被験者は本事象を理由に試験を中止した。

ELIQUIS が投与された。

The patient's past medications include:

COUMADIN for DVT and PULMONARY EMBOLUS (20[redacted] - 20[redacted])

TRIAMCINOLONE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BRYHALI for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Deep vein thrombosis leg (10065052) (Deep vein thrombosis (10051055)) [v.23.0] [10065052]

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 DEEP VEIN THROMBOSIS LEFT LOWER LEG

- **Investigator:** Not applicable

- **AbbVie:** Event more likely related to underlying prothrombin (FACTOR II) 20210G A MUTATION. Additional factors include prior history of deep venous thrombosis, pulmonary embolism and family history of deep venous thrombosis.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANC:** 1750 NO UNITS

[redacted] **20[redacted] ANTI-THROMBIN III ACTIVITY:** 111 % (normal 83 to 128)

[redacted] **20[redacted] BLOOD PRESSURE:** 141/85 mmHg

[redacted] **20[redacted] HEMOGLOBIN:** 11.6 NO UNITS

[redacted] **20[redacted] IGE:** 2844 IU/mL

[redacted] **20[redacted] IGG:** 2847 NO UNITS

[redacted] **20[redacted] INR SPECIAL COAG:** 1.1 RATIO

[redacted] **20[redacted] LUPUS INTERPRETATION:** Not detected

[redacted] **20[redacted] PLATELETS:** 196 NO UNITS

[redacted] **20[redacted] PROTHROMBIN (FACTOR II) 20210G>A MUTATION:** HETEROZYGOUS

[redacted] **20[redacted] PROTIME:** 12.4 SEC (normal 9.4 to 12.5)

[redacted] **20[redacted] SPO2:** 98 %

[redacted] **20[redacted] ULTRASOUND:** There is a nonocclusive thrombus of the popliteal vein. Echogenic linear component is clearly chronic. Less specific rounded nonocclusive thrombus is age indeterminate. Possibly acute on chronic deep venous thrombosis of the popliteal vein.

[redacted] **20[redacted] WBC:** 3.67 NO UNITS

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3.3 K/MM3

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	1[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
ASTHMA	20[redacted]
ATOPIC DERMATITIS	20[redacted]
BENIGN HEART MURMUR	20[redacted]
ENVIRONMENTAL ALLERGIES	20[redacted]
BLEPHARITIS	20[redacted]
OBESITY	20[redacted]
MENSTRUAL CRAMPS	20[redacted]
ANGULAR CHELITIS	20[redacted]
ANXIETY	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: BLEACH BATH	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted] / 1	[redacted] / 112	112
UPA	15 MG	ORAL	QD	[redacted] / 113	[redacted] / 138	26

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
HYDROCORTISONE	2.5 %	BID	Y: [redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
HYDROXYZINE	5 mg	PRN	Y: [redacted]
HYPOCHLOROUS ACID	N/A OTHER: UNK	QD	Y: [redacted]
SALBUTAMOL	1 OTHER: VIAL	OTHER: Q4-6 HRS, PRN	Y-M: [redacted]
CETIRIZINE	10 mg	PRN	Y: [redacted]
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	PRN	Y: [redacted]
TRIAMCINOLONE	0.1 %	PRN	Y: [redacted]
BETAMETHASONE	1 OTHER: APPLLICATION	BID	Y: [redacted]
IBUPROFEN	400 mg	QD	Y: [redacted]
METHOTREXATE	15 mg	OTHER: EVERY WEEK	Y-M: [redacted]
KETOCONAZOLE	1 OTHER: APP	OTHER: BID, PRN	Y-M: [redacted] / -346
OLOPATADINE	1 DROP, BOTH EYES gtt	QD	Y-M: [redacted] / -344
METHOTREXATE	25 mg	OTHER: EVERY WEEK	Y-M: [redacted] / -329
CLOBETASOL	0.05 %	PRN	Y: [redacted] / -191
MENINGOCOCCAL VACCINE	0.5 mL	OTHER: X1	Y-M: [redacted] / -48
EMOLLIENTS AND PROTECTIVES	N/A OTHER: UNKNOWN	BID	Y-M: [redacted] / -14

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
HYDROXYZINE	5 mg	PRN	Y: [redacted]	ONGOING
SALBUTAMOL	1 OTHER: VIAL	OTHER: Q4-6 HRS, PRN	Y-M: [redacted]	ONGOING
CETIRIZINE	10 mg	PRN	Y: [redacted]	ONGOING
IBUPROFEN	400 mg	QD	Y: [redacted]	ONGOING
KETOCONAZOLE	1 OTHER: APP	OTHER: BID, PRN	Y-M: [redacted] / -346	ONGOING
OLOPATADINE	1 DROP, BOTH EYES gtt	QD	Y-M: [redacted] / -344	ONGOING

EMOLLIENTS AND PROTECTIVES	N/A OTHER: UNKNOWN	BID	Y-M: 20[redacted] / - 14	ONGOING
MUPIROCIN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 56
CEFALEXIN	500 mg	BID	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 75
CLINDAMYCIN	300 mg	TID	Y-M: 20[redacted] / 76	Y-M: 20[redacted] / 82
MUPIROCIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 78	ONGOING
ESCITALOPRAM	5 mg	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 91
HYDROCORTISONE	2.5 %	TID	Y-M: 20[redacted] / 83	ONGOING
VANCOMYCIN	1 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 83
CLINDAMYCIN	900 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 84
CLINDAMYCIN	600 mg	TID	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 95
ESCITALOPRAM	10 mg	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 112
ESCITALOPRAM	15 mg	QD	Y-M: 20[redacted] / 113	ONGOING
INFLUENZA VACCINE	0.5 mL	OTHER: ONCE	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 125
CLINDAMYCIN	600 mg	TID	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 128
TRIAMCINOLONE	0.1 %	QD	Y-M: 20[redacted] / 141	ONGOING

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

Event Description	WORSENING IMPETIGO AROUND LIPS
Preferred term	膿痂疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 82
Age at AE Onset	1[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 83): Leukocytes: 8.6 [3.5 - 10.6] 10^9/L; Lymphocytes: 2.8 [1 - 3.8] UNIT NOT REPORTED; Neutrophils: 5.0 [1.58 - 7.13] UNIT NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 82): WOUND NPTST047-CULTURE: POSITIVE-RARE CORYNEBACTERIUM SPECIES; [redacted]20[redacted] (RX DAY 83): BLOOD NPTST047-CULTURE: NEGATIVE; WOUND NPTST075-HERPES SIMPLEX VIRUS 1/2: NEGATIVE
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	155 (17 DAYS AFTER LAST TREATMENT)
Duration of AE	74 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED

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

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者は米国の 1[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，口唇周囲の膿痂疹増悪を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎，環境アレルギー及び口角口唇炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は口唇周囲の膿痂疹増悪を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，口唇周囲の膿痂疹増悪は消失した。

本事象発現に先行し，被験者は 20[redacted] 年 [redacted] 月に膿痂疹（非重篤）を 2 回発現していた。1 回目の患部は下唇，2 回目の患部は口周囲及び前額部であった。外来治療として mupirocin の外用軟膏，並びに Keflex 及び clindamycin の経口薬が投与されたが，全体的な改善が得られなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，症状として口唇乾燥，1 ヵ月持続する口周囲の漿液性痂皮病変及び漿液性排液，中等度のそう痒を伴うびまん性湿疹性顔面皮疹，皮膚乾燥，及び皮膚剥離を呈していた。治療薬として，vancomycin の静脈内投与及び静脈内補液が行われた。その後，clindamycin の静脈内投与に変更された。創部検体培養の結果はコリネバクテリウム属菌陽性であった。バイタルサインは安定しており，入院期間中の発熱はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，口周囲の病変は軽快して漿液性排液もなく，被験者は退院した。

BACTROBAN，clindamycin，vancomycin 及びヒドロコルチゾンが投与された。

The patient's past medications include:

HYDROCORTISONE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

TRIAMCINOLONE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

BETAMETHASONE DIPROPIONATE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

METHOTREXATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted] - [redacted] 20[redacted])

CLOBETASOL for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

KEFLEX for IMPETIGO ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Impetigo (10021531) (Impetigo (10021531)) [v.23.0] [10021531]

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 IMPETIGO AROUND LIPS

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing angular cheilitis and atopic dermatitis.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BLOOD TEST:** Negative

[redacted] **WHITE BLOOD CELLS:** 8.6 K/CUMM (normal 3.5 to 10.6)

[redacted] **WOUND CULTURES:** Negative for HERPES SIMPLEX VIRUS 1/2.

