.2)	0	0	1 (0.5)	0	2 (0.2)
筋骨格系胸痛	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
筋骨格系および結合組織障害 (Cont.)								
筋骨格痛	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
筋骨格硬直	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
筋肉痛	3 (0.5)	2 (0.8)	5 (0.9)	0	0	0	2 (0.7)	7 (0.7)
頸部痛	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
四肢痛	2 (0.3)	0	2 (0.3)	1 (2.0)	0	0	2 (0.7)	4 (0.4)
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 (0.5)	0	1 (<0.1)
足底筋膜炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
横紋筋融解症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
腱炎	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
良性、悪性および詳細不明の新生物 (嚢胞およびボリーブを含む)	1 (0.2)	7 (2.8)	8 (1.4)	0	0	0	2 (0.7)	10 (1.0)
血管肉腫	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
良性、悪性および詳細不明の新生物（囊胞およびポリープを含む） (Cont.)								
基底細胞癌	0	2 (0.8)	2 (0.3)	0	0	0	1 (0.4)	3 (0.3)
ボーエン病	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
皮膚乳頭腫	0	2 (0.8)	2 (0.3)	0	0	0	0	2 (0.2)
皮膚有棘細胞癌	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
舌扁平上皮癌	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
神経系障害	9 (1.6)	6 (2.4)	15 (2.6)	0	0	1 (0.5)	3 (1.1)	19 (1.8)
灼熱感	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
頸髄圧迫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
注意力障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
浮動性めまい	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)	2 (0.8)	7 (1.2)	0	0	1 (0.5)	2 (0.7)	10 (1.0)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
神経系障害 (Cont.)								
知覚過敏	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
感覚鈍麻	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
片頭痛	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
脊髄症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
錯感覚	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
会話障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
失神	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
視野欠損	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
精神障害	3 (0.5)	0	3 (0.5)	1 (2.0)	0	0	1 (0.4)	4 (0.4)
不安	3 (0.5)	0	3 (0.5)	0	0	0	0	3 (0.3)
うつ病	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
睡眠障害	0	0	0	1 (2.0)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
腎および尿路障害	7 (1.2)	5 (2.0)	11 (1.9)	1 (2.0)	0	0	3 (1.1)	14 (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 (0.8)	2 (0.3)	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 (2.0)	0	0	0	0
腎結石症	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
蛋白尿	2 (0.3)	1 (0.4)	3 (0.5)	1 (2.0)	0	0	3 (1.1)	6 (0.6)
腎仙痛	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
腎機能障害	2 (0.3)	0	2 (0.3)	0	0	0	0	2 (0.2)
生殖系および乳房障害	5 (0.9)	4 (1.6)	9 (1.6)	0	0	0	0	9 (0.9)
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)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
生殖系および乳房障害 (Cont.)								
性器びらん	0	1 (0.4)	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)
前立腺炎	1 (0.2)	2 (0.8)	3 (0.5)	0	0	0	0	3 (0.3)
精液変色	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
外陰腫そう痒症	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	16 (2.8)	5 (2.0)	21 (3.7)	0	0	1 (0.5)	4 (1.5)	26 (2.5)
咳嗽	5 (0.9)	0	5 (0.9)	0	0	1 (0.5)	1 (0.4)	7 (0.7)
鼻出血	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
鼻閉	0	2 (0.8)	2 (0.3)	0	0	0	0	2 (0.2)
鼻中隔穿孔	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
口腔咽頭痛	8 (1.4)	0	8 (1.4)	0	0	0	0	8 (0.8)
胸水	0	1 (0.4)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=574) n (%)	(N=249) n (%)	Total (N=574) n (%)	(N=51) n (%)	(N=1) n (%)	(N=190) n (%)	(N=272) n (%)	(N=1037) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)								
湿性咳嗽	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
肺塞栓症	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
肺腫瘍	0	0	0	0	0	1 (0.5)	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)
副鼻腔うっ血	2 (0.3)	1 (0.4)	3 (0.5)	0	0	0	0	3 (0.3)
上気道咳嗽症候群	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
皮膚および皮下組織障害	28 (4.9)	19 (7.6)	45 (7.8)	0	0	6 (3.2)	12 (4.4)	63 (6.1)
ざ瘡	3 (0.5)	4 (1.6)	7 (1.2)	0	0	5 (2.6)	3 (1.1)	15 (1.4)
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)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
脱毛症	4 (0.7)	2 (0.8)	6 (1.0)	0	0	0	0	6 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
皮膚および皮下組織障害 (Cont.)								
ざ瘡様皮膚炎	1 (0.2)	0	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
アレルギー性皮膚炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
アトピー性皮膚炎	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
剥脱性皮膚炎	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
皮膚乾燥	1 (0.2)	2 (0.8)	3 (0.5)	0	0	0	0	3 (0.3)
異汗性湿疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
湿疹	0	1 (0.4)	1 (0.2)	0	0	0	1 (0.4)	2 (0.2)
紅斑	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
環状紅斑	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
多汗症	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
間擦疹	1 (0.2)	0	1 (0.2)	0	0	0	0	1 (<0.1)
毛孔性角化症	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
皮膚および皮下組織障害 (Cont.)								
寝汗	0	0	0	0	0	1 (0.5)	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)	0	1 (0.2)	0	0	0	0	1 (<0.1)
光線過敏性反応	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
そう痒症	2 (0.3)	2 (0.8)	4 (0.7)	0	0	0	0	4 (0.4)
発疹	8 (1.4)	3 (1.2)	11 (1.9)	0	0	0	3 (1.1)	14 (1.4)
紅斑性皮疹	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
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 (0.4)	1 (<0.1)
丘疹性皮疹	1 (0.2)	1 (0.4)	2 (0.3)	0	0	0	0	2 (0.2)
そう痒性皮疹	0	1 (0.4)	1 (0.2)	0	0	0	0	1 (<0.1)
酒さ	1 (0.2)	1 (0.4)	2 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) n (%)	UPA 30 mg QD (N=249) n (%)	Total (N=574) n (%)	Placebo (N=51) n (%)	UPA 7.5 mg QD (N=1) n (%)	UPA 15 mg QD (N=190) n (%)	UPA 30 mg QD (N=272) n (%)	All UPA (N=1037) n (%)
皮膚および皮下組織障害 (Cont.)								
脂漏性皮膚炎	0	2 (0.8)	2 (0.3)	0	0	0	0	2 (0.2)
皮膚変色	0	1 (0.4)	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 (0.3)	0	2 (0.3)	0	0	0	2 (0.7)	4 (0.4)
血管障害	9 (1.6)	2 (0.8)	11 (1.9)	0	0	0	0	11 (1.1)
深部静脈血栓症	1 (0.2)	1 (0.4)	2 (0.3)	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	4 (0.7)	1 (0.4)	5 (0.9)	0	0	0	0	5 (0.5)
高血圧クレーゼ	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD			Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
Any adverse event	520 (63.3)	249 (71.4)	769 (65.7)	34 (74.2)	0	90 (44.9)	167 (70.1)	1026 (63.7)
血液およびリンパ系障害	31 (3.8)	17 (4.9)	48 (4.1)	4 (8.7)	0	8 (4.0)	20 (8.4)	76 (4.7)
貧血	6 (0.7)	0	6 (0.5)	1 (2.2)	0	1 (0.5)	2 (0.8)	9 (0.6)
周期性好中球減少症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
内出血発生の増加傾向	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
鉄欠乏性貧血	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
白血球増加症	0	1 (0.3)	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
白血球減少症	5 (0.6)	3 (0.9)	8 (0.7)	1 (2.2)	0	3 (1.5)	8 (3.4)	19 (1.2)
リンパ球増加症	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
血液およびリンパ系障害 (Cont.)								
リンパ球減少症	9 (1.1)	5 (1.4)	14 (1.2)	0	0	1 (0.5)	2 (0.8)	17 (1.1)
好中球減少症	10 (1.2)	5 (1.4)	15 (1.3)	2 (4.4)	0	1 (0.5)	6 (2.5)	22 (1.4)
好中球増加症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
汎血球減少症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
網状赤血球増加症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
心臓障害	2 (0.2)	4 (1.1)	6 (0.5)	0	0	0	1 (0.4)	7 (0.4)
急性心筋梗塞	1 (0.1)	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 (0.4)	1 (<0.1)
期外収縮	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
心臓障害 (Cont.)								
動悸	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
心嚢液貯留	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
心膜炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
頻脈	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
耳および迷路障害	3 (0.4)	2 (0.6)	5 (0.4)	0	0	0	1 (0.4)	6 (0.4)
耳痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
外耳の炎症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
内耳障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
メニエール病	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
耳および迷路障害 (Cont.)								
耳鳴	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
回転性めまい	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
内分泌障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
クッシング様症状	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
眼障害	0	2 (0.6)	2 (0.2)	2 (4.4)	0	0	0	2 (0.1)
眼精疲労	0	0	0	1 (2.2)	0	0	0	0
眼瞼炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
角膜炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ぶどう膜炎	0	0	0	1 (2.2)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
胃腸障害	44 (5.4)	20 (5.7)	64 (5.5)	7 (15.3)	0	9 (4.5)	14 (5.9)	87 (5.4)
腹部膨満	1 (0.1)	0	1 (<0.1)	1 (2.2)	0	0	0	1 (<0.1)
腹痛	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)
下腹部痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腹部圧痛	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
口角口唇炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
アフタ性潰瘍	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
大腸炎	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)
潰瘍性大腸炎	15 (1.8)	10 (2.9)	25 (2.1)	2 (4.4)	0	2 (1.0)	6 (2.5)	33 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
結腸異形成	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
便秘	1 (0.1)	1 (0.3)	2 (0.2)	0	0	4 (2.0)	1 (0.4)	7 (0.4)
便意切迫	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
下痢	3 (0.4)	1 (0.3)	4 (0.3)	1 (2.2)	0	0	0	4 (0.2)
大腿ヘルニア	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
鼓腸	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
胃炎	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
胃食道逆流性疾患	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
血便排泄	0	0	0	1 (2.2)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
胃腸障害 (Cont.)								
痔核	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
腸閉塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
口腔内潰瘍形成	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
悪心	4 (0.5)	0	4 (0.3)	1 (2.2)	0	1 (0.5)	1 (0.4)	6 (0.4)
膵炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
直腸出血	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
口内炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
歯痛	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
胃腸障害 (Cont.)								
嘔吐	2 (0.2)	0	2 (0.2)	1 (2.2)	0	1 (0.5)	2 (0.8)	5 (0.3)
一般・全身障害および投与部位の状態	19 (2.3)	10 (2.9)	29 (2.5)	2 (4.4)	0	2 (1.0)	4 (1.7)	35 (2.2)
無力症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
悪寒	1 (0.1)	1 (0.3)	2 (0.2)	1 (2.2)	0	2 (1.0)	1 (0.4)	5 (0.3)
疲労	4 (0.5)	1 (0.3)	5 (0.4)	0	0	0	1 (0.4)	6 (0.4)
治癒不良	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
インフルエンザ様疾患	3 (0.4)	2 (0.6)	5 (0.4)	0	0	0	1 (0.4)	6 (0.4)
注射部位疼痛	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
倦怠感	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
疼痛	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
末梢腫脹	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
発熱	4 (0.5)	5 (1.4)	9 (0.8)	1 (2.2)	0	0	0	9 (0.6)
評価不能の事象	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肝胆道系障害	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	0	4 (0.2)
硬化性胆管炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脂肪肝	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肝障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
非アルコール性脂肪性肝疾患	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)			--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)	
免疫系障害	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)
薬物過敏症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
過敏症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
感染症および寄生虫症	182 (22.2)	74 (21.2)	256 (21.9)	10 (21.8)	0	24 (12.0)	32 (13.4)	312 (19.4)
腹部膿瘍	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
腹壁膿瘍	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
急性副鼻腔炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肛門膿瘍	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
無症候性COVID-19	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
細菌感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
細菌性膣症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
気管支炎	7 (0.9)	2 (0.6)	9 (0.8)	0	0	1 (0.5)	0	10 (0.6)
COVID-19	2 (0.2)	2 (0.6)	4 (0.3)	0	0	0	3 (1.3)	7 (0.4)
COVID-19肺炎	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	1 (0.4)	3 (0.2)
カンジダ感染	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
蜂巣炎	2 (0.2)	0	2 (0.2)	0	0	4 (2.0)	0	6 (0.4)
感染性胆嚢炎	1 (0.1)	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 (0.5)	1 (0.3)	5 (0.4)	0	0	0	1 (0.4)	6 (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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/							
	UPA 15 mg QD	UPA 30 mg QD	Total	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
Events	Events	Events	Events	Events	Events	Events	Events	
(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
感染症および寄生虫症 (Cont.)								
結膜炎	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
ウイルス性結膜炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
サイトメガロウイルス感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
毛嚢虫症	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
爪の皮膚糸状菌症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
感染性下痢	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
耳感染	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
丹毒	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
眼感染	1 (0.1)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/							
	UPA 15 mg QD	UPA 30 mg QD	Total	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
Events	Events	Events	Events	Events	Events	Events	Events	
(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
感染症および寄生虫症 (Cont.)								
毛包炎	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
皮膚真菌感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
せつ	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