[redacted] **WOUND CULTURES:** Positive for rare Corynebacterium species.

Subject [redacted] ([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
コロナウイルス感染	X			X
細菌性肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
PLACEBO/UPA 30 MG QD	5[redacted]	MALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
ASTHMA	19[redacted]
ATOPIC DERMATITIS	19[redacted]
CHRONIC KIDNEY DISEASE	19[redacted]
ATOPIC DERMATITIS	19[redacted]
FOOD ALLERGIES: FISH	19[redacted]
GOUT	20[redacted]
CARDIOVASCULAR DISEASE - MYOCARDIAL INFARCTION	20[redacted]
CORONARY ARTERY DISEASE	20[redacted]
HYPERCHOLESTEROLEMIA	20[redacted]
HYPERTENSION	20[redacted]
KERATOCONUS	20[redacted]
OSTEOARTHRITIS OF RIGHT KNEE	20[redacted]
ALLERGIC RHINITIS	20[redacted]
ACUTE OTITIS MEDIA	20[redacted]
RIGHT ROTATOR CUFF INJURY	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ANEMIA	NOT REPORTED
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED
OBSTRUCTIVE SLEEP APNEA	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: HIP REPLACEMENT- RIGHT	19[redacted]
PRIOR PROCEDURES: EXCISION OF GOUT NODULE	20[redacted]
PRIOR PROCEDURES: CORONARY ANGIOPLASTY	20[redacted]
PRIOR PROCEDURES: CORONARY STENT	20[redacted]
PRIOR PROCEDURES: HIP REPLACEMENT - RIGHT	20[redacted]
PRIOR PROCEDURES: BUNIONECTOMY	20[redacted]
PRIOR PROCEDURES: HIP REPLACEMENT - LEFT	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	5 CIGARETTE	13	19[redacted]

CIGARS	NEVER
E-CIGARETTES	NEVER
PIPES	NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 112	112
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 113		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARAFFIN	4 g	BID	Y: 19[redacted]
ATORVASTATIN	80 mg	QD	Y: 20[redacted]
CLOPIDOGREL	75 mg	QD	Y: 20[redacted]
METOPROLOL	50 mg	BID	Y: 20[redacted]
ALLOPURINOL	100 mg	PRN	Y-M: 20[redacted]
FLUOCINONIDE	0.05 %	BID	Y: 20[redacted]
CRISABOROLE	2 %	BID	Y-M: 20[redacted]
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / -148
FLUTICASONE	88 ug	BID	Y-M: 20[redacted] / -35
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / -30
AUGMENTIN	875/125 mg	BID	Y-M: 20[redacted] / -13
COLCHICINE	0.6 mg	PRN	Y-M: 20[redacted] / -13

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
PARAFFIN	4 g	BID	Y: 19[redacted]	NOT REPORTED
ATORVASTATIN	80 mg	QD	Y: 20[redacted]	ONGOING
CLOPIDOGREL	75 mg	QD	Y: 20[redacted]	ONGOING
METOPROLOL	50 mg	BID	Y: 20[redacted]	ONGOING
ALLOPURINOL	100 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
FLUTICASONE	88 ug	BID	Y-M: 20[redacted] / -35	ONGOING
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / -30	Y-M: 20[redacted] / 393
COLCHICINE	0.6 mg	PRN	Y-M: 20[redacted] / -13	ONGOING
HEPARIN	5000 OTHER: UNITS	OTHER: Q8H	Y-M: 20[redacted] / 294	Y-M: 20[redacted] / 299
SODIUM CHLORIDE	100 OTHER: ML/HR	OTHER: CONTINIOUS	Y-M: 20[redacted] / 294	Y-M: 20[redacted] / 299
PARACETAMOL	650 mg	OTHER: Q6H	Y-M: 20[redacted] / 294	Y-M: 20[redacted] / 308
VANCOMYCIN	1500 mg	OTHER: ONCE	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 295
HYDROXYCHLOROQUINE	400 mg	BID	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 296
LEVETIRACETAM	1000 mg	QD	Y-M: 20[redacted] / 296	Y-M: 20[redacted] / 296
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted] / 296	Y-M: 20[redacted] / 297
HYDROXYCHLOROQUINE	400 mg	QD	Y-M: 20[redacted] / 296	Y-M: 20[redacted] / 299
PIP/TAZO	2.25 g	QID	Y-M: 20[redacted] / 297	Y-M: 20[redacted] / 299
VANCOMYCIN	1500 mg	QD	Y-M: 20[redacted] / 297	Y-M: 20[redacted] / 299
POTASSIUM	40 mEq	PRN	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 299

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

Event Description COVID-19 INFECTION

Preferred term コロナウイルス感染

AE Onset Date / Rx Day [redacted]20[redacted] / 292

Age at AE Onset 5[redacted]

Laboratory Testing [redacted]20[redacted] (RX DAY 294): Basophils: 0.0 [0 - 0.05] UNIT NOT REPORTED; Basophils/Leukocytes: 0 [0 - 2] %; Blood Urea Nitrogen: 9.3 [1.8 - 7.1] MMOL/L; Calcium: 2.07 [2.12 - 2.62] MMOL/L; Chloride: 94 [98 - 108] MMOL/L; Creatinine: 233 [0 - 133] UMOL/L; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4.29 [4.5 - 5.9] UNIT NOT REPORTED; Glucose: 7 [3.9 - 7.8] MMOL/L; Hematocrit: 0.38 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 127 [140 - 174] G/L; Leukocytes: 5.3 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.6 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 11 [20 - 44] %; NPTST039-CO2: 26 [20 - 30] MEQ/L; NPTST097-MCH: 29.6 [27 - 33] PG; NPTST100-MCV: 88.6 [80 - 96] FL; NPTST129-RDW: 15.5 [12.2 - 16.1] %; Neutrophils: 4.4 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 84 [50 - 70] %; Platelets: 119 [150 - 400] UNIT NOT REPORTED; Potassium: 3.5 [3.5 - 5] MMOL/L; Sodium: 136 [135 - 145] MMOL/L; [redacted]20[redacted] (RX