胃腸炎	0	2 (0.6)	2 (0.2)	1 (2.2)	0	0	0	2 (0.1)
ウイルス性胃腸炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
性器カンジダ症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
陰部ヘルペス	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
陰部単純ヘルペス	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
真菌性性器感染	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
歯肉炎	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
単径部膿瘍	1 (0.1)	0	1 (<0.1)	1 (2.2)	0	0	0	1 (<0.1)
手足口病	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
ヘルペス眼感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
単純ヘルペス	5 (0.6)	1 (0.3)	6 (0.5)	0	0	0	0	6 (0.4)
単純ヘルペス性咽頭炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
帯状疱疹	31 (3.8)	12 (3.4)	43 (3.7)	2 (4.4)	0	5 (2.5)	8 (3.4)	56 (3.5)
耳帯状疱疹	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
麦粒腫	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)			--SA UPA-- All UPA (N=1037) (PYs=1611.6)	
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
伝染性単核症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
インフルエンザ	5 (0.6)	1 (0.3)	6 (0.5)	1 (2.2)	0	0	0	6 (0.4)
潜伏結核	5 (0.6)	0	5 (0.4)	0	0	1 (0.5)	1 (0.4)	7 (0.4)
限局性感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
下気道感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
上咽頭炎	12 (1.5)	10 (2.9)	22 (1.9)	0	0	2 (1.0)	2 (0.8)	26 (1.6)
爪真菌症	2 (0.2)	0	2 (0.2)	0	0	2 (1.0)	0	4 (0.2)
口腔カンジダ症	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
口腔ヘルペス	9 (1.1)	5 (1.4)	14 (1.2)	1 (2.2)	0	0	1 (0.4)	15 (0.9)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
精巣炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
中耳炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
爪囲炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
直腸周囲膿瘍	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
咽頭炎	0	2 (0.6)	2 (0.2)	1 (2.2)	0	0	0	2 (0.1)
肺炎	5 (0.6)	3 (0.9)	8 (0.7)	0	0	0	0	8 (0.5)
膿疱	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腎盂腎炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
直腸膿瘍	0	1 (0.3)	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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574) (PYs=821.6) Events (E/100 PYs)	(N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	(N=51) (PYs=45.8) Events (E/100 PYs)	(N=1) (PYs=2.8) Events (E/100 PYs)	(N=190) (PYs=200.6) Events (E/100 PYs)	(N=272) (PYs=238.1) Events (E/100 PYs)	(N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
気道感染	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
ウイルス性気道感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
鼻炎	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
根管感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
敗血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
副鼻腔炎	8 (1.0)	1 (0.3)	9 (0.8)	0	0	0	0	9 (0.6)
皮膚感染	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
皮下組織膿瘍	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
股部白癬	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
足部白癬	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
扁桃炎	0	1 (0.3)	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
歯膿瘍	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
歯感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
結核	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
上気道感染	33 (4.0)	8 (2.3)	41 (3.5)	1 (2.2)	0	1 (0.5)	2 (0.8)	44 (2.7)
尿路感染	9 (1.1)	2 (0.6)	11 (0.9)	2 (4.4)	0	2 (1.0)	0	13 (0.8)
膣感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
水痘	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
ウイルス感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ウイルス性上気道感染	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
外陰部腔カンジダ症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
外陰腔真菌感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
傷害、中毒および処置合併症	2 (0.2)	3 (0.9)	5 (0.4)	0	0	0	0	5 (0.3)
筋断裂	0	3 (0.9)	3 (0.3)	0	0	0	0	3 (0.2)
皮膚裂傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
皮下血腫	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
臨床検査	108 (13.1)	39 (11.2)	147 (12.6)	3 (6.6)	0	17 (8.5)	55 (23.1)	219 (13.6)
アラニンアミノトランスフェラーゼ増加	10 (1.2)	2 (0.6)	12 (1.0)	0	0	0	2 (0.8)	14 (0.9)
アスパラギン酸アミノトランスフェラーゼ増加	9 (1.1)	4 (1.1)	13 (1.1)	0	0	0	3 (1.3)	16 (1.0)
細菌検査陽性	0	0	0	1 (2.2)	0	0	0	0
血中アルカリホスファターゼ増加	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
血中ビリルビン増加	1 (0.1)	0	1 (<0.1)	0	0	0	3 (1.3)	4 (0.2)
血中コレステロール増加	4 (0.5)	1 (0.3)	5 (0.4)	0	0	0	1 (0.4)	6 (0.4)
血中クレアチンホスホキナーゼ増加	34 (4.1)	22 (6.3)	56 (4.8)	1 (2.2)	0	1 (0.5)	13 (5.5)	70 (4.3)
血中クレアチニン増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血中葉酸減少	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
血圧上昇	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
血中トリグリセリド増加	3 (0.4)	0	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
尿中血陽性	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
凝固時間延長	1 (0.1)	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	4 (0.5)	0	4 (0.3)	0	0	0	2 (0.8)	6 (0.4)
ヘマトクリット減少	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ヘモグロビン減少	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
肝酵素上昇	2 (0.2)	2 (0.6)	4 (0.3)	0	0	0	1 (0.4)	5 (0.3)
高比重リポ蛋白増加	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
臨床検査異常	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肝機能検査異常	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肝機能検査値上昇	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
低比重リボ蛋白増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
リンパ球数減少	5 (0.6)	3 (0.9)	8 (0.7)	0	0	2 (1.0)	4 (1.7)	14 (0.9)
リンパ球百分率減少	0	0	0	0	0	0	2 (0.8)	2 (0.1)
平均赤血球容積増加	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
好中球数減少	6 (0.7)	0	6 (0.5)	0	0	5 (2.5)	7 (2.9)	18 (1.1)
好中球数増加	2 (0.2)	0	2 (0.2)	0	0	2 (1.0)	1 (0.4)	5 (0.3)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
血小板数減少	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血小板数増加	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
尿蛋白	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
尿中蛋白陽性	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
赤血球数減少	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
網状赤血球数増加	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
トランスアミナーゼ上昇	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
尿中ケトン体陽性	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
尿中白血球エステラーゼ陽性	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	(N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
体重増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
白血球数減少	7 (0.9)	0	7 (0.6)	1 (2.2)	0	4 (2.0)	4 (1.7)	15 (0.9)
尿中白血球陽性	1 (0.1)	1 (0.3)	2 (0.2)	0	0	1 (0.5)	1 (0.4)	4 (0.2)
代謝および栄養障害	12 (1.5)	3 (0.9)	15 (1.3)	0	0	6 (3.0)	3 (1.3)	24 (1.5)
脂質異常症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
痛風	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
高コレステロール血症	5 (0.6)	1 (0.3)	6 (0.5)	0	0	1 (0.5)	2 (0.8)	9 (0.6)
高血糖	1 (0.1)	0	1 (<0.1)	0	0	2 (1.0)	0	3 (0.2)
高脂血症	2 (0.2)	0	2 (0.2)	0	0	2 (1.0)	0	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
代謝および栄養障害 (Cont.)								
低リン酸血症	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)
低蛋白血症	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
肥満	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
筋骨格系および結合組織障害	18 (2.2)	11 (3.2)	29 (2.5)	3 (6.6)	0	11 (5.5)	8 (3.4)	48 (3.0)
関節痛	5 (0.6)	4 (1.1)	9 (0.8)	2 (4.4)	0	2 (1.0)	4 (1.7)	15 (0.9)
関節障害	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)
背部痛	2 (0.2)	1 (0.3)	3 (0.3)	0	0	1 (0.5)	0	4 (0.2)
指炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
四肢拘縮	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
筋拘縮	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
筋痙縮	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
筋骨格系胸痛	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
筋骨格痛	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
筋骨格硬直	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
筋肉痛	3 (0.4)	2 (0.6)	5 (0.4)	0	0	0	2 (0.8)	7 (0.4)
頸部痛	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
四肢痛	2 (0.2)	0	2 (0.2)	1 (2.2)	0	0	2 (0.8)	4 (0.2)
顎痛	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) 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 (1.0)	0	2 (0.1)
足底筋膜炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
横紋筋融解症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
腱炎	0	0	0	0	0	1 (0.5)	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 (0.1)	10 (2.9)	11 (0.9)	0	0	0	2 (0.8)	13 (0.8)
血管肉腫	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
基底細胞癌	0	3 (0.9)	3 (0.3)	0	0	0	1 (0.4)	4 (0.2)
ボーエン病	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
皮膚乳頭腫	0	4 (1.1)	4 (0.3)	0	0	0	0	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む） (Cont.)								
皮膚有棘細胞癌	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
舌扁平上皮癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
神経系障害	12 (1.5)	6 (1.7)	18 (1.5)	0	0	4 (2.0)	5 (2.1)	27 (1.7)
灼熱感	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頸髄圧迫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
注意力障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
浮動性めまい	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
構語障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頭痛	7 (0.9)	2 (0.6)	9 (0.8)	0	0	2 (1.0)	2 (0.8)	13 (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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/							
	UPA 15 mg QD	UPA 30 mg QD	Total	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
Events	Events	Events	Events	Events	Events	Events	Events	
(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
神經系障害 (Cont.)								
知覚過敏	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
感覚鈍麻	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
片頭痛	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
脊髄症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
錯感覚	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
会話障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
失神	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
視野欠損	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
精神障害	3 (0.4)	0	3 (0.3)	1 (2.2)	0	0	1 (0.4)	4 (0.2)
不安	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
うつ病	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
睡眠障害	0	0	0	1 (2.2)	0	0	0	0
腎および尿路障害	8 (1.0)	5 (1.4)	13 (1.1)	2 (4.4)	0	0	3 (1.3)	16 (1.0)
急性腎障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
排尿困難	2 (0.2)	2 (0.6)	4 (0.3)	0	0	0	0	4 (0.2)
血尿	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ケトン尿	0	0	0	1 (2.2)	0	0	0	0
腎結石症	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
腎および尿路障害 (Cont.)								
蛋白尿	2 (0.2)	1 (0.3)	3 (0.3)	1 (2.2)	0	0	3 (1.3)	6 (0.4)
腎仙痛	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
腎機能障害	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
生殖系および乳房障害	5 (0.6)	4 (1.1)	9 (0.8)	0	0	0	0	9 (0.6)
良性前立腺肥大症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
勃起不全	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
性器びらん	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
不規則月経	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
前立腺炎	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
生殖系および乳房障害 (Cont.)								
精液変色	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
外陰膣そう痒症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
呼吸器、胸郭および縦隔障害	21 (2.6)	8 (2.3)	29 (2.5)	0	0	2 (1.0)	4 (1.7)	35 (2.2)
咳嗽	5 (0.6)	0	5 (0.4)	0	0	1 (0.5)	1 (0.4)	7 (0.4)
鼻出血	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
鼻閉	0	3 (0.9)	3 (0.3)	0	0	0	0	3 (0.2)
鼻中隔穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
口腔咽頭痛	9 (1.1)	0	9 (0.8)	0	0	0	0	9 (0.6)
胸水	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total			-----SA 2 Population-----				--SA UPA--
	(N=574) (PYs=821.6) Events (E/100 PYs)	(N=249) (PYs=348.5) Events (E/100 PYs)	(N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
湿性咳嗽	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
肺塞栓症	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
肺腫瘍	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
アレルギー性鼻炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
鼻漏	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
副鼻腔うっ血	2 (0.2)	3 (0.9)	5 (0.4)	0	0	0	0	5 (0.3)
上気道咳症候群	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
皮膚および皮下組織障害	36 (4.4)	26 (7.5)	62 (5.3)	0	0	7 (3.5)	14 (5.9)	83 (5.2)
ざ瘡	3 (0.4)	4 (1.1)	7 (0.6)	0	0	5 (2.5)	3 (1.3)	15 (0.9)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574) (PYs=821.6) Events (E/100 PYs)	(N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	(N=51) (PYs=45.8) Events (E/100 PYs)	(N=1) (PYs=2.8) Events (E/100 PYs)	(N=190) (PYs=200.6) Events (E/100 PYs)	(N=272) (PYs=238.1) Events (E/100 PYs)	(N=1037) (PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
膿疱性湿疹	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
光線角化症	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
脱毛症	4 (0.5)	2 (0.6)	6 (0.5)	0	0	0	0	6 (0.4)
湿疹様皮膚炎	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
アレルギー性皮膚炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
アトピー性皮膚炎	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
剥脱性皮膚炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
皮膚乾燥	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)
異汗性湿疹	1 (0.1)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
湿疹	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
紅斑	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
環状紅斑	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
多汗症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
間擦疹	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
毛孔性角化症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
寝汗	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
丘疹	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
口囲皮膚炎	1 (0.1)	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.

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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.

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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/ UPA 15 mg QD			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				--SA UPA-- All UPA
	(N=574)	(N=249)	Total (N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events	Events	Events	Events	Events	Events	Events	Events
	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
光線過敏性反応	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
そう痒症	2 (0.2)	2 (0.6)	4 (0.3)	0	0	0	0	4 (0.2)
発疹	8 (1.0)	5 (1.4)	13 (1.1)	0	0	0	3 (1.3)	16 (1.0)
紅斑性皮疹	1 (0.1)	2 (0.6)	3 (0.3)	0	0	0	0	3 (0.2)
毛孔性皮疹	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
斑状皮疹	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
丘疹性皮疹	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
そう痒性皮疹	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
酒さ	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
脂漏性皮膚炎	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)
皮膚変色	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
皮膚剥脱	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
皮膚病変	2 (0.2)	0	2 (0.2)	0	0	0	2 (0.8)	4 (0.2)
血管障害	9 (1.1)	2 (0.6)	11 (0.9)	0	0	0	0	11 (0.7)
深部静脈血栓症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
ほてり	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
高血圧	4 (0.5)	1 (0.3)	5 (0.4)	0	0	0	0	5 (0.3)
高血圧クリーゼ	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
血管障害 (Cont.)								
レイノー現象	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
静脈血栓症	1 (0.1)	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.

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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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD			Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All_UPA
	(N=574) (PYs=821.6) Events (E/100 PYs)	(N=249) (PYs=348.5) Events (E/100 PYs)	(N=574) (PYs=1170.1) Events (E/100 PYs)	(N=51) (PYs=45.8) Events (E/100 PYs)	(N=1) (PYs=2.8) Events (E/100 PYs)	(N=190) (PYs=200.6) Events (E/100 PYs)	(N=272) (PYs=238.1) Events (E/100 PYs)	(N=1037) (PYs=1611.6) Events (E/100 PYs)
Any adverse event	71 (8.6)	44 (12.6)	115 (9.8)	3 (6.6)	1 (35.7)	15 (7.5)	28 (11.8)	159 (9.9)
血液およびリンパ系障害	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
リンパ球減少症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
好中球減少症	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
心臓障害	2 (0.2)	2 (0.6)	4 (0.3)	0	0	1 (0.5)	0	5 (0.3)
急性心筋梗塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
心房細動	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
完全房室ブロック	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
心嚢液貯留	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
心臟障害 (Cont.)								
心膜炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
耳および迷路障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
突発性難聴	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
胃腸障害	23 (2.8)	7 (2.0)	30 (2.6)	2 (4.4)	0	1 (0.5)	5 (2.1)	36 (2.2)
腹痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
裂肛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
痔瘻	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
潰瘍性大腸炎	18 (2.2)	5 (1.4)	23 (2.0)	2 (4.4)	0	1 (0.5)	3 (1.3)	27 (1.7)
結腸異形成	0	1 (0.3)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
大腿ヘルニア	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
膵炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
埋伏歯	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
一般・全身障害および投与部位の状態	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
疲労	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
疼痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
発熱	1 (0.1)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)			--SA UPA-- All UPA (N=1037) (PYs=1611.6)	
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
肝胆道系障害	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
胆嚢炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
感染症および寄生虫症	8 (1.0)	16 (4.6)	24 (2.1)	1 (2.2)	1 (35.7)	5 (2.5)	9 (3.8)	39 (2.4)
腹部膿瘍	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
虫垂炎	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
COVID-19	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	3 (1.3)	5 (0.3)
COVID-19肺炎	0	2 (0.6)	2 (0.2)	0	0	2 (1.0)	3 (1.3)	7 (0.4)
蜂巣炎	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
感染性胆嚢炎	1 (0.1)	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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
クロストリジウム・ディフィシレ感染	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)
サイトメガロウイルス感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
医療機器関連敗血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸菌感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸菌性敗血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
消化管感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
带状疱疹	1 (0.1)	1 (0.3)	2 (0.2)	1 (2.2)	0	0	1 (0.4)	3 (0.2)
耳带状疱疹	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
毛巣嚢胞	0	4 (1.1)	4 (0.3)	0	0	0	0	4 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
肺炎	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
細菌性肺炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ウイルス性肺炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
直腸膿瘍	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
敗血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
尿路性敗血症	0	0	0	0	1 (35.7)	0	0	1 (<0.1)
傷害、中毒および処置合併症	5 (0.6)	1 (0.3)	6 (0.5)	0	0	3 (1.5)	0	9 (0.6)
腓骨骨折	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
企図の過量投与	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
靱帯捻挫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
処置による腸管穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
橈骨骨折	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肋骨骨折	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脛骨骨折	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
創傷	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
臨床検査	5 (0.6)	0	5 (0.4)	0	0	1 (0.5)	2 (0.8)	8 (0.5)
血中クレアチンホスホキナーゼ増加	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
臨床検査 (Cont.)								
血中トリグリセリド増加	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肝酵素上昇	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
肝機能検査値上昇	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
リンパ球数減少	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
好中球数減少	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
代謝および栄養障害	2 (0.2)	3 (0.9)	5 (0.4)	0	0	0	0	5 (0.3)
脱水	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
高血糖	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
低リン酸血症	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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/ UPA 15 mg QD UPA 30 mg QD (N=574) (N=249) Total (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)			--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
代謝および栄養障害 (Cont.)							
過少体重	1 (0.1)	0	1 (<0.1)	0	0	0	1 (<0.1)
筋骨格系および結合組織障害	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	5 (0.3)
関節痛	1 (0.1)	0	1 (<0.1)	0	0	0	1 (<0.1)
滑液包炎	0	0	0	0	0	1 (0.4)	1 (<0.1)
骨壊死	1 (0.1)	0	1 (<0.1)	0	0	0	1 (<0.1)
四肢痛	0	1 (0.3)	1 (<0.1)	0	0	0	1 (<0.1)
肩回旋筋腱板症候群	1 (0.1)	0	1 (<0.1)	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 (0.2)	3 (0.9)	5 (0.4)	0	0	0	7 (0.4)
膵腺癌	0	0	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む） (Cont.)								
血管肉腫	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
基底細胞癌	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
乳癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮頸部扁平上皮癌	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
精巣（純粹）セミノーマ	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精巣癌	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
神経系障害	3 (0.4)	3 (0.9)	6 (0.5)	0	0	0	1 (0.4)	7 (0.4)
脳損傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頭痛	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
神経系障害 (Cont.)								
片頭痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
神経炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
坐骨神経痛	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
失神	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精神障害	5 (0.6)	1 (0.3)	6 (0.5)	0	0	3 (1.5)	1 (0.4)	10 (0.6)
不安	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
双極1型障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
うつ病	4 (0.5)	0	4 (0.3)	0	0	1 (0.5)	1 (0.4)	6 (0.4)
自殺念慮	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
精神障害 (Cont.)								
自殺企図	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腎および尿路障害	3 (0.4)	3 (0.9)	6 (0.5)	0	0	0	0	6 (0.4)
排尿困難	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腎結石症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
腎仙痛	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
尿管閉塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
尿管結石症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
生殖系および乳房障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮頸部の炎症	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
呼吸器、胸郭および縦隔障害	2 (0.2)	2 (0.6)	4 (0.3)	0	0	1 (0.5)	3 (1.3)	8 (0.5)
喘息	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
胸水	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肺塞栓症	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	3 (1.3)	5 (0.3)
睡眠時無呼吸症候群	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
皮膚および皮下組織障害	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
ざ瘡	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
脱毛症	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
血管障害	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
深部静脈血栓症	1 (0.1)	0	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
静脈血栓症	1 (0.1)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 15 mg QD/ UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All_UPA (N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events	Events	Events	Events	Events	Events	Events	Events
	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
Any adverse event	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	3 (1.3)	5 (0.3)
感染症および寄生虫症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
COVID-19	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
良性、悪性および詳細不明の新生物（囊胞およびポリープを含む）	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
膵腺癌	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
血管肉腫	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
神経系障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脳損傷	1 (0.1)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
呼吸器、胸郭および縦隔障害	0	0	0	0	0	0	1 (0.4)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
肺塞栓症	0	0	0	0	0	0	1 (0.4)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD (N=574) (N=249) Total (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)			--SA UPA-- All_UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)	
Any adverse event	101 (12.3)	64 (18.4)	165 (14.1)	5 (10.9)	1 (35.7)	20 (10.0)	41 (17.2)	227 (14.1)
血液およびリンパ系障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
小球性貧血	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
心臓障害	7 (0.9)	2 (0.6)	9 (0.8)	0	0	1 (0.5)	0	10 (0.6)
急性心筋梗塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
不安定狭心症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
心房細動	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
完全房室ブロック	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
心筋梗塞	1 (0.1)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
心臓障害 (Cont.)								
心嚢液貯留	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
心膜炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
心室性頻脈	3 (0.4)	0	3 (0.3)	0	0	0	0	3 (0.2)
耳および迷路障害	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
回転性めまい	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
眼障害	0	0	0	0	0	0	2 (0.8)	2 (0.1)
無水晶体眼	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
角膜浮腫	0	0	0	0	0	0	1 (0.4)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
胃腸障害	26 (3.2)	10 (2.9)	36 (3.1)	2 (4.4)	0	0	4 (1.7)	40 (2.5)
腹痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
裂肛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
痔瘻	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
潰瘍性大腸炎	12 (1.5)	7 (2.0)	19 (1.6)	2 (4.4)	0	0	1 (0.4)	20 (1.2)
下痢	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
胃炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
胃食道逆流性疾患	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
イレウス	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
単径ヘルニア	0	2 (0.6)	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
胃腸障害 (Cont.)								
腸閉塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	4 (0.5)	0	4 (0.3)	0	0	0	0	4 (0.2)
悪心	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
埋伏歯	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
嘔吐	1 (0.1)	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 (0.6)	0	5 (0.4)	0	0	0	0	5 (0.3)
胸痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
異形成	1 (0.1)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
疲労	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
倦怠感	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
疼痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肝胆道系障害	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
胆嚢炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
感染症および寄生虫症	19 (2.3)	19 (5.5)	38 (3.2)	2 (4.4)	1 (35.7)	8 (4.0)	18 (7.6)	65 (4.0)
腹部膿瘍	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肛門膿瘍	0	0	0	0	0	0	2 (0.8)	2 (0.1)
虫垂炎	1 (0.1)	0	1 (<0.1)	0	0	0	2 (0.8)	3 (0.2)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.

E/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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
気管支炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
COVID-19	3 (0.4)	1 (0.3)	4 (0.3)	0	0	1 (0.5)	4 (1.7)	9 (0.6)
COVID-19肺炎	1 (0.1)	2 (0.6)	3 (0.3)	0	0	4 (2.0)	7 (2.9)	14 (0.9)
蜂巣炎	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
感染性胆嚢炎	1 (0.1)	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	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
サイトメガロウイルス感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
医療機器関連敗血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸菌感染	0	1 (0.3)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
大腸菌性敗血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
胃腸炎	1 (0.1)	3 (0.9)	4 (0.3)	1 (2.2)	0	0	0	4 (0.2)
消化管感染	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ヘリコバクター性胃炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
带状疱疹	2 (0.2)	1 (0.3)	3 (0.3)	1 (2.2)	0	0	2 (0.8)	5 (0.3)
耳带状疱疹	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
伝染性単核症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精巣炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
毛巣嚢胞	0	1 (0.3)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
肺炎	4 (0.5)	0	4 (0.3)	0	0	0	0	4 (0.2)
細菌性肺炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ウイルス性肺炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
術後創感染	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
腎盂腎炎	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
直腸膿瘍	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
敗血症	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)
尿路性敗血症	0	0	0	0	1 (35.7)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1)				--SA UPA-- All UPA (N=1037) (PYs=1611.6)
	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)
傷害、中毒および処置合併症	9 (1.1)	2 (0.6)	11 (0.9)	0	0	2 (1.0)	0	13 (0.8)
挫傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腓骨骨折	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
企図の過量投与	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
過量投与	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
処置後出血	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
術後イレウス	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
処置による腸管穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
橈骨骨折	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肋骨骨折	1 (0.1)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
腱断裂	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脛骨骨折	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
子宮穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
代謝および栄養障害	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)
低リン酸血症	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)
筋骨格系および結合組織障害	6 (0.7)	4 (1.1)	10 (0.9)	0	0	0	1 (0.4)	11 (0.7)
背部痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
滑液包炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
椎間板障害	1 (0.1)	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.