	DAY 295): Alanine Aminotransferase: 50 [0 - 40] U/L; Albumin: 38 [35 - 50] G/L; Alkaline Phosphatase: 38 [0 - 130] U/L; Aspartate Aminotransferase: 104 [0 - 50] U/L; Basophils: 0.01 [0 - 0.05] UNIT NOT REPORTED; Basophils/Leukocytes: 0 [0 - 2] %; Bilirubin: 12 [0 - 21] UMOL/L; Blood Urea Nitrogen: 9.6 [1.8 - 7.1] MMOL/L; Calcium: 1.72 [2.12 - 2.62] MMOL/L; Chloride: 94 [98 - 108] MMOL/L; Creatine Kinase: 1575 [0 - 200] U/L; Creatinine: 201 [0 - 133] UMOL/L; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4.18 [4.5 - 5.9] UNIT NOT REPORTED; Glucose: 6.7 [3.9 - 7.8] MMOL/L; Hematocrit: 0.37 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 125 [140 - 174] G/L; Leukocytes: 3.8 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.7 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 19 [20 - 44] %; Monocytes: 0.1 [0.3 - 0.5] UNIT NOT REPORTED; Monocytes/Leukocytes: 2 [2 - 9] %; NPTST025-BILLIRUBIN - CONJUGATED: 0.2 [0 - 0.3] MG/DL; NPTST039-CO2: 21 [20 - 30] MEQ/L; NPTST087-LDH: 518 [0 - 240] U/L; NPTST096-MAGNESIUM: 1.2 [1.7 - 2.8] MG/DL; NPTST097-MCH: 29.9 [27 - 33] PG; NPTST100-MCV: 87.6 [80 - 96] FL; NPTST122-PHOSPHORUS: 2.5 [2.5 - 4.5] MG/DL; NPTST129-RDW: 15.6 [12.2 - 16.1] %; Neutrophils: 3.0 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 78 [50 - 70] %; Platelets: 99 [150 - 400] UNIT NOT REPORTED; Potassium: 3.1 [3.5 - 5] MMOL/L; Protein: 62 [60 - 80] G/L; Sodium: 131 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 296): Basophils: 0.01 [0 - 0.05] UNIT NOT REPORTED; Basophils/Leukocytes: 0 [0 - 2] %; Blood Urea Nitrogen: 10.4 [1.8 - 7.1] MMOL/L; Calcium: 1.75 [2.12 - 2.62] MMOL/L; Chloride: 98 [98 - 108] MMOL/L; Creatine Kinase: 1863 [0 - 200] U/L; Creatinine: 210 [0 - 133] UMOL/L; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4.33 [4.5 - 5.9] UNIT NOT REPORTED; Glucose: 7.3 [3.9 - 7.8] MMOL/L; Hematocrit: 0.38 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 126 [140 - 174] G/L; Leukocytes: 3.7 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.8 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 20 [20 - 44] %; Monocytes: 0.1 [0.3 - 0.5] UNIT NOT REPORTED; Monocytes/Leukocytes: 4 [2 - 9] %; NPTST039-CO2: 16 [20 - 30] MEQ/L; NPTST096-MAGNESIUM: 1.5 [1.7 - 2.8] MG/DL; NPTST097-MCH: 29.1 [27 - 33] PG; NPTST100-MCV: 87.8 [80 - 96] FL; NPTST122-PHOSPHORUS: 2.5 [2.5 - 4.5] MG/DL; NPTST129-RDW: 15.6 [12.2 - 16.1] %; NPTST150-TROPONIN: 0.01 [0 - 0.1] NG/ML; Neutrophils: 2.8 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 75 [50 - 70] %; Platelets: 115 [150 - 400] UNIT NOT REPORTED; Potassium: 3.1 [3.5 - 5] MMOL/L; Sodium: 132 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 297): NPTST124-PROCALCITONIN: 3.6 [0 - 0.1] NG/ML; [redacted]20[redacted] (RX DAY 298): Basophils: 0.00 [0 - 0.05] UNIT NOT REPORTED; Blood Urea Nitrogen: 7.5 [1.8 - 7.1] MMOL/L; Calcium: 1.62 [2.12 - 2.62] MMOL/L; Chloride: 99 [98 - 108] MMOL/L; Creatinine: 197 [0 - 133] UMOL/L; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 3.80 [4.5 - 5.9] UNIT NOT REPORTED; Glucose: 5.7 [3.9 - 7.8] MMOL/L; Hematocrit: 0.33 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 111 [140 - 174] G/L; Leukocytes: 3.8 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.6 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 16 [20 - 44] %; Monocytes: 0.3 [0.3 - 0.5] UNIT NOT REPORTED; Monocytes/Leukocytes: 7 [2 - 9] %; NPTST039-CO2: 21 [20 - 30] MEQ/L; NPTST096-MAGNESIUM: 1.5 [1.7 - 2.8] MG/DL; NPTST097-MCH: 29.2 [27 - 33] PG; NPTST100-MCV: 87.4 [80 - 96] FL; NPTST122-PHOSPHORUS: 2 [2.5 - 4.5] MG/DL; NPTST129-RDW: 15.7 [12.2 - 16.1] %; Neutrophils: 2.9 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 76 [50 - 70] %; Platelets: 108 [150 - 400] UNIT NOT REPORTED; Potassium: 3 [3.5 - 5] MMOL/L; Sodium: 138 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 299): Basophils: 0.01 [0 - 0.05] UNIT NOT REPORTED; Basophils/Leukocytes: 0 [0 - 2] %; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 3.72 [4.5 - 5.9] UNIT NOT REPORTED; Hematocrit: 0.33 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 111 [140 - 174] G/L; Leukocytes: 3.3 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.3 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 10 [20 - 44] %; Monocytes: 0.4 [0.3 - 0.5] UNIT NOT REPORTED; Monocytes/Leukocytes: 12 [2 - 9] %; NPTST097-MCH: 29.8 [27 - 33] PG; NPTST100-MCV: 88.4 [80 - 96] FL; NPTST129-RDW: 15.6 [12.2 - 16.1] %; Neutrophils: 2.5 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 76 [50 - 70] %; Platelets: 131 [150 - 400] UNIT NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 294): BLOOD NPTST026-BLOOD CULTURE: POSITIVE-STAPHYLOCOCCUS EPIDERMIDIS; OTHER NASOPHARYNGEAL SWAB NPTST043-COVID-19 PCR: POSITIVE-NOVEL CORONAVIRUS; OTHER NASOPHARYNGEAL SWAB NPTST082-INFLUENZA A/B: NEGATIVE-INFLUENZA A/B; OTHER NASOPHARYNGEAL SWAB NPTST134-RESPIRATORY SYNCYTIAL VIRUS: NEGATIVE-RESPIRATORY SYNCYTIAL