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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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total			-----SA 2 Population-----				--SA UPA--
	(N=574) (PYs=821.6) Events (E/100 PYs)	(N=249) (PYs=348.5) Events (E/100 PYs)	(N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
椎間板突出	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
腰部脊柱管狭窄症	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
骨壊死	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
四肢痛	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
横紋筋融解症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肩回旋筋腱板症候群	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脊柱変形	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
変形性脊椎症	0	1 (0.3)	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.

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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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.2)	5 (1.4)	7 (0.6)	0	0	4 (2.0)	2 (0.8)	13 (0.8)
結腸腺癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
膵腺癌	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
エナメル上皮腫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
血管肉腫	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
肛門性器疣贅	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
基底細胞癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
乳癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
前立腺癌	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
子宮頸部扁平上皮癌	0	0	0	0	0	0	1 (0.4)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む） (Cont.)								
精巣（純粋）セミノーマ	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精巣癌	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
甲状腺腺腫	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮平滑筋腫	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
神経系障害	6 (0.7)	6 (1.7)	12 (1.0)	1 (2.2)	0	0	2 (0.8)	14 (0.9)
健忘	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
脳損傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
手根管症候群	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
大脳障害	1 (0.1)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	(N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
神経系障害 (Cont.)								
頸髄圧迫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
構語障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頭痛	1 (0.1)	1 (0.3)	2 (0.2)	1 (2.2)	0	0	0	2 (0.1)
ラクナ梗塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
片頭痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脊髄症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
発作様現象	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
失神	0	2 (0.6)	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574)	UPA 30 mg QD (N=249)	Total (N=574)	Placebo (N=51)	UPA 7.5 mg QD (N=1)	UPA 15 mg QD (N=190)	UPA 30 mg QD (N=272)	All UPA (N=1037)
	(PYs=821.6) Events (E/100 PYs)	(PYs=348.5) Events (E/100 PYs)	(PYs=1170.1) Events (E/100 PYs)	(PYs=45.8) Events (E/100 PYs)	(PYs=2.8) Events (E/100 PYs)	(PYs=200.6) Events (E/100 PYs)	(PYs=238.1) Events (E/100 PYs)	(PYs=1611.6) Events (E/100 PYs)
妊娠、産褥および周産期の状態	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
自然流産	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精神障害	5 (0.6)	1 (0.3)	6 (0.5)	0	0	3 (1.5)	3 (1.3)	12 (0.7)
不安	0	0	0	0	0	1 (0.5)	1 (0.4)	2 (0.1)
双極1型障害	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
うつ病	4 (0.5)	0	4 (0.3)	0	0	1 (0.5)	1 (0.4)	6 (0.4)
薬物依存	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
自殺念慮	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
自殺企図	1 (0.1)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)			--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)	
腎および尿路障害	6 (0.7)	6 (1.7)	12 (1.0)	0	0	0	2 (0.8)	14 (0.9)
急性腎障害	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
膀胱タンポナーデ	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
膀胱結石	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
尿路結石	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
腎結石症	3 (0.4)	2 (0.6)	5 (0.4)	0	0	0	0	5 (0.3)
腎仙痛	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
尿管閉塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
尿管結石症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
生殖系および乳房障害	1 (0.1)	4 (1.1)	5 (0.4)	0	0	1 (0.5)	1 (0.4)	7 (0.4)
良性前立腺肥大症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
子宮頸部障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮頸部の炎症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
子宮内膜症	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
前立腺炎	0	3 (0.9)	3 (0.3)	0	0	0	0	3 (0.2)
呼吸器、胸郭および縦隔障害	5 (0.6)	1 (0.3)	6 (0.5)	0	0	1 (0.5)	4 (1.7)	11 (0.7)
喘息	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
口腔咽頭痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
胸水	0	1 (0.3)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
肺塞栓症	2 (0.2)	0	2 (0.2)	0	0	1 (0.5)	4 (1.7)	7 (0.4)
肺腫瘍	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血管障害	3 (0.4)	1 (0.3)	4 (0.3)	0	0	0	0	4 (0.2)
深部静脈血栓症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
静脈瘤	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
静脈血栓症	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)			--SA UPA-- All_UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)	
Any adverse event	41 (5.0)	33 (9.5)	74 (6.3)	3 (6.6)	0	11 (5.5)	16 (6.7)	101 (6.3)
血液およびリンパ系障害	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
リンパ球減少症	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
小球性貧血	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
心臓障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
急性心筋梗塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
眼障害	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
網膜静脈閉塞	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
胃腸障害	18 (2.2)	13 (3.7)	31 (2.6)	3 (6.6)	0	5 (2.5)	2 (0.8)	38 (2.4)
腹痛	1 (0.1)	0	1 (<0.1)	0	0	1 (0.5)	0	2 (0.1)
潰瘍性大腸炎	14 (1.7)	9 (2.6)	23 (2.0)	3 (6.6)	0	3 (1.5)	2 (0.8)	28 (1.7)
結腸異形成	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
クローン病	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
イレウス	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
大腸ポリープ	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
悪心	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
膵炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
直腸異形成	0	0	0	0	0	1 (0.5)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
一般・全身障害および投与部位の状態 異形成	1 (0.1) 1 (0.1)	0 0	1 (<0.1) 1 (<0.1)	0 0	0 0	1 (0.5) 1 (0.5)	0 0	2 (0.1) 2 (0.1)
肝胆道系障害 硬化性胆管炎	1 (0.1) 1 (0.1)	0 0	1 (<0.1) 1 (<0.1)	0 0	0 0	0 0	0 0	1 (<0.1) 1 (<0.1)
感染症および寄生虫症 腹部膿瘍	1 (0.1) 0	5 (1.4) 1 (0.3)	6 (0.5) 1 (<0.1)	0 0	0 0	2 (1.0) 0	3 (1.3) 0	11 (0.7) 1 (<0.1)
虫垂炎	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
COVID-19	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
COVID-19肺炎	0	0	0	0	0	1 (0.5)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD	UPA 30 mg QD	Total	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
	Events	Events	Events	Events	Events	Events	Events	Events
	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
感染症および寄生虫症 (Cont.)								
クロストリジウム・ディフィシレ感染	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
真菌性性器感染	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
带状疱疹	0	2 (0.6)	2 (0.2)	0	0	1 (0.5)	0	3 (0.2)
肺炎	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
結核	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
傷害、中毒および処置合併症								
処置による腸管穿孔	2 (0.2)	0	2 (0.2)	0	0	0	0	2 (0.1)
子宮穿孔	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
	1 (0.1)	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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/							
	UPA 15 mg QD	UPA 30 mg QD	Total	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=574)	(N=249)	(N=574)	(N=51)	(N=1)	(N=190)	(N=272)	(N=1037)
	(PYs=821.6)	(PYs=348.5)	(PYs=1170.1)	(PYs=45.8)	(PYs=2.8)	(PYs=200.6)	(PYs=238.1)	(PYs=1611.6)
Events	Events	Events	Events	Events	Events	Events	Events	
(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)
臨床検査	4 (0.5)	4 (1.1)	8 (0.7)	0	0	0	1 (0.4)	9 (0.6)
アラニンアミノトランスフェラーゼ増加	1 (0.1)	1 (0.3)	2 (0.2)	0	0	0	0	2 (0.1)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (0.3)	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 (0.3)	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	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
肝酵素上昇	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
B型肝炎DNA測定陽性	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
リンパ球数減少	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
白血球数減少	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
代謝および栄養障害	0	1 (0.3)	1 (<0.1)	0	0	0	1 (0.4)	2 (0.1)
高ナトリウム血症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
低リン酸血症	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
筋骨格系および結合組織障害	2 (0.2)	1 (0.3)	3 (0.3)	0	0	0	0	3 (0.2)
関節痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
筋肉痛	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
横紋筋融解症	0	1 (0.3)	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 (0.2)	4 (1.1)	6 (0.5)	0	0	1 (0.5)	3 (1.3)	10 (0.6)
結腸腺癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
膵腺癌	0	0	0	0	0	0	1 (0.4)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
良性、悪性および詳細不明の新生物（囊 胞およびポリープを含む） (Cont.)								
血管肉腫	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
乳癌	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
喉頭扁平上皮癌	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
髄膜腫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
前立腺癌	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
子宮頸部扁平上皮癌	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
精巣（純粹）セミノーマ	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
精巣癌	1 (0.1)	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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=574) (PYs=821.6) Events (E/100 PYs)	UPA 30 mg QD (N=249) (PYs=348.5) Events (E/100 PYs)	Total (N=574) (PYs=1170.1) Events (E/100 PYs)	Placebo (N=51) (PYs=45.8) Events (E/100 PYs)	UPA 7.5 mg QD (N=1) (PYs=2.8) Events (E/100 PYs)	UPA 15 mg QD (N=190) (PYs=200.6) Events (E/100 PYs)	UPA 30 mg QD (N=272) (PYs=238.1) Events (E/100 PYs)	All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
神経系障害	2 (0.2)	3 (0.9)	5 (0.4)	0	0	0	2 (0.8)	7 (0.4)
健忘	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
脳損傷	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
頸髄圧迫	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
頭痛	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
ラクナ梗塞	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
脊髄症	0	0	0	0	0	0	1 (0.4)	1 (<0.1)
発作様現象	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
妊娠、産褥および周産期の状態	0	1 (0.3)	1 (<0.1)	0	0	0	0	1 (<0.1)
自然流産	0	1 (0.3)	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.

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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/ UPA 15 mg QD UPA 30 mg QD Total (N=574) (N=249) (N=574) (PYs=821.6) (PYs=348.5) (PYs=1170.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=51) (N=1) (N=190) (N=272) (PYs=45.8) (PYs=2.8) (PYs=200.6) (PYs=238.1) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=1037) (PYs=1611.6) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害	1 (0.1)	0	1 (<0.1)	0	0	0	3 (1.3)	4 (0.2)
肺塞栓症	1 (0.1)	0	1 (<0.1)	0	0	0	3 (1.3)	4 (0.2)
皮膚および皮下組織障害	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
ざ瘡	1 (0.1)	0	1 (<0.1)	0	0	0	0	1 (<0.1)
血管障害	3 (0.4)	0	3 (0.3)	0	0	1 (0.5)	1 (0.4)	5 (0.3)
深部静脈血栓症	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.4)	3 (0.2)
末梢静脈疾患	0	0	0	0	0	1 (0.5)	0	1 (<0.1)
静脈血栓症	1 (0.1)	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:

表11

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 UPADACITINIB (ULCERATIVE COLITIS)
 STUDY M14-533 (CUTOFF 20)
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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=61)	UPA 15 mg QD/ UPA 30 mg QD (N=19)	Total (N=61)	Placebo (N=10)	UPA 7.5 mg QD (N=0)	UPA 15 mg QD (N=40)	UPA 30 mg QD (N=49)	All UPA (N=150)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Subjects with:								
Any adverse event (AE)	47 (77.0)	16 (84.2)	56 (91.8)	6 (60.0)	0	27 (67.5)	36 (73.5)	119 (79.3)
Any AE with reasonable possibility of being related to study drug\$	24 (39.3)	11 (57.9)	34 (55.7)	3 (30.0)	0	7 (17.5)	15 (30.6)	56 (37.3)
Any severe AE	3 (4.9)	1 (5.3)	4 (6.6)	2 (20.0)	0	1 (2.5)	6 (12.2)	11 (7.3)
Any serious AE	7 (11.5)	2 (10.5)	8 (13.1)	1 (10.0)	0	2 (5.0)	6 (12.2)	16 (10.7)
Any AE leading to discontinuation of study drug	3 (4.9)	3 (15.8)	6 (9.8)	1 (10.0)	0	2 (5.0)	3 (6.1)	11 (7.3)
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:

表12

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 UPADACITINIB (ULCERATIVE COLITIS)
 STUDY M14-533 (CUTOFF 20)
 R&D/21/1541 - CLINICAL/STATISTICAL
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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=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD/ (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
Any treatment-emergent:								
Any adverse event (AE)	319 (267.4)	93 (344.4)	412 (281.8)	16 (222.2)	0	78 (187.1)	112 (275.9)	602 (263.5)
Any AE with reasonable possibility of being related to study drug\$	69 (57.8)	23 (85.2)	92 (62.9)	4 (55.6)	0	13 (31.2)	22 (54.2)	127 (55.6)
Any severe AE	3 (2.5)	1 (3.7)	4 (2.7)	2 (27.8)	0	1 (2.4)	7 (17.2)	12 (5.3)
Any serious AE	16 (13.4)	4 (14.8)	20 (13.7)	1 (13.9)	0	2 (4.8)	6 (14.8)	28 (12.3)
Any AE leading to discontinuation of study drug	3 (2.5)	3 (11.1)	6 (4.1)	1 (13.9)	0	2 (4.8)	3 (7.4)	11 (4.8)
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:

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 UPADACITINIB (ULCERATIVE COLITIS)
 STUDY M14-533 (CUTOFF 20)
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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/ UPA 15 mg QD UPA 30 mg QD Total			Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All UPA
	(N=61)	(N=19)	(N=61)	(N=10)	(N=0)	(N=40)	(N=49)	(N=150)
	(PYs=119.3)	(PYs=27.0)	(PYs=146.2)	(PYs=7.2)	(PYs=0.0)	(PYs=41.7)	(PYs=40.6)	(PYs=228.5)
	Events	Events	Events	Events	Events	Events	Events	Events
	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(E/100 PYs)	(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:

表13

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 UPADACITINIB (ULCERATIVE COLITIS)
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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD							
	UPA 15 mg QD (N=61) n (%)	UPA 30 mg QD (N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All_UPA (N=150) n (%)
Any adverse event	47 (77.0)	16 (84.2)	56 (91.8)	6 (60.0)	0	27 (67.5)	36 (73.5)	119 (79.3)
血液およびリンパ系障害	7 (11.5)	2 (10.5)	9 (14.8)	0	0	3 (7.5)	2 (4.1)	14 (9.3)
貧血	1 (1.6)	0	1 (1.6)	0	0	1 (2.5)	0	2 (1.3)
鉄欠乏性貧血	2 (3.3)	0	2 (3.3)	0	0	1 (2.5)	0	3 (2.0)
白血球減少症	2 (3.3)	2 (10.5)	4 (6.6)	0	0	1 (2.5)	1 (2.0)	6 (4.0)
リンパ節症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
リンパ球減少症	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
好中球減少症	3 (4.9)	1 (5.3)	4 (6.6)	0	0	0	2 (4.1)	6 (4.0)
心臓障害	1 (1.6)	0	1 (1.6)	0	0	1 (2.5)	2 (4.1)	4 (2.7)
完全房室ブロック	0	0	0	0	0	1 (2.5)	0	1 (0.7)
上室性期外収縮	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
心室性期外収縮	0	0	0	0	0	0	2 (4.1)	2 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61)	UPA 30 mg QD (N=19)	Total (N=61)	Placebo (N=10)	UPA 7.5 mg QD (N=0)	UPA 15 mg QD (N=40)	UPA 30 mg QD (N=49)	All UPA (N=150)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
先天性、家族性および遺伝性障害	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
歯原性嚢胞	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
耳および迷路障害	0	1 (5.3)	1 (1.6)	0	0	1 (2.5)	3 (6.1)	5 (3.3)
メニエール病	0	0	0	0	0	0	1 (2.0)	1 (0.7)
耳漏	0	0	0	0	0	0	1 (2.0)	1 (0.7)
耳鳴	0	1 (5.3)	1 (1.6)	0	0	0	1 (2.0)	2 (1.3)
回転性めまい	0	0	0	0	0	1 (2.5)	1 (2.0)	2 (1.3)
内分泌障害	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	0	2 (1.3)
副腎機能不全	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
甲状腺腫	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
眼障害	8 (13.1)	1 (5.3)	9 (14.8)	2 (20.0)	0	1 (2.5)	2 (4.1)	12 (8.0)
白内障	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD							
	UPA 15 mg QD (N=61) n (%)	UPA 30 mg QD (N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All UPA (N=150) n (%)
眼障害 (Cont.)								
結膜嚢胞	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
結膜出血	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
アレルギー性結膜炎	1 (1.6)	1 (5.3)	2 (3.3)	1 (10.0)	0	0	1 (2.0)	3 (2.0)
ドライアイ	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
緑内障	0	0	0	0	0	0	1 (2.0)	1 (0.7)
黄斑浮腫	0	0	0	0	0	1 (2.5)	0	1 (0.7)
眼充血	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
網膜静脈閉塞	0	0	0	0	0	1 (2.5)	0	1 (0.7)
ぶどう膜炎	0	0	0	1 (10.0)	0	0	0	0
硝子体浮遊物	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
胃腸障害	22 (36.1)	6 (31.6)	28 (45.9)	1 (10.0)	0	11 (27.5)	8 (16.3)	47 (31.3)
腹部膨満	0	2 (10.5)	2 (3.3)	0	0	0	0	2 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61)	UPA 30 mg QD (N=19)	Total (N=61)	Placebo (N=10)	UPA 7.5 mg QD (N=0)	UPA 15 mg QD (N=40)	UPA 30 mg QD (N=49)	All UPA (N=150)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸障害 (Cont.)								
腹痛	2 (3.3)	0	2 (3.3)	0	0	0	1 (2.0)	3 (2.0)
下腹部痛	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
上腹部痛	1 (1.6)	0	1 (1.6)	0	0	0	1 (2.0)	2 (1.3)
肛門ポリープ	0	0	0	0	0	0	1 (2.0)	1 (0.7)
口角口唇炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
アフタ性潰瘍	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
潰瘍性大腸炎	4 (6.6)	1 (5.3)	5 (8.2)	1 (10.0)	0	2 (5.0)	1 (2.0)	8 (5.3)
便秘	2 (3.3)	1 (5.3)	3 (4.9)	0	0	1 (2.5)	1 (2.0)	5 (3.3)
齲齒	1 (1.6)	1 (5.3)	2 (3.3)	0	0	1 (2.5)	0	3 (2.0)
下痢	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
消化不良	2 (3.3)	1 (5.3)	3 (4.9)	0	0	0	0	3 (2.0)
腸炎	1 (1.6)	0	1 (1.6)	0	0	0	2 (4.1)	3 (2.0)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All UPA (N=150) n (%)
	(N=61) n (%)	(N=19) n (%)	Total (N=61) n (%)					
胃腸障害 (Cont.)								
胃ポリープ	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
胃炎	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	0	2 (1.3)
胃食道逆流性疾患	4 (6.6)	0	4 (6.6)	0	0	1 (2.5)	0	5 (3.3)
痔核	0	0	0	0	0	2 (5.0)	0	2 (1.3)
腸管ポリープ	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
大腸ポリープ	4 (6.6)	1 (5.3)	5 (8.2)	0	0	1 (2.5)	0	6 (4.0)
口唇障害	0	0	0	0	0	1 (2.5)	0	1 (0.7)
悪心	0	0	0	0	0	2 (5.0)	0	2 (1.3)
口腔扁平苔癬	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
歯周病	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
直腸炎	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
直腸ポリープ	0	0	0	0	0	0	1 (2.0)	1 (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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=61) n (%)	(N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	(N=150) n (%)
胃腸障害 (Cont.)								
口内炎	3 (4.9)	1 (5.3)	4 (6.6)	0	0	0	0	4 (2.7)
埋伏歯	0	0	0	0	0	0	1 (2.0)	1 (0.7)
歯痛	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
嘔吐	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
一般・全身障害および投与部位の状態	15 (24.6)	2 (10.5)	16 (26.2)	1 (10.0)	0	6 (15.0)	4 (8.2)	26 (17.3)
胸痛	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	0	2 (1.3)
異常感	0	0	0	0	0	1 (2.5)	0	1 (0.7)
注射部位疼痛	2 (3.3)	0	2 (3.3)	0	0	2 (5.0)	3 (6.1)	7 (4.7)
倦怠感	1 (1.6)	0	1 (1.6)	1 (10.0)	0	0	0	1 (0.7)
末梢性浮腫	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
発熱	10 (16.4)	1 (5.3)	11 (18.0)	1 (10.0)	0	3 (7.5)	2 (4.1)	16 (10.7)
腫脹	0	0	0	0	0	1 (2.5)	0	1 (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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=61) n (%)	(N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	(N=150) n (%)
一般・全身障害および投与部位の状態 (Cont.)								
評価不能の事象	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
肝胆道系障害	5 (8.2)	2 (10.5)	7 (11.5)	0	0	0	2 (4.1)	9 (6.0)
胆嚢炎	0	0	0	0	0	0	1 (2.0)	1 (0.7)
胆石症	0	0	0	0	0	0	1 (2.0)	1 (0.7)
肝機能異常	3 (4.9)	1 (5.3)	4 (6.6)	0	0	0	1 (2.0)	5 (3.3)
脂肪肝	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
肝障害	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
免疫系障害	1 (1.6)	0	1 (1.6)	0	0	0	1 (2.0)	2 (1.3)
アナフィラキシー反応	0	0	0	0	0	0	1 (2.0)	1 (0.7)
季節性アレルギー	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
感染症および寄生虫症	34 (55.7)	11 (57.9)	41 (67.2)	1 (10.0)	0	8 (20.0)	16 (32.7)	65 (43.3)
肛門膿瘍	1 (1.6)	0	1 (1.6)	0	0	0	1 (2.0)	2 (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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD							
	UPA 15 mg QD (N=61) n (%)	UPA 30 mg QD (N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All UPA (N=150) n (%)
感染症および寄生虫症 (Cont.)								
虫垂炎	0	0	0	0	0	0	1 (2.0)	1 (0.7)
細菌感染	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
バルトリン腺炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
気管支炎	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
COVID-19	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
COVID-19肺炎	0	0	0	0	0	0	1 (2.0)	1 (0.7)
カンピロバクター胃腸炎	1 (1.6)	0	1 (1.6)	0	0	1 (2.5)	1 (2.0)	3 (2.0)
カンジダ感染	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
クロストリジウム・ディフィシレ感染	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	0	2 (1.3)
結膜炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
ウイルス性結膜炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
膀胱炎	2 (3.3)	0	2 (3.3)	0	0	0	1 (2.0)	3 (2.0)

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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=61) n (%)	(N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	(N=40) n (%)	(N=49) n (%)	(N=150) n (%)
感染症および寄生虫症 (Cont.)								
サイトメガロウイルス感染	0	0	0	0	0	0	1 (2.0)	1 (0.7)
感染性皮膚炎	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
爪の皮膚糸状菌症	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	0	2 (1.3)
感染性腸炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
毛包炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
胃腸炎	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	1 (2.0)	3 (2.0)
ウイルス性胃腸炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
歯肉炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
ヘリコバクター感染	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
ヘルペス眼感染	0	0	0	0	0	0	1 (2.0)	1 (0.7)
単純ヘルペス	1 (1.6)	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
带状疱疹	10 (16.4)	1 (5.3)	11 (18.0)	1 (10.0)	0	1 (2.5)	3 (6.1)	15 (10.0)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD							
	UPA 15 mg QD (N=61) n (%)	UPA 30 mg QD (N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All UPA (N=150) n (%)
感染症および寄生虫症 (Cont.)								
麦粒腫	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
膿痂疹	0	0	0	0	0	1 (2.5)	0	1 (0.7)
インフルエンザ	4 (6.6)	2 (10.5)	6 (9.8)	0	0	0	0	6 (4.0)
クレブシエラ感染	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
大腸感染	0	0	0	0	0	0	1 (2.0)	1 (0.7)
潜伏結核	1 (1.6)	0	1 (1.6)	0	0	0	1 (2.0)	2 (1.3)
上咽頭炎	18 (29.5)	5 (26.3)	21 (34.4)	1 (10.0)	0	4 (10.0)	3 (6.1)	28 (18.7)
口腔ヘルペス	3 (4.9)	1 (5.3)	4 (6.6)	0	0	0	4 (8.2)	8 (5.3)
骨髓炎	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
爪囲炎	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
歯冠周囲炎	0	0	0	0	0	1 (2.5)	0	1 (0.7)
歯周炎	2 (3.3)	0	2 (3.3)	0	0	0	2 (4.1)	4 (2.7)