	VIRUS; [redacted]20[redacted] (RX DAY 295): BLOOD NPTST026-BLOOD CULTURE: NEGATIVE-NO GROWTH AT 48 HRS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 294): ELECTROCARDIOGRAM: NORMAL; PORTABLE AP CHEST X RAY: CLEAR LUNGS; VITAL SIGNS: TEMPERATURE(F): 102.4 PULSE: 115 BP: 103/67 RR: 22 SP02(%):100 ROOM AIR; VITAL SIGNS: TEMPERATURE(F):102.4 PULSE: 87 BP: 102/68 RR:18 SP02(%):97% ROOM AIR; VITAL SIGNS: TEMPERATURE(F): 99.2 PULSE: 85 BP: 113/74 RR: 18 SP02(%): 99 ROOM AIR; [redacted]20[redacted] (RX DAY 295): VITAL SIGNS: TEMPERATURE(F): 101.3 PULSE: 93 BP: 111/72 RR: 18 SP02(%): 99 ROOM AIR; [redacted]20[redacted] (RX DAY 296): CT HEAD: NORMAL CT OF BRAIN; PARTIAL RIGHT-SIDED PARANASAL SINUS OPACIFICATION; VITAL SIGNS: TEMPERATURE(F): 102 PULSE: 93 BP: 109/52 RR: NA SP02(%): 95 ON 02 2 LITERS NASAL CANNULA; VITAL SIGNS: TEMPERATURE(F): 100.7 PULSE: 103 BP: 107/70 RR: 22 SP02(%): 99 ROOM AIR; XR CHEST- PORTABLE AP: BILATERAL PATCHY PERIPHERAL AND LEFT PERIHILIAR INFILTRATES WITH AIR BRONCHOGRAMS ARE NOTED, NOT VISUALIZED ON THE MOST RECENT PREVIOUS EXAMINATION; [redacted]20[redacted] (RX DAY 297): VITAL SIGNS: TEMPERATURE(F): 99.8 PULSE: 96 BP: 106/66 RR: 20 SPO2(%):97 ON 02 2 LITERS ON NASAL CANNULA; VITAL SIGNS: TEMPERATURE(F): 99.2 PULSE: 86 BP: 87/49 RR: 20 SP02(%): 93 ON 02 2 LITERS NASAL CANUNLA; [redacted]20[redacted] (RX DAY 298): VITAL SIGNS: TEMPERATURE(F): 98.2 PULSE: 87 BP: 119/70 RR: 20 SPO2(%):100 ON 02 2 LITERS ON NASAL CANNULA; VITAL SIGNS: TEMPERATURE(F): 99.4 PULSE: 74 BP: 136/95 RR: 20 SPO2(%):92 ON 02 2 LITERS ON NASAL CANNULA; [redacted]20[redacted] (RX DAY 299): VITAL SIGNS: TEMPERATURE(F): 102.1 PULSE: 107 BP: 107/59 RR: 20 SPO2(%):99 ROOM AIR; VITAL SIGNS: TEMPERATURE(F): 97.9 PULSE: 98 BP: 121/76 RR: 20 SPO2(%):98 ON 02 2 LITERS ON NASAL CANNULA
AE Stopped Rx Day	328
Duration of AE	37 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Event of Interest - Renal Dysfunction

Event Description	ACUTE KIDNEY INJURY
Preferred term	急性腎障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 294
Age at AE Onset	5[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	299
Duration of AE	6 DAYS
Toxicity Grade	2
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE

Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	BACTERIAL PNEUMONIA
Preferred term	細菌性肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 296
Age at AE Onset	5[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 294): Basophils: 0.0 [0 - 0.05] UNIT NOT REPORTED; Basophils/Leukocytes: 0 [0 - 2] %; Blood Urea Nitrogen: 9.3 [1.8 - 7.1] MMOL/L; Calcium: 2.07 [2.12 - 2.62] MMOL/L; Chloride: 94 [98 - 108] MMOL/L; Creatinine: 233 [0 - 133] UMOL/L; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4.29 [4.5 - 5.9] UNIT NOT REPORTED; Glucose: 7 [3.9 - 7.8] MMOL/L; Hematocrit: 0.38 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 127 [140 - 174] G/L; Leukocytes: 5.3 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.6 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 11 [20 - 44] %; NPTST039-CO2: 26 [20 - 30] MEQ/L; NPTST097-MCH: 29.6 [27 - 33] PG; NPTST100-MCV: 88.6 [80 - 96] FL; NPTST129-RDW: 15.5 [12.2 - 16.1] %; Neutrophils: 4.4 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 84 [50 - 70] %; Platelets: 119 [150 - 400] UNIT NOT REPORTED; Potassium: 3.5 [3.5 - 5] MMOL/L; Sodium: 136 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 295): Alanine Aminotransferase: 50 [0 - 40] U/L; Albumin: 38 [35 - 50] G/L; Alkaline Phosphatase: 38 [0 - 130] U/L; Aspartate Aminotransferase: 104 [0 - 50] U/L; Basophils: 0.01 [0 - 0.05] UNIT NOT REPORTED; Basophils/Leukocytes: 0 [0 - 2] %; Bilirubin: 12 [0 - 21] UMOL/L; Blood Urea Nitrogen: 9.6 [1.8 - 7.1] MMOL/L; Calcium: 1.72 [2.12 - 2.62] MMOL/L; Chloride: 94 [98 - 108] MMOL/L; Creatine Kinase: 1575 [0 - 200] U/L; Creatinine: 201 [0 - 133] UMOL/L; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4.18 [4.5 - 5.9] UNIT NOT REPORTED; Glucose: 6.7 [3.9 - 7.8] MMOL/L; Hematocrit: 0.37 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 125 [140 - 174] G/L; Leukocytes: 3.8 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.7 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 19 [20 - 44] %; Monocytes: 0.1 [0.3 - 0.5] UNIT NOT REPORTED; Monocytes/Leukocytes: 2 [2 - 9] %; NPTST025-BILLIRUBIN - CONJUGATED: 0.2 [0 - 0.3] MG/DL; NPTST039-CO2: 21 [20 - 30] MEQ/L; NPTST087-LDH: 518 [0 - 240] U/L; NPTST096-MAGNESIUM: 1.2 [1.7 - 2.8] MG/DL; NPTST097-MCH: 29.9 [27 - 33] PG; NPTST100-MCV: 87.6 [80 - 96] FL; NPTST122-PHOSPHORUS: 2.5 [2.5 - 4.5] MG/DL; NPTST129-RDW: 15.6 [12.2 - 16.1] %; Neutrophils: 3.0 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 78 [50 - 70] %; Platelets: 99 [150 - 400] UNIT NOT REPORTED; Potassium: 3.1 [3.5 - 5] MMOL/L; Protein: 62 [60 - 80] G/L; Sodium: 131 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 296): Basophils: 0.01 [0 - 0.05] UNIT NOT REPORTED; Basophils/Leukocytes: 0 [0 - 2] %; Blood Urea Nitrogen: 10.4 [1.8 - 7.1] MMOL/L; Calcium: 1.75 [2.12 - 2.62] MMOL/L; Chloride: 98 [98 - 108] MMOL/L; Creatine Kinase: 1863 [0 - 200] U/L; Creatinine: 210 [0 - 133] UMOL/L; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4.33 [4.5 - 5.9] UNIT NOT REPORTED; Glucose: 7.3 [3.9 - 7.8] MMOL/L; Hematocrit: 0.38 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 126 [140 - 174] G/L; Leukocytes: 3.7 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.8 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 20 [20 - 44] %; Monocytes: 0.1 [0.3 - 0.5] UNIT NOT REPORTED; Monocytes/Leukocytes: 4 [2 - 9] %; NPTST039-CO2: 16 [20 - 30] MEQ/L; NPTST096-MAGNESIUM: 1.5 [1.7 - 2.8] MG/DL; NPTST097-MCH: 29.1 [27 - 33] PG; NPTST100-MCV: 87.8 [80 - 96] FL; NPTST122-PHOSPHORUS: 2.5 [2.5 - 4.5] MG/DL; NPTST129-RDW: 15.6 [12.2 - 16.1] %; NPTST150-TROPONIN: 0.01 [0 - 0.1] NG/ML; Neutrophils: 2.8 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 75 [50 - 70] %; Platelets: 115 [150 - 400] UNIT NOT REPORTED; Potassium: 3.1 [3.5 - 5] MMOL/L; Sodium: 132 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 297): NPTST124-PROCALCITONIN: 3.6 [0 - 0.1] NG/ML; [redacted]20[redacted] (RX DAY 298): Basophils: 0.00 [0 - 0.05] UNIT NOT REPORTED; Blood Urea Nitrogen: 7.5 [1.8 - 7.1] MMOL/L; Calcium: 1.62 [2.12 - 2.62] MMOL/L; Chloride: 99 [98 - 108] MMOL/L; Creatinine: 197 [0 - 133] UMOL/L; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 3.80 [4.5 - 5.9] UNIT NOT REPORTED; Glucose: 5.7 [3.9 - 7.8] MMOL/L; Hematocrit:

	0.33 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 111 [140 - 174] G/L; Leukocytes: 3.8 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.6 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 16 [20 - 44] %; Monocytes: 0.3 [0.3 - 0.5] UNIT NOT REPORTED; Monocytes/Leukocytes: 7 [2 - 9] %; NPTST039-CO2: 21 [20 - 30] MEQ/L; NPTST096-MAGNESIUM: 1.5 [1.7 - 2.8] MG/DL; NPTST097-MCH: 29.2 [27 - 33] PG; NPTST100-MCV: 87.4 [80 - 96] FL; NPTST122-PHOSPHORUS: 2 [2.5 - 4.5] MG/DL; NPTST129-RDW: 15.7 [12.2 - 16.1] %; Neutrophils: 2.9 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 76 [50 - 70] %; Platelets: 108 [150 - 400] UNIT NOT REPORTED; Potassium: 3 [3.5 - 5] MMOL/L; Sodium: 138 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 299): Basophils: 0.01 [0 - 0.05] UNIT NOT REPORTED; Basophils/Leukocytes: 0 [0 - 2] %; Eosinophils: 0.0 [0.1 - 0.3] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 3.72 [4.5 - 5.9] UNIT NOT REPORTED; Hematocrit: 0.33 [0.42 - 0.5] FRACTION OF 1; Hemoglobin: 111 [140 - 174] G/L; Leukocytes: 3.3 [4.8 - 10.8] UNIT NOT REPORTED; Lymphocytes: 0.3 [1 - 4.8] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 10 [20 - 44] %; Monocytes: 0.4 [0.3 - 0.5] UNIT NOT REPORTED; Monocytes/Leukocytes: 12 [2 - 9] %; NPTST097-MCH: 29.8 [27 - 33] PG; NPTST100-MCV: 88.4 [80 - 96] FL; NPTST129-RDW: 15.6 [12.2 - 16.1] %; Neutrophils: 2.5 [1.8 - 7.7] UNIT NOT REPORTED; Neutrophils/Leukocytes: 76 [50 - 70] %; Platelets: 131 [150 - 400] UNIT NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 294): BLOOD NPTST026-BLOOD CULTURE: POSITIVE-STAPHYLOCOCCUS EPIDERMIDIS; OTHER NASOPHARYNGEAL SWAB NPTST043-COVID-19 PCR: POSITIVE-NOVEL CORONAVIRUS; OTHER NASOPHARYNGEAL SWAB NPTST082-INFLUENZA A/B: NEGATIVE-INFLUENZA A/B; OTHER NASOPHARYNGEAL SWAB NPTST134-RESPIRATORY SYNCYTIAL VIRUS: NEGATIVE-RESPIRATORY SYNCYTIAL VIRUS; [redacted]20[redacted] (RX DAY 295): BLOOD NPTST026-BLOOD CULTURE: NEGATIVE-NO GROWTH AT 48 HRS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 294): ELECTROCARDIOGRAM: NORMAL; PORTABLE AP CHEST X RAY: CLEAR LUNGS; VITAL SIGNS: TEMPERATURE(F): 102.4 PULSE: 115 BP: 103/67 RR: 22 SP02(%):100 ROOM AIR; VITAL SIGNS: TEMPERATURE(F):102.4 PULSE: 87 BP: 102/68 RR:18 SP02(%):97% ROOM AIR; VITAL SIGNS: TEMPERATURE(F): 99.2 PULSE: 85 BP: 113/74 RR: 18 SP02(%): 99 ROOM AIR; [redacted]20[redacted] (RX DAY 295): VITAL SIGNS: TEMPERATURE(F): 101.3 PULSE: 93 BP: 111/72 RR: 18 SP02(%): 99 ROOM AIR; [redacted]20[redacted] (RX DAY 296): CT HEAD: NORMAL CT OF BRAIN; PARTIAL RIGHT-SIDED PARANASAL SINUS OPACIFICATION; VITAL SIGNS: TEMPERATURE(F): 102 PULSE: 93 BP: 109/52 RR: NA SP02(%): 95 ON 02 2 LITERS NASAL CANNULA; VITAL SIGNS: TEMPERATURE(F): 100.7 PULSE: 103 BP: 107/70 RR: 22 SP02(%): 99 ROOM AIR; XR CHEST- PORTABLE AP: BILATERAL PATCHY PERIPHERAL AND LEFT PERIHILIAR INFILTRATES WITH AIR BRONCHOGRAMS ARE NOTED, NOT VISUALIZED ON THE MOST RECENT PREVIOUS EXAMINATION; [redacted]20[redacted] (RX DAY 297): VITAL SIGNS: TEMPERATURE(F): 99.8 PULSE: 96 BP: 106/66 RR: 20 SPO2(%):97 ON 02 2 LITERS ON NASAL CANNULA; VITAL SIGNS: TEMPERATURE(F): 99.2 PULSE: 86 BP: 87/49 RR: 20 SP02(%): 93 ON 02 2 LITERS NASAL CANUNLA; [redacted]20[redacted] (RX DAY 298): VITAL SIGNS: TEMPERATURE(F): 98.2 PULSE: 87 BP: 119/70 RR: 20 SPO2(%):100 ON 02 2 LITERS ON NASAL CANNULA; VITAL SIGNS: TEMPERATURE(F): 99.4 PULSE: 74 BP: 136/95 RR: 20 SPO2(%):92 ON 02 2 LITERS ON NASAL CANNULA; [redacted]20[redacted] (RX DAY 299): VITAL SIGNS: TEMPERATURE(F): 102.1 PULSE: 107 BP: 107/59 RR: 20 SPO2(%):99 ROOM AIR; VITAL SIGNS: TEMPERATURE(F): 97.9 PULSE: 98 BP: 121/76 RR: 20 SPO2(%):98 ON 02 2 LITERS ON NASAL CANNULA
AE Stopped Rx Day	299
Duration of AE	4 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SOCONDARY INFECTION DUE TO COVID 19

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

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

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を投与され，新型コロナウイルス感染症（以下，「COVID-19」）及び細菌性肺炎を発現した。被験者は元喫煙者（紙巻タバコ 5 本／日，13 年間）かつ飲酒者（2 杯未満／日）であり，関連する病歴は喘息，慢性腎臓病，アトピー性皮膚炎，心血管疾患（心筋梗塞），冠動脈疾患，高コレステロール血症，高血圧，アレルギー性鼻炎，貧血及び閉塞性睡眠時無呼吸であり，冠動脈形成及び冠動脈ステントによる治療歴があった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は COVID-19 を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は細菌性肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，細菌性肺炎は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，COVID-19 は消失した。

入院前，被験者は COVID-19 のホットラインに電話して症状について相談し，検査のため受診するよう指導された。

20[redacted] 年 [redacted] 月 [redacted] 日，1 日間続く発熱（40°C）の自覚，筋肉痛，及び乾性咳嗽に関連した頭痛があり，被験者は入院した。身体的診察で発達及び発育良好な男性と確認され，急性窮迫症状はなかった。呼吸器の診察所見は断続性ラ音なし，低音性連続性ラ音なし，喘鳴なしであった。循環器の診察所見は正常であり，心拍数及び心調律正常で，心雑音なし，心膜摩擦音なし，ギャロップ・リズムなしであった。バイタルサインは体温 39.1°C，心拍数 115 bpm，呼吸数 22 回／分，血圧 103/67 mmHg，酸素飽和度 100%（室内気）であった。20[redacted] 年 [redacted] 月に発現した感冒／RS ウイルス感染（非重篤）と類似した症状であったが，最近流行している COVID-19 を除外する必要があった。COVID-19 を検査するため検体を採取した。被験者は急性腎障害（非重篤）も発現しており，敗血症の続発症と考えられた。クレアチニン値は 2.63 mg/dL であり，ベースラインの 1.8 から上昇していた。被験者は内科病棟に入院し，発熱に対しアセトアミノフェンを 6 時間ごとに投与され，静脈内補液を受けた。