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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) n (%)	UPA 30 mg QD (N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All UPA (N=150) n (%)
感染症および寄生虫症 (Cont.)								
扁桃周囲炎	0	0	0	0	0	1 (2.5)	0	1 (0.7)
咽頭炎	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	2 (4.1)	4 (2.7)
肺炎	0	2 (10.5)	2 (3.3)	0	0	0	0	2 (1.3)
歯髄炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
腎盂腎炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
鼻炎	0	0	0	0	0	1 (2.5)	0	1 (0.7)
副鼻腔炎	1 (1.6)	0	1 (1.6)	0	0	1 (2.5)	0	2 (1.3)
皮膚感染	1 (1.6)	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
足部白癬	2 (3.3)	0	2 (3.3)	0	0	1 (2.5)	1 (2.0)	4 (2.7)
上気道感染	2 (3.3)	2 (10.5)	4 (6.6)	0	0	0	0	4 (2.7)
水痘	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
外陰部腔カンジダ症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD							
	UPA 15 mg QD (N=61) n (%)	UPA 30 mg QD (N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All UPA (N=150) n (%)
感染症および寄生虫症 (Cont.)								
創傷感染	0	0	0	0	0	0	1 (2.0)	1 (0.7)
傷害、中毒および処置合併症	7 (11.5)	2 (10.5)	9 (14.8)	0	0	5 (12.5)	1 (2.0)	15 (10.0)
動物咬傷	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
節足動物咬傷	0	0	0	0	0	1 (2.5)	1 (2.0)	2 (1.3)
挫傷	0	0	0	0	0	1 (2.5)	0	1 (0.7)
上顎炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
足骨折	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	1 (2.0)	3 (2.0)
熱射病	0	0	0	0	0	1 (2.5)	0	1 (0.7)
過量投与	0	0	0	0	0	1 (2.5)	0	1 (0.7)
処置後出血	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
肋骨骨折	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
皮膚擦過傷	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=61) n (%)	UPA 30 mg QD (N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All UPA (N=150) n (%)
傷害、中毒および処置合併症 (Cont.)								
ストレス骨折	0	0	0	0	0	1 (2.5)	0	1 (0.7)
皮下血腫	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
脛骨骨折	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
ワクチン接種合併症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
臨床検査	11 (18.0)	5 (26.3)	16 (26.2)	0	0	4 (10.0)	11 (22.4)	31 (20.7)
アラニンアミノトランスフェラーゼ増加	1 (1.6)	0	1 (1.6)	0	0	0	2 (4.1)	3 (2.0)
アスパラギン酸アミノトランスフェラーゼ増加	1 (1.6)	0	1 (1.6)	0	0	0	2 (4.1)	3 (2.0)
血中クレアチンホスホキナーゼ増加	5 (8.2)	3 (15.8)	8 (13.1)	0	0	1 (2.5)	3 (6.1)	12 (8.0)
γ-グルタミルトランスフェラーゼ増加	2 (3.3)	1 (5.3)	3 (4.9)	0	0	1 (2.5)	0	4 (2.7)
高比重リボ蛋白増加	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
リンパ球数減少	1 (1.6)	1 (5.3)	2 (3.3)	0	0	1 (2.5)	2 (4.1)	5 (3.3)
好中球数減少	2 (3.3)	0	2 (3.3)	0	0	1 (2.5)	3 (6.1)	6 (4.0)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=61) n (%)	(N=19) n (%)	Total (N=61) n (%)	(N=10) n (%)	(N=0) n (%)	(N=40) n (%)	(N=49) n (%)	(N=150) n (%)
臨床検査 (Cont.)								
尿中白血球エステラーゼ陽性	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
白血球数減少	4 (6.6)	0	4 (6.6)	0	0	1 (2.5)	2 (4.1)	7 (4.7)
代謝および栄養障害	8 (13.1)	2 (10.5)	10 (16.4)	1 (10.0)	0	4 (10.0)	3 (6.1)	17 (11.3)
糖尿病	0	0	0	1 (10.0)	0	0	1 (2.0)	1 (0.7)
脂質異常症	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
高コレステロール血症	4 (6.6)	0	4 (6.6)	0	0	0	1 (2.0)	5 (3.3)
高脂血症	2 (3.3)	1 (5.3)	3 (4.9)	0	0	3 (7.5)	1 (2.0)	7 (4.7)
高尿酸血症	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
低蛋白血症	0	0	0	0	0	1 (2.5)	0	1 (0.7)
筋骨格系および結合組織障害	14 (23.0)	5 (26.3)	17 (27.9)	2 (20.0)	0	7 (17.5)	5 (10.2)	29 (19.3)
関節痛	3 (4.9)	1 (5.3)	4 (6.6)	0	0	1 (2.5)	1 (2.0)	6 (4.0)
関節炎	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	0	2 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61)	UPA 30 mg QD (N=19)	Total (N=61)	Placebo (N=10)	UPA 7.5 mg QD (N=0)	UPA 15 mg QD (N=40)	UPA 30 mg QD (N=49)	All UPA (N=150)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
筋骨格系および結合組織障害 (Cont.)								
関節障害	0	0	0	0	0	1 (2.5)	0	1 (0.7)
背部痛	3 (4.9)	0	3 (4.9)	0	0	1 (2.5)	0	4 (2.7)
頸部脊柱管狭窄症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
側腹部痛	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
椎間板突出	4 (6.6)	1 (5.3)	5 (8.2)	0	0	1 (2.5)	2 (4.1)	8 (5.3)
腰部脊柱管狭窄症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
筋痙縮	2 (3.3)	1 (5.3)	3 (4.9)	0	0	0	1 (2.0)	4 (2.7)
筋骨格系胸痛	0	0	0	0	0	1 (2.5)	0	1 (0.7)
筋骨格痛	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
筋骨格硬直	1 (1.6)	0	1 (1.6)	1 (10.0)	0	0	0	1 (0.7)
筋肉痛	1 (1.6)	0	1 (1.6)	0	0	1 (2.5)	1 (2.0)	3 (2.0)
変形性関節症	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD							
	UPA 15 mg QD (N=61) n (%)	UPA 30 mg QD (N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	All UPA (N=150) n (%)
筋骨格系および結合組織障害 (Cont.)								
骨端症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
骨壊死	0	1 (5.3)	1 (1.6)	0	0	1 (2.5)	0	2 (1.3)
骨粗鬆症	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
四肢痛	1 (1.6)	1 (5.3)	2 (3.3)	1 (10.0)	0	0	2 (4.1)	4 (2.7)
関節周囲炎	0	0	0	0	0	1 (2.5)	0	1 (0.7)
横紋筋融解症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
変形性脊椎症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
弾発指	0	0	0	0	0	1 (2.5)	0	1 (0.7)
良性、悪性および詳細不明の新生物（囊胞およびポリープを含む）	4 (6.6)	0	4 (6.6)	1 (10.0)	0	2 (5.0)	1 (2.0)	7 (4.7)
肛門性器疣贅	0	0	0	0	0	1 (2.5)	0	1 (0.7)
大腸腺腫	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
線維腫	0	0	0	0	0	0	1 (2.0)	1 (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.

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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-----			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=61) n (%)	(N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	(N=150) n (%)
良性、悪性および詳細不明の新生物（囊胞およびポリープを含む） (Cont.)	0	0	0	1 (10.0)	0	0	0	0
脂漏性角化症	2 (3.3)	0	2 (3.3)	0	0	0	1 (2.0)	3 (2.0)
皮膚乳頭腫	0	0	0	0	0	1 (2.5)	0	1 (0.7)
子宮平滑筋腫								
神経系障害	8 (13.1)	4 (21.1)	12 (19.7)	0	0	0	4 (8.2)	16 (10.7)
大脳障害	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
浮動性めまい	1 (1.6)	2 (10.5)	3 (4.9)	0	0	0	1 (2.0)	4 (2.7)
異常感覚	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
頭痛	3 (4.9)	1 (5.3)	4 (6.6)	0	0	0	2 (4.1)	6 (4.0)
感覚鈍麻	0	2 (10.5)	2 (3.3)	0	0	0	1 (2.0)	3 (2.0)
片頭痛	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
後頭神経痛	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
傾眠	0	0	0	0	0	0	1 (2.0)	1 (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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=61) n (%)	(N=19) n (%)	Total (N=61) n (%)	(N=10) n (%)	(N=0) n (%)	(N=40) n (%)	(N=49) n (%)	(N=150) n (%)
神経系障害 (Cont.)								
失神	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
精神障害	2 (3.3)	2 (10.5)	4 (6.6)	0	0	1 (2.5)	1 (2.0)	6 (4.0)
不安	1 (1.6)	0	1 (1.6)	0	0	1 (2.5)	0	2 (1.3)
不眠症	1 (1.6)	2 (10.5)	3 (4.9)	0	0	0	1 (2.0)	4 (2.7)
腎および尿路障害	4 (6.6)	1 (5.3)	5 (8.2)	0	0	0	0	5 (3.3)
排尿困難	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
腎結石症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
腎機能障害	2 (3.3)	0	2 (3.3)	0	0	0	0	2 (1.3)
尿管結石症	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
生殖系および乳房障害	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
閉経期症状	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61)	UPA 30 mg QD (N=19)	Total (N=61)	Placebo (N=10)	UPA 7.5 mg QD (N=0)	UPA 15 mg QD (N=40)	UPA 30 mg QD (N=49)	All UPA (N=150)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害	5 (8.2)	4 (21.1)	8 (13.1)	0	0	2 (5.0)	2 (4.1)	12 (8.0)
喘息	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
咳嗽	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
発声障害	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
過換気	0	0	0	0	0	0	1 (2.0)	1 (0.7)
口腔咽頭不快感	0	1 (5.3)	1 (1.6)	0	0	1 (2.5)	0	2 (1.3)
口腔咽頭痛	1 (1.6)	1 (5.3)	2 (3.3)	0	0	1 (2.5)	1 (2.0)	4 (2.7)
アレルギー性鼻炎	0	3 (15.8)	3 (4.9)	0	0	0	0	3 (2.0)
睡眠時無呼吸症候群	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
上気道の炎症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
皮膚および皮下組織障害	14 (23.0)	4 (21.1)	18 (29.5)	2 (20.0)	0	5 (12.5)	7 (14.3)	30 (20.0)
ざ瘡	3 (4.9)	0	3 (4.9)	0	0	1 (2.5)	1 (2.0)	5 (3.3)
皮膚嚢腫	0	0	0	0	0	0	1 (2.0)	1 (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.

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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.

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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/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=61)	UPA 30 mg QD (N=19)	Total (N=61)	Placebo (N=10)	UPA 7.5 mg QD (N=0)	UPA 15 mg QD (N=40)	UPA 30 mg QD (N=49)	All UPA (N=150)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
皮膚および皮下組織障害 (Cont.)								
皮膚炎	0	0	0	1 (10.0)	0	0	0	0
ざ瘡様皮膚炎	0	0	0	0	0	1 (2.5)	0	1 (0.7)
接触皮膚炎	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
薬疹	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
異汗性湿疹	0	0	0	0	0	0	1 (2.0)	1 (0.7)
湿疹	5 (8.2)	2 (10.5)	7 (11.5)	0	0	0	1 (2.0)	8 (5.3)
皮脂欠乏性湿疹	0	0	0	0	0	0	2 (4.1)	2 (1.3)
紅斑	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
毛孔性角化症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
汗疹	1 (1.6)	0	1 (1.6)	0	0	1 (2.5)	0	2 (1.3)
そう痒症	1 (1.6)	1 (5.3)	2 (3.3)	0	0	0	1 (2.0)	3 (2.0)
発疹	2 (3.3)	0	2 (3.3)	1 (10.0)	0	1 (2.5)	1 (2.0)	4 (2.7)

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.

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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-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			UPA 15 mg QD UPA 30 mg QD				All UPA
	(N=61) n (%)	(N=19) n (%)	Total (N=61) n (%)	Placebo (N=10) n (%)	UPA 7.5 mg QD (N=0) n (%)	UPA 15 mg QD (N=40) n (%)	UPA 30 mg QD (N=49) n (%)	(N=150) n (%)
皮膚および皮下組織障害 (Cont.)								
脂漏性皮膚炎	0	1 (5.3)	1 (1.6)	0	0	0	0	1 (0.7)
皮膚潰瘍	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
蕁麻疹	0	1 (5.3)	1 (1.6)	0	0	1 (2.5)	0	2 (1.3)
乾皮症	0	0	0	0	0	0	1 (2.0)	1 (0.7)
血管障害	4 (6.6)	1 (5.3)	5 (8.2)	1 (10.0)	0	0	1 (2.0)	6 (4.0)
深部静脈血栓症	1 (1.6)	0	1 (1.6)	0	0	0	0	1 (0.7)
高血圧	4 (6.6)	1 (5.3)	5 (8.2)	1 (10.0)	0	0	0	5 (3.3)
静脈炎	0	0	0	0	0	0	1 (2.0)	1 (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.

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UPADACITINIB (ULCERATIVE COLITIS)

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population-----			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD/ UPA 15 mg QD			Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	All_UPA
	(N=61)	(N=19)	(N=61)	(N=10)	(N=0)	(N=40)	(N=49)	(N=150)
	(PYs=119.3) Events (E/100 PYs)	(PYs=27.0) Events (E/100 PYs)	(PYs=146.2) Events (E/100 PYs)	(PYs=7.2) Events (E/100 PYs)	(PYs=0.0) Events (E/100 PYs)	(PYs=41.7) Events (E/100 PYs)	(PYs=40.6) Events (E/100 PYs)	(PYs=228.5) Events (E/100 PYs)
Any adverse event	319 (267.4)	93 (344.4)	412 (281.8)	16 (222.2)	0	78 (187.1)	112 (275.9)	602 (263.5)
血液およびリンパ系障害	11 (9.2)	3 (11.1)	14 (9.6)	0	0	4 (9.6)	3 (7.4)	21 (9.2)
貧血	1 (0.8)	0	1 (0.7)	0	0	1 (2.4)	0	2 (0.9)
鉄欠乏性貧血	2 (1.7)	0	2 (1.4)	0	0	1 (2.4)	0	3 (1.3)
白血球減少症	2 (1.7)	2 (7.4)	4 (2.7)	0	0	2 (4.8)	1 (2.5)	7 (3.1)
リンパ節症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
リンパ球減少症	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
好中球減少症	3 (2.5)	1 (3.7)	4 (2.7)	0	0	0	2 (4.9)	6 (2.6)
心臓障害	1 (0.8)	0	1 (0.7)	0	0	1 (2.4)	2 (4.9)	4 (1.8)
完全房室ブロック	0	0	0	0	0	1 (2.4)	0	1 (0.4)
上室性期外収縮	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total (N=61) (N=19) (N=61) (PYs=119.3) (PYs=27.0) (PYs=146.2) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=10) (N=0) (N=40) (N=49) (PYs=7.2) (PYs=0.0) (PYs=41.7) (PYs=40.6) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
心臓障害 (Cont.)								
心室性期外収縮	0	0	0	0	0	0	2 (4.9)	2 (0.9)
先天性、家族性および遺伝性障害	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
歯原性嚢胞	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
耳および迷路障害	0	1 (3.7)	1 (0.7)	0	0	2 (4.8)	4 (9.9)	7 (3.1)
メニエール病	0	0	0	0	0	0	1 (2.5)	1 (0.4)
耳漏	0	0	0	0	0	0	1 (2.5)	1 (0.4)
耳鳴	0	1 (3.7)	1 (0.7)	0	0	0	1 (2.5)	2 (0.9)
回転性めまい	0	0	0	0	0	2 (4.8)	1 (2.5)	3 (1.3)
内分泌障害	1 (0.8)	1 (3.7)	2 (1.4)	0	0	0	0	2 (0.9)
副腎機能不全	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
甲状腺腫	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
眼障害	9 (7.5)	1 (3.7)	10 (6.8)	2 (27.8)	0	2 (4.8)	2 (4.9)	14 (6.1)
白内障	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
結膜嚢胞	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
結膜出血	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
アレルギー性結膜炎	1 (0.8)	1 (3.7)	2 (1.4)	1 (13.9)	0	0	1 (2.5)	3 (1.3)
ドライアイ	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
緑内障	0	0	0	0	0	0	1 (2.5)	1 (0.4)
黄斑浮腫	0	0	0	0	0	1 (2.4)	0	1 (0.4)
眼充血	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
網膜静脈閉塞	0	0	0	0	0	1 (2.4)	0	1 (0.4)
ぶどう膜炎	0	0	0	1 (13.9)	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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
眼障害 (Cont.)								
硝子体浮遊物	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
胃腸障害	47 (39.4)	14 (51.9)	61 (41.7)	1 (13.9)	0	12 (28.8)	10 (24.6)	83 (36.3)
腹部膨満	0	4 (14.8)	4 (2.7)	0	0	0	0	4 (1.8)
腹痛	3 (2.5)	0	3 (2.1)	0	0	0	1 (2.5)	4 (1.8)
下腹部痛	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
上腹部痛	1 (0.8)	0	1 (0.7)	0	0	0	1 (2.5)	2 (0.9)
肛門ポリープ	0	0	0	0	0	0	1 (2.5)	1 (0.4)
口角口唇炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
アフタ性潰瘍	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
潰瘍性大腸炎	4 (3.4)	1 (3.7)	5 (3.4)	1 (13.9)	0	3 (7.2)	2 (4.9)	10 (4.4)
便秘	5 (4.2)	1 (3.7)	6 (4.1)	0	0	1 (2.4)	1 (2.5)	8 (3.5)

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.

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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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
胃腸障害 (Cont.)								
齲齒	1 (0.8)	2 (7.4)	3 (2.1)	0	0	1 (2.4)	0	4 (1.8)
下痢	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
消化不良	4 (3.4)	1 (3.7)	5 (3.4)	0	0	0	0	5 (2.2)
腸炎	1 (0.8)	0	1 (0.7)	0	0	0	2 (4.9)	3 (1.3)
胃ポリープ	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
胃炎	1 (0.8)	1 (3.7)	2 (1.4)	0	0	0	0	2 (0.9)
胃食道逆流性疾患	4 (3.4)	0	4 (2.7)	0	0	1 (2.4)	0	5 (2.2)
痔核	0	0	0	0	0	2 (4.8)	0	2 (0.9)
腸管ポリープ	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
大腸ポリープ	8 (6.7)	1 (3.7)	9 (6.2)	0	0	1 (2.4)	0	10 (4.4)
口唇障害	0	0	0	0	0	1 (2.4)	0	1 (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.

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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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
胃腸障害 (Cont.)								
悪心	0	0	0	0	0	2 (4.8)	0	2 (0.9)
口腔扁平苔癬	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
歯周病	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
直腸炎	0	2 (7.4)	2 (1.4)	0	0	0	0	2 (0.9)
直腸ポリープ	0	0	0	0	0	0	1 (2.5)	1 (0.4)
口内炎	3 (2.5)	1 (3.7)	4 (2.7)	0	0	0	0	4 (1.8)
埋伏歯	0	0	0	0	0	0	1 (2.5)	1 (0.4)
歯痛	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
嘔吐	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
一般・全身障害および投与部位の状態	21 (17.6)	2 (7.4)	23 (15.7)	2 (27.8)	0	8 (19.2)	7 (17.2)	38 (16.6)
胸痛	1 (0.8)	1 (3.7)	2 (1.4)	0	0	0	0	2 (0.9)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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--
	UPA 15 mg QD (N=61)	UPA 30 mg QD (N=19)	Total (N=61)	Placebo (N=10)	UPA 7.5 mg QD (N=0)	UPA 15 mg QD (N=40)	UPA 30 mg QD (N=49)	All UPA (N=150)
MedDRA 23.0 System Organ Class Preferred Term	(PYs=119.3) Events (E/100 PYs)	(PYs=27.0) Events (E/100 PYs)	(PYs=146.2) Events (E/100 PYs)	(PYs=7.2) Events (E/100 PYs)	(PYs=0.0) Events (E/100 PYs)	(PYs=41.7) Events (E/100 PYs)	(PYs=40.6) Events (E/100 PYs)	(PYs=228.5) Events (E/100 PYs)
一般・全身障害および投与部位の状態 (Cont.)								
異常感	0	0	0	0	0	1 (2.4)	0	1 (0.4)
注射部位疼痛	3 (2.5)	0	3 (2.1)	0	0	3 (7.2)	4 (9.9)	10 (4.4)
倦怠感	1 (0.8)	0	1 (0.7)	1 (13.9)	0	0	0	1 (0.4)
末梢性浮腫	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
発熱	13 (10.9)	1 (3.7)	14 (9.6)	1 (13.9)	0	3 (7.2)	3 (7.4)	20 (8.8)
腫脹	0	0	0	0	0	1 (2.4)	0	1 (0.4)
評価不能の事象	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
肝胆道系障害	6 (5.0)	2 (7.4)	8 (5.5)	0	0	0	3 (7.4)	11 (4.8)
胆嚢炎	0	0	0	0	0	0	1 (2.5)	1 (0.4)
胆石症	0	0	0	0	0	0	1 (2.5)	1 (0.4)
肝機能異常	4 (3.4)	1 (3.7)	5 (3.4)	0	0	0	1 (2.5)	6 (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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
肝胆道系障害 (Cont.)								
脂肪肝	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
肝障害	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
免疫系障害	1 (0.8)	0	1 (0.7)	0	0	0	1 (2.5)	2 (0.9)
アナフィラキシー反応	0	0	0	0	0	0	1 (2.5)	1 (0.4)
季節性アレルギー	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
感染症および寄生虫症	102 (85.5)	30 (111.1)	132 (90.3)	3 (41.7)	0	13 (31.2)	30 (73.9)	175 (76.6)
肛門膿瘍	1 (0.8)	0	1 (0.7)	0	0	0	1 (2.5)	2 (0.9)
虫垂炎	0	0	0	0	0	0	1 (2.5)	1 (0.4)
細菌感染	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
バルトリン腺炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
気管支炎	3 (2.5)	0	3 (2.1)	0	0	0	0	3 (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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
COVID-19	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
COVID-19肺炎	0	0	0	0	0	0	1 (2.5)	1 (0.4)
カンピロバクター胃腸炎	1 (0.8)	0	1 (0.7)	0	0	1 (2.4)	1 (2.5)	3 (1.3)
カンジダ感染	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
クロストリジウム・ディフィシレ感染	1 (0.8)	5 (18.5)	6 (4.1)	0	0	0	0	6 (2.6)
結膜炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
ウイルス性結膜炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
膀胱炎	6 (5.0)	0	6 (4.1)	0	0	0	1 (2.5)	7 (3.1)
サイトメガロウイルス感染	0	0	0	0	0	0	1 (2.5)	1 (0.4)
感染性皮膚炎	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
爪の皮膚糸状菌症	1 (0.8)	1 (3.7)	2 (1.4)	0	0	0	0	2 (0.9)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61)	UPA 30 mg QD (N=19)	Total (N=61)	Placebo (N=10)	UPA 7.5 mg QD (N=0)	UPA 15 mg QD (N=40)	UPA 30 mg QD (N=49)	All UPA (N=150)
	(PYs=119.3) Events (E/100 PYs)	(PYs=27.0) Events (E/100 PYs)	(PYs=146.2) Events (E/100 PYs)	(PYs=7.2) Events (E/100 PYs)	(PYs=0.0) Events (E/100 PYs)	(PYs=41.7) Events (E/100 PYs)	(PYs=40.6) Events (E/100 PYs)	(PYs=228.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
感染性腸炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
毛包炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
胃腸炎	1 (0.8)	1 (3.7)	2 (1.4)	0	0	0	1 (2.5)	3 (1.3)
ウイルス性胃腸炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
歯肉炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
ヘリコバクター感染	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
ヘルペス眼感染	0	0	0	0	0	0	1 (2.5)	1 (0.4)
単純ヘルペス	2 (1.7)	1 (3.7)	3 (2.1)	0	0	0	0	3 (1.3)
带状疱疹	11 (9.2)	1 (3.7)	12 (8.2)	2 (27.8)	0	1 (2.4)	3 (7.4)	16 (7.0)
麦粒腫	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
膿痂疹	0	0	0	0	0	1 (2.4)	0	1 (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.

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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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total (N=61) (N=19) (N=61) (PYs=119.3) (PYs=27.0) (PYs=146.2) Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=10) (N=0) (N=40) (N=49) (PYs=7.2) (PYs=0.0) (PYs=41.7) (PYs=40.6) Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
インフルエンザ	4 (3.4)	2 (7.4)	6 (4.1)	0	0	0	0	6 (2.6)
クレブシエラ感染	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
大腸感染	0	0	0	0	0	0	1 (2.5)	1 (0.4)
潜伏結核	1 (0.8)	0	1 (0.7)	0	0	0	1 (2.5)	2 (0.9)
上咽頭炎	28 (23.5)	6 (22.2)	34 (23.3)	1 (13.9)	0	4 (9.6)	3 (7.4)	41 (17.9)
口腔ヘルペス	15 (12.6)	1 (3.7)	16 (10.9)	0	0	0	8 (19.7)	24 (10.5)
骨髓炎	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
爪囲炎	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
歯冠周囲炎	0	0	0	0	0	2 (4.8)	0	2 (0.9)
歯周炎	2 (1.7)	0	2 (1.4)	0	0	0	2 (4.9)	4 (1.8)
扁桃周囲炎	0	0	0	0	0	1 (2.4)	0	1 (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.