20[redacted] 年 [redacted] 月 [redacted] 日，COVID-19 検査の結果は陽性であり，隔離が継続された。hydroxychloroquine の経口投与が開始され，始めの 2 回は 400 mg を 12 時間ごとに，その後は 400 mg を 24 時間ごとに 4 日間投与した。被験者の発熱は持続したが，その他の状態は安定した。バイタルサイン

は体温 39.8°C，心拍数 92 bpm，呼吸数 19 回／分，血圧 103/67 mmHg，酸素飽和度 100%（室内気）であった。血液培養で *Staphylococcus epidermidis* の増殖が認められた。医療チームは検体が汚染されていたのではないかと考えたが，vancomycin 1500 mg の経験的投与を 1 回行った。vancomycin の再投与を要する状態悪化を感知できるよう，臨床症状をモニターした。被験者が常用していた薬剤の投与は，いずれも適宜再開された。

20[redacted] 年 [redacted] 月 [redacted] 日，症状軽減のためにアセトアミノフェンの投与が継続され，食事は経口摂取であった。被験者は洗面所に行った際に浮動性めまいを発現して転倒し，頭部に外傷を負い，尿失禁で汚れた床の上で発見された。看護師によると，被験者に異常な身体活動が認められ，院内急変対応チームが呼ばれた。血圧 107/68 mmHg，酸素飽和度 90%台後半（室内気），ブドウ糖値 104 であった。Keppra の導入用量が投与され，心電図検査及び頭部コンピュータ断層撮影（以下「CT」）が行われた。心電図では洞調律が認められ，頭部 CT 像に急性所見はなかった。後の被験者の訴えによると，入浴後に浮動性めまいを自覚し，意識を失うような感覚があり，床に座り込んで気絶した。このときは，発熱，悪寒，息切れ，脱力及び胸痛はなかった。痙攣発作に対する血管迷走神経性失神であり心原性ではなさそうだと医療チームは考えたが，持続的遠隔モニタリングを開始し，軽度洞性頻脈を確認した。被験者は発熱，悪寒，息切れ及び脱力が持続しており，必要に応じて酸素が投与された。胸部 X 線像に透過性の更なる低下及び間質の肺紋理増強が認められた。ceftriaxone の投与が開始された。プロカルシトニン値は 3.6 であり，細菌性肺炎の併発が示された。vancomycin（血中濃度により調整）及び Zosyn を含む広域抗生物質に変更した。2 回目の血液培養検査で微生物の増殖は認められなかった。被験者は低酸素状態が持続していたものの，酸素要求量は 2 L/min に減少した。その後，血行動態は安定し，被験者は胸痛を否定した。息切れ及び酸素飽和度は改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

この他のリスク因子として，被験者に喘息の病歴があり，COVID-19 が流行する人口密度の高い地域に居住していたことが挙げられた。

アセトアミノフェン，生理食塩液，hydroxychloroquine，ceftriaxone，vancomycin 及び ZOSYN が投与された。

The patient's past medications include:

FLUOCINONIDE for ATOPIC DERMATITIS and ATOPIC DERMATITIS RESCUE THERAPY (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

EUCRISA for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ATOPIC DERMATITIS RESCUE THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ATROVENT for COMMON COLD ([redacted] 20[redacted] - [redacted] 20[redacted])

TAMILFLU for INITIAL FLU-LIKE SYMPTOMS ([redacted] 20[redacted] - [redacted] 20[redacted])

TESSALON PERLE for COMMON COLD ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Coronavirus infection (10051905) (Coronavirus infection (10051905)) [v.23.0] [10051905]

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) Pneumonia bacterial (10060946) (Pneumonia bacterial (10060946)) [v.23.0] [10060946]

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 INFECTION

- Investigator: Not applicable.

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

Event of BACTERIAL PNEUMONIA

- Investigator: Secondary infection due to COVID 19.

- AbbVie: Event is more likely related to concurrt COVID-19 infection.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 50 U/L (normal 0 to 40)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 104 U/L (normal 0 to 50)

[redacted] **20[redacted] BASOPHILS %:** 0 %

[redacted] **20[redacted] BASOPHILS %:** 0 %

[redacted] **20[redacted] BASOPHILS ABS:** 0.0 K/UL (normal 0.0 to 0.05)

[redacted] **20[redacted] BASOPHILS ABS:** 0.00 K/UL (normal 0.0 to 0.05)

[redacted] **20[redacted] BLOOD CULTURE:** Positive; Staphylococcus epidermidis

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

[redacted] **20[redacted] BLOOD PRESSURE:** 103/70 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 103/67 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 121/75 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 113/74 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 111/72 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 109/52 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 111/72 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:**107/68 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 87/49 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 106/66 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 136/95 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 119/70 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 121/76 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 107/59 mmHg

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 26 mg/dL (normal 5 to 20)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 27 mg/dL (normal 5 to 20)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 29 mg/dL (normal 5 to 20)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 21 mg/dL (normal 5 to 20)

[redacted] **20[redacted] BODY TEMPERATURE:** 104 F

[redacted] **20[redacted] BODY TEMPERATURE:** 102.4 F

[redacted] **20[redacted] BODY TEMPERATURE:** 103.7 F

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

[redacted] **20[redacted] BODY TEMPERATURE:** 101.3 F

[redacted] **20[redacted] CALCIUM:** 8.3 mg/dL (normal 8.5 to 10.5)

[redacted] **20[redacted] CALCIUM:** 6.9 mg/dL (normal 8.5 to 10.5)

[redacted] **20[redacted] CALCIUM:** 6.5 mg/dL (normal 8.5 to 10.5)

[redacted] **20[redacted] CHLORIDE:** 94 MEQ/L (normal 98 to 108)

[redacted] **20[redacted] CHLORIDE:** 99 MEQ/L (normal 98 to 108)

[redacted] **20[redacted] CO2:** 26 MEQ/L (normal 20 to 30)

[redacted] **20[redacted] CO2:** 21 MEQ/L (normal 20 to 30)

[redacted] **20[redacted] CREATINE KINASE:** 1575 U/L (normal 0 to 200)

[redacted] **20[redacted] CREATINE KINASE:** 1863 U/L (normal 0 to 200)

20[redacted] CREATININE: (Baseline): 1.8

[redacted] **20[redacted] CREATININE:** 2.63 mg/dL (normal 0 to 1.5)

[redacted] **20[redacted] CREATININE:** 2.27 mg/dL (normal 0 to 1.5)

[redacted] **20[redacted] CREATININE:** 2.37 mg/dL (normal 0 to 1.5)

[redacted] **20[redacted] CREATININE:** 2.23 mg/dL (normal 0 to 1.5)

[redacted] **20[redacted] CT HEAD:** Normal CT of brain; partial right-sided paranasal sinus opacification.