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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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----			--SA UPA--	
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
咽頭炎	2 (1.7)	1 (3.7)	3 (2.1)	0	0	0	2 (4.9)	5 (2.2)
肺炎	0	2 (7.4)	2 (1.4)	0	0	0	0	2 (0.9)
歯髄炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
腎盂腎炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
鼻炎	0	0	0	0	0	1 (2.4)	0	1 (0.4)
副鼻腔炎	1 (0.8)	0	1 (0.7)	0	0	1 (2.4)	0	2 (0.9)
皮膚感染	2 (1.7)	1 (3.7)	3 (2.1)	0	0	0	0	3 (1.3)
足部白癬	2 (1.7)	0	2 (1.4)	0	0	1 (2.4)	1 (2.5)	4 (1.8)
上気道感染	3 (2.5)	2 (7.4)	5 (3.4)	0	0	0	0	5 (2.2)
水痘	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
外陰部腔カンジダ症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (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.

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The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)								
創傷感染	0	0	0	0	0	0	1 (2.5)	1 (0.4)
傷害、中毒および処置合併症	9 (7.5)	2 (7.4)	11 (7.5)	0	0	5 (12.0)	2 (4.9)	18 (7.9)
動物咬傷	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
節足動物咬傷	0	0	0	0	0	1 (2.4)	1 (2.5)	2 (0.9)
挫傷	0	0	0	0	0	1 (2.4)	0	1 (0.4)
上顎炎	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
足骨折	1 (0.8)	1 (3.7)	2 (1.4)	0	0	0	1 (2.5)	3 (1.3)
熱射病	0	0	0	0	0	1 (2.4)	0	1 (0.4)
過量投与	0	0	0	0	0	1 (2.4)	0	1 (0.4)
処置後出血	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
肋骨骨折	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (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.

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The SA_UPA population includes all subjects who received at least one dose of upadacitinib in Cohort 1 or Cohort 2.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD Total (N=61) (N=19) (N=61) (PYs=119.3) (PYs=27.0) (PYs=146.2) Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs)			-----SA 2 Population----- Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD (N=10) (N=0) (N=40) (N=49) (PYs=7.2) (PYs=0.0) (PYs=41.7) (PYs=40.6) Events Events Events Events (E/100 PYs) (E/100 PYs) (E/100 PYs) (E/100 PYs)				--SA UPA-- All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)								
皮膚擦過傷	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
ストレス骨折	0	0	0	0	0	1 (2.4)	0	1 (0.4)
皮下血腫	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
脛骨骨折	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
ワクチン接種合併症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
臨床検査	21 (17.6)	5 (18.5)	26 (17.8)	0	0	6 (14.4)	15 (36.9)	47 (20.6)
アラニンアミノトランスフェラーゼ増加	1 (0.8)	0	1 (0.7)	0	0	0	2 (4.9)	3 (1.3)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.8)	0	1 (0.7)	0	0	0	2 (4.9)	3 (1.3)
血中クレアチンホスホキナーゼ増加	6 (5.0)	3 (11.1)	9 (6.2)	0	0	1 (2.4)	3 (7.4)	13 (5.7)
γ-グルタミルトランスフェラーゼ増加	2 (1.7)	1 (3.7)	3 (2.1)	0	0	2 (4.8)	0	5 (2.2)
高比重リポ蛋白増加	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
臨床検査 (Cont.)								
リンパ球数減少	1 (0.8)	1 (3.7)	2 (1.4)	0	0	1 (2.4)	2 (4.9)	5 (2.2)
好中球数減少	3 (2.5)	0	3 (2.1)	0	0	1 (2.4)	4 (9.9)	8 (3.5)
尿中白血球エステラーゼ陽性	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
白血球数減少	4 (3.4)	0	4 (2.7)	0	0	1 (2.4)	2 (4.9)	7 (3.1)
代謝および栄養障害	8 (6.7)	2 (7.4)	10 (6.8)	1 (13.9)	0	4 (9.6)	3 (7.4)	17 (7.4)
糖尿病	0	0	0	1 (13.9)	0	0	1 (2.5)	1 (0.4)
脂質異常症	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
高コレステロール血症	4 (3.4)	0	4 (2.7)	0	0	0	1 (2.5)	5 (2.2)
高脂血症	2 (1.7)	1 (3.7)	3 (2.1)	0	0	3 (7.2)	1 (2.5)	7 (3.1)
高尿酸血症	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
低蛋白血症	0	0	0	0	0	1 (2.4)	0	1 (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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
筋骨格系および結合組織障害	30 (25.1)	7 (25.9)	37 (25.3)	2 (27.8)	0	11 (26.4)	9 (22.2)	57 (24.9)
関節痛	3 (2.5)	1 (3.7)	4 (2.7)	0	0	1 (2.4)	2 (4.9)	7 (3.1)
関節炎	1 (0.8)	1 (3.7)	2 (1.4)	0	0	0	0	2 (0.9)
関節障害	0	0	0	0	0	1 (2.4)	0	1 (0.4)
背部痛	6 (5.0)	0	6 (4.1)	0	0	1 (2.4)	0	7 (3.1)
頸部脊柱管狭窄症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
側腹部痛	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
椎間板突出	4 (3.4)	1 (3.7)	5 (3.4)	0	0	1 (2.4)	2 (4.9)	8 (3.5)
腰部脊柱管狭窄症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
筋痙縮	2 (1.7)	1 (3.7)	3 (2.1)	0	0	0	1 (2.5)	4 (1.8)
筋骨格系胸痛	0	0	0	0	0	2 (4.8)	0	2 (0.9)

Note: PYs is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
 E/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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
筋骨格痛	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
筋骨格硬直	1 (0.8)	0	1 (0.7)	1 (13.9)	0	0	0	1 (0.4)
筋肉痛	1 (0.8)	0	1 (0.7)	0	0	1 (2.4)	1 (2.5)	3 (1.3)
変形性関節症	3 (2.5)	0	3 (2.1)	0	0	0	0	3 (1.3)
骨端症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
骨壊死	0	1 (3.7)	1 (0.7)	0	0	1 (2.4)	0	2 (0.9)
骨粗鬆症	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
四肢痛	2 (1.7)	1 (3.7)	3 (2.1)	1 (13.9)	0	0	3 (7.4)	6 (2.6)
関節周囲炎	0	0	0	0	0	2 (4.8)	0	2 (0.9)
横紋筋融解症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
変形性脊椎症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (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.

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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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)								
弾発指	0	0	0	0	0	1 (2.4)	0	1 (0.4)
良性、悪性および詳細不明の新生物 (嚢胞およびポリープを含む)	4 (3.4)	0	4 (2.7)	1 (13.9)	0	2 (4.8)	2 (4.9)	8 (3.5)
肛門性器疣贅	0	0	0	0	0	1 (2.4)	0	1 (0.4)
大腸腺腫	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
線維腫	0	0	0	0	0	0	1 (2.5)	1 (0.4)
脂漏性角化症	0	0	0	1 (13.9)	0	0	0	0
皮膚乳頭腫	2 (1.7)	0	2 (1.4)	0	0	0	1 (2.5)	3 (1.3)
子宮平滑筋腫	0	0	0	0	0	1 (2.4)	0	1 (0.4)
神経系障害	8 (6.7)	6 (22.2)	14 (9.6)	0	0	0	5 (12.3)	19 (8.3)
大脳障害	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
浮動性めまい	1 (0.8)	2 (7.4)	3 (2.1)	0	0	0	1 (2.5)	4 (1.8)

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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				---SA UPA---
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
神経系障害 (Cont.)								
異常感覚	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
頭痛	3 (2.5)	1 (3.7)	4 (2.7)	0	0	0	2 (4.9)	6 (2.6)
感覚鈍麻	0	2 (7.4)	2 (1.4)	0	0	0	1 (2.5)	3 (1.3)
片頭痛	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
後頭神経痛	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
傾眠	0	0	0	0	0	0	1 (2.5)	1 (0.4)
失神	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
精神障害	2 (1.7)	4 (14.8)	6 (4.1)	0	0	1 (2.4)	1 (2.5)	8 (3.5)
不安	1 (0.8)	0	1 (0.7)	0	0	1 (2.4)	0	2 (0.9)
不眠症	1 (0.8)	4 (14.8)	5 (3.4)	0	0	0	1 (2.5)	6 (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.

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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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
腎および尿路障害	5 (4.2)	2 (7.4)	7 (4.8)	0	0	0	0	7 (3.1)
排尿困難	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
腎結石症	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
腎機能障害	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
尿管結石症	0	2 (7.4)	2 (1.4)	0	0	0	0	2 (0.9)
生殖系および乳房障害	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
閉経期症状	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
呼吸器、胸郭および縦隔障害	7 (5.9)	5 (18.5)	12 (8.2)	0	0	2 (4.8)	2 (4.9)	16 (7.0)
喘息	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
咳嗽	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
発声障害	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
過換気	0	0	0	0	0	0	1 (2.5)	1 (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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
呼吸器、胸郭および縦隔障害 (Cont.)								
口腔咽頭不快感	0	1 (3.7)	1 (0.7)	0	0	1 (2.4)	0	2 (0.9)
口腔咽頭痛	1 (0.8)	1 (3.7)	2 (1.4)	0	0	1 (2.4)	1 (2.5)	4 (1.8)
アレルギー性鼻炎	0	3 (11.1)	3 (2.1)	0	0	0	0	3 (1.3)
睡眠時無呼吸症候群	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
上気道の炎症	2 (1.7)	0	2 (1.4)	0	0	0	0	2 (0.9)
皮膚および皮下組織障害	18 (15.1)	5 (18.5)	23 (15.7)	3 (41.7)	0	5 (12.0)	10 (24.6)	38 (16.6)
ざ瘡	4 (3.4)	0	4 (2.7)	0	0	1 (2.4)	1 (2.5)	6 (2.6)
皮膚嚢腫	0	0	0	0	0	0	1 (2.5)	1 (0.4)
皮膚炎	0	0	0	1 (13.9)	0	0	0	0
ざ瘡様皮膚炎	0	0	0	0	0	1 (2.4)	0	1 (0.4)
接触皮膚炎	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (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.

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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)

MedDRA 23.0 System Organ Class Preferred Term	-----SA 1 Population----- UPA 15 mg QD/ UPA 15 mg QD UPA 30 mg QD			-----SA 2 Population-----				--SA UPA--
	UPA 15 mg QD (N=61) (PYs=119.3) Events (E/100 PYs)	UPA 30 mg QD (N=19) (PYs=27.0) Events (E/100 PYs)	Total (N=61) (PYs=146.2) Events (E/100 PYs)	Placebo (N=10) (PYs=7.2) Events (E/100 PYs)	UPA 7.5 mg QD (N=0) (PYs=0.0) Events (E/100 PYs)	UPA 15 mg QD (N=40) (PYs=41.7) Events (E/100 PYs)	UPA 30 mg QD (N=49) (PYs=40.6) Events (E/100 PYs)	All UPA (N=150) (PYs=228.5) Events (E/100 PYs)
皮膚および皮下組織障害 (Cont.)								
薬疹	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
異汗性湿疹	0	0	0	0	0	0	1 (2.5)	1 (0.4)
湿疹	5 (4.2)	2 (7.4)	7 (4.8)	0	0	0	1 (2.5)	8 (3.5)
皮脂欠乏性湿疹	0	0	0	0	0	0	3 (7.4)	3 (1.3)
紅斑	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
毛孔性角化症	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (0.4)
汗疹	1 (0.8)	0	1 (0.7)	0	0	1 (2.4)	0	2 (0.9)
そう痒症	1 (0.8)	1 (3.7)	2 (1.4)	0	0	0	1 (2.5)	3 (1.3)
発疹	2 (1.7)	0	2 (1.4)	2 (27.8)	0	1 (2.4)	1 (2.5)	4 (1.8)
脂漏性皮膚炎	0	1 (3.7)	1 (0.7)	0	0	0	0	1 (0.4)
皮膚潰瘍	1 (0.8)	0	1 (0.7)	0	0	0	0	1 (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.
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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.

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