[redacted] **20[redacted] ECG:** Normal sinus rhythm

[redacted] **20[redacted] ELECTROCARDIOGRAM:** NORMAL

[redacted] **20[redacted] EOSINOPHILS %:** 0 %

[redacted] **20[redacted] EOSINOPHILS %:** 0 %

[redacted] **20[redacted] EOSINOPHILS ABS:** 0.0 K/UL (normal 0.1 to 0.3)

[redacted] **20[redacted] EOSINOPHILS ABS:** 0.0 K/UL (normal 0.1 to 0.3)

[redacted] **20[redacted] HEART RATE:** 138 BPM

[redacted] **20[redacted] HEART RATE:** 115 BPM

[redacted] **20[redacted] HEART RATE:** 92 BPM

[redacted] **20[redacted] HEART RATE:** Upper 90s BPM

[redacted] **20[redacted] HEART RATE:** 93 BPM

[redacted] **20[redacted] HEMATOCRIT:** 38.0 % (normal 41.5 to 50.4)

[redacted] **20[redacted] HEMATOCRIT:** 36.6 % (normal 41.5 to 50.4)

[redacted] **20[redacted] HEMATOCRIT:** 38.0 % (normal 41.5 to 50.4)

[redacted] **20[redacted] HEMOGLOBIN:** 12.7 G/DL (normal 14.0 to 17.4)

[redacted] **20[redacted] HEMOGLOBIN:** 12.5 G/DL (normal 14.0 to 17.4)

[redacted] **20[redacted] HEMOGLOBIN:** 11.1 G/DL (normal 14.0 to 17.4)

[redacted] **20[redacted] LDH:** 518 U/L (normal 0 to 240)

[redacted] **20[redacted] LYMPHOCYTES %:** 11 %

[redacted] **20[redacted] LYMPHOCYTES %:** 19 %

[redacted] **20[redacted] LYMPHOCYTES %:** 16 %

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.6 K/UL (normal 1.0 to 4.8)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.8 K/UL (normal 1.0 to 4.8)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.6 K/UL (normal 1.0 to 4.8)

[redacted] **20[redacted] MAGNESIUM:** 1.2 mg/dL (normal 1.7 to 2.8)

[redacted] **20[redacted] MAGNESIUM:** 1.5 mg/dL (normal 1.7 to 2.8)

[redacted] **20[redacted] MONOCYTES %:** 2 %

[redacted] **20[redacted] MONOCYTES %:** 7 %

[redacted] **20[redacted] MONOCYTES ABS:** 0.1 K/UL (normal 0.3 to 0.5)

[redacted] **20[redacted] MONOCYTES ABS:** 0.3 K/UL (normal 0.3 to 0.5)

[redacted] **20[redacted] NASOPHARYNGEAL SWAB COVID-19 PCR:** Positive; Novel coronavirus

[redacted] 20[redacted] **NASOPHARYNGEAL SWAB INFLUENZA A/B:** Negative

[redacted] 20[redacted] **NASOPHARYNGEAL SWAB RESPIRATORY SYNCYTIAL VIRUS:** Negative

[redacted] 20[redacted] **NEUTROPHILS %:** 84 %

[redacted] 20[redacted] **NEUTROPHILS %:** 78 %

[redacted] 20[redacted] **NEUTROPHILS %:** 76 %

[redacted] 20[redacted] **NEUTROPHILS ABS:** 4.4 K/UL (normal 1.8 to 7.7)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 3.0 K/UL (normal 1.8 to 7.7)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 2.9 K/UL (normal 1.8 to 7.7)

[redacted] 20[redacted] **OXYGEN SATURATION:** 99% at room air

[redacted] 20[redacted] **OXYGEN SATURATION:** 100% at room air

[redacted] 20[redacted] **OXYGEN SATURATION:** 97% at room air

[redacted] 20[redacted] **OXYGEN SATURATION:** 99% at room air

[redacted] 20[redacted] **OXYGEN SATURATION:** 95% on oxygen therapy

[redacted] 20[redacted] **OXYGEN SATURATION:** 99% at room air

[redacted] 20[redacted] **OXYGEN SATURATION:** 100% at room air

[redacted] 20[redacted] **OXYGEN SATURATION:** 93% on oxygen therapy 2 Liters on nasal cannula

[redacted] 20[redacted] **OXYGEN SATURATION:** 97% on oxygen therapy 2 Liters on nasal cannula

[redacted] 20[redacted] **OXYGEN SATURATION:** 92% on oxygen therapy 2 Liters on nasal cannula[redacted] 20[redacted] OXYGEN SATURATION: 100% on oxygen therapy 2 Liters on nasal cannula

[redacted] 20[redacted] **OXYGEN SATURATION:** 98% on oxygen therapy 2 Liters on nasal cannula

[redacted] 20[redacted] **OXYGEN SATURATION:** 99% at room air

[redacted] 20[redacted] **PHOSPHORUS:** 2.0 mg/dL (normal 2.5 to 4.5)

[redacted] 20[redacted] **PLATELET COUNT:** 119 K/UL (normal 150 to 400)

[redacted] 20[redacted] **PLATELET COUNT:** 99 K/UL (normal 150 to 400)

[redacted] 20[redacted] **PLATELET COUNT:** 108 K/UL (normal 150 to 400)

[redacted] 20[redacted] **PORTABLE AP CHEST X RAY:** CLEAR LUNGS

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

[redacted] 20[redacted] **POTASSIUM:** 3.1 MEQ/L (normal 3.5 to 5.0)

[redacted] 20[redacted] **POTASSIUM:** 3.0 MEQ/L (normal 3.5 to 5.0)

[redacted] 20[redacted] **PROCALCITONIN:** 3.6 NG/ML (normal 0 to 0.1)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.29 MIL/UL (normal 4.5 to 5.9)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.18 MIL/UL (normal 4.5 to 5.9)

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.80 MIL/UL (normal 4.5 to 5.9)

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

[redacted] 20[redacted] **RESPIRATORY RATE:** 22 /min

[redacted] 20[redacted] **RESPIRATORY RATE:** 19 /min

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

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

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

[redacted] 20[redacted] **SCREENING CHEST X-RAY:** Normal

[redacted] 20[redacted] **SODIUM:** 136 MEQ/L (normal 135 to 145)

[redacted] 20[redacted] **SODIUM:** 131 MEQ/L (normal 135 to 145)

[redacted] 20[redacted] **SODIUM:** 138 MEQ/L (normal 135 to 145)

[redacted] 20[redacted] **TROPONIN:** 0.01 NG/ML (normal 0 to 0.1)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 5.3 K/UL (normal 4.8 to 10.8)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.8 K/UL (normal 4.8 to 10.8)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.7 K/UL (normal 4.8 to 10.8)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.8 K/UL (normal 4.8 to 10.8)

[redacted] 20[redacted] **XR CHEST PORTABLE AP:** Bilateral patchy peripheral and left perihiliar infiltrates with air bronchograms are noted, not visualized on the most recent previous examination.

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
背部痛	X			
椎間板突出	X			
椎間板炎	X			X
瘢痕	X			
坐骨神経痛	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
ALLERGIC RHINITIS	19[redacted]
ASTHMA	19[redacted]
ABDOMINAL PAIN DURING PERIOD	19[redacted]
ATOPIC DERMATITIS	19[redacted]
FRACTURE OF THE JAW	19[redacted]
ACNE	19[redacted]
IMPETIGO INFECTION	20[redacted]
LUMBAGO	20[redacted]
VAGINITIS	20[redacted]
DEPRESSIVE SYNDROME	20[redacted]
OTITIS	20[redacted]
ABORTION	20[redacted]
ACNE	NOT REPORTED
ALERGGY MITES	NOT REPORTED
ALLERGIC CONJUNCTIVITIS	NOT REPORTED
ALLERGIC RHINITIS	NOT REPORTED
ALLERGY CHROME	NOT REPORTED
ALLGERY TO PERON BALM	NOT REPORTED
ASTHMA	NOT REPORTED
CHLORURE BENZALKONIUM ALLERGY	NOT REPORTED
DEPRESSIVE SYNDROME	NOT REPORTED
FOOD ALLERGY	NOT REPORTED
LABIAL HERPES SIMPLEX INFECTION	NOT REPORTED
NICKEL ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 115	115
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 116		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SALBUTAMOL	200 ug	OTHER: IF NEEDED	Y-M: 19[redacted]
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	UK OTHER: UK	OTHER: UK	Y-M: 20[redacted]
METHOTREXATE	UNK OTHER: UNK	OTHER: UNK	Y-M: 20[redacted]
INFLIXIMAB	UK OTHER: UK	EVERY 2 WEEKS	Y-M: 20[redacted]
MYCOPHENOLIC ACID	500 mg	BID	Y-M: 20[redacted]
TACROLIMUS	UK %	QD	Y-M: 20[redacted]
CICLOSPORIN	250 mg	QD	Y-M: 20[redacted]
CICLOSPORIN	150 mg	BID	Y-M: 20[redacted]
BILASTINE	20 mg	QD	Y-M: 20[redacted]
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]
CLOBETASOL	0.05 %	QD	Y-M: 20[redacted]
DIFLUCORTOLONE	0.1 %	QD	Y-M: 20[redacted]
INTRAUTERINE CONTRACEPTIVE DEVICE	DIU UT 380 FILS 1.5CM OTHER: NA	OTHER: NA	Y-M: 20[redacted]
UREA	NA OTHER: UNK	BID	Y-M: 20[redacted] / -41

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
SALBUTAMOL	200 ug	OTHER: IF NEEDED	Y-M: 19[redacted]	NOT REPORTED
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 203
INTRAUTERINE CONTRACEPTIVE DEVICE	DIU UT 380 FILS 1.5CM OTHER: NA	OTHER: NA	Y-M: 20[redacted]	NOT REPORTED
UREA	NA OTHER: UNK	BID	Y-M: 20[redacted] / -41	Y-M: 20[redacted] / 288

DIFLUCORTOLONE	0.1 %	QD	Y-M: 20[redacted]-[redacted] / 141	NOT REPORTED
PARACETAMOL	1 g	PRN	Y-M: 20[redacted]-[redacted] / 195	NOT REPORTED
KETOPROFEN	100 mg	BID	Y-M: 20[redacted]-[redacted] / 195	Y-M: 20[redacted]-[redacted] / 201
MACROGOL	20 g	QD	Y-M: 20[redacted]-[redacted] / 196	Y-M: 20[redacted]-[redacted] / 200
MORPHINE	5 mg	PRN	Y-M: 20[redacted]-[redacted] / 196	Y-M: 20[redacted]-[redacted] / 201
ENOXAPARIN	4000 IU	QD	Y-M: 20[redacted]-[redacted] / 214	Y-M: 20[redacted]-[redacted] / 235
ALPRAZOLAM	0.5 mg	QD	Y-M: 20[redacted]-[redacted] / 215	Y-M: 20[redacted]-[redacted] / 219
METHOCARBAMOL	500 mg	BID	Y-M: 20[redacted]-[redacted] / 219	Y-M: 20[redacted]-[redacted] / 220
ALPRAZOLAM	0.5 mg	BID	Y-M: 20[redacted]-[redacted] / 219	Y-M: 20[redacted]-[redacted] / 251
THIOCOLCHICOSIDE	4 mg	QD	Y-M: 20[redacted]-[redacted] / 220	Y-M: 20[redacted]-[redacted] / 231
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted]-[redacted] / 270	Y-M: 20[redacted]-[redacted] / 285
RIFAMPICIN	300 mg	BID	Y-M: 20[redacted]-[redacted] / 270	Y-M: 20[redacted]-[redacted] / 298
AMPHOTERICIN B	100MG/ML OTHER: MG/ML	TID	Y-M: 20[redacted]-[redacted] / 286	Y-M: 20[redacted]-[redacted] / 292
ECONAZOLE	1 %	BID	Y-M: 20[redacted]-[redacted] / 286	Y-M: 20[redacted]-[redacted] / 292
BACTRIM	800/160 mg	BID	Y-M: 20[redacted]-[redacted] / 286	Y-M: 20[redacted]-[redacted] / 298
TOLERIANE	NA OTHER: NA	QD	Y-M: 20[redacted]-[redacted] / 288	NOT REPORTED
FOLIC ACID	0.4 mg	TID	Y-M: 20[redacted]-[redacted] / 288	Y-M: 20[redacted]-[redacted] / 298
DESONIDE	0.1 %	QD	Y-M: 20[redacted]-[redacted] / 288	Y-M: 20[redacted]-[redacted] / 360
FUSIDIC ACID	2 %	QD	Y-M: 20[redacted]-[redacted] / 351	Y-M: 20[redacted]-[redacted] / 367
SPIRULINA SPP.	1 g	QD	Y-M: 20[redacted]-[redacted] / 372	Y-M: 20[redacted]-[redacted] / 409
RACECADOTRIL	100 mg	TID	Y-M: 20[redacted]-[redacted] / 400	Y-M: 20[redacted]-[redacted] / 409
SACCHAROMYCES BOULARDII	100 mg	TID	Y-M: 20[redacted]-[redacted] / 400	Y-M: 20[redacted]-[redacted] / 409

Event #1: Serious Adverse Event

Event Description	SCIATICA
Preferred term	坐骨神経痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 185
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 201): HERNIATED DISC CURE L5-S1: EXCISION DISC, ROOT FREEDOM AND ABSENCE OF RESIDUAL FRAGMENT
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DISCAL HERNIA L5S1
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #2: Serious Adverse Event

Event Description	LOW BACK PAIN, SCAR FROM THE SURGERY OF INFLAMMATORY DISC HERNIATION.
Preferred term	背部痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 210
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 266): WOUND NPTST105-MICROBIAL CULTURE: POSITIVE-STAPHYLOCOCCUS CAPITIS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 222): LUMBAR RACHIS MRI: RECURRENCE OF POSTEROMEDIAL AND POSTEROLATERAL LEFT L5S1 DISC HERNIATION IN CONFLICT WITH THE EMERGENCE OF THE LEFT S1 ROOT.; [redacted]20[redacted] (RX DAY 266): BIOPSY OF THE OPERATING SITE WITH BACTERIOLOGICAL SAMPLES: STAPHYLOCOCCUS CAPITIS INFECTION
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RECENT OPERATION OF A HERNIATED DISC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #3: Serious Adverse Event

Event Description	LOW BACK PAIN, SCAR FROM THE SURGERY OF INFLAMMATORY DISC HERNIATION.
Preferred term	椎間板突出
AE Onset Date / Rx Day	[redacted]20[redacted] / 210
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 266): WOUND NPTST105-MICROBIAL CULTURE: POSITIVE-STAPHYLOCOCCUS CAPITIS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 222): LUMBAR RACHIS MRI: RECURRENCE OF POSTEROMEDIAL AND POSTEROLATERAL LEFT L5S1 DISC HERNIATION IN CONFLICT WITH THE EMERGENCE OF THE LEFT S1 ROOT.; [redacted]20[redacted] (RX DAY 266): BIOPSY OF THE OPERATING SITE WITH BACTERIOLOGICAL SAMPLES: STAPHYLOCOCCUS CAPITIS INFECTION
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RECENT OPERATION OF A HERNIATED DISC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #4: Serious Adverse Event

Event Description	LOW BACK PAIN, SCAR FROM THE SURGERY OF INFLAMMATORY DISC HERNIATION.
Preferred term	瘢痕
AE Onset Date / Rx Day	[redacted]20[redacted] / 210
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 266): WOUND NPTST105-MICROBIAL CULTURE: POSITIVE-STAPHYLOCOCCUS CAPITIS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 222): LUMBAR RACHIS MRI: RECURRENCE OF POSTEROMEDIAL AND POSTEROLATERAL LEFT L5S1 DISC HERNIATION IN CONFLICT WITH THE EMERGENCE OF THE LEFT S1 ROOT.; [redacted]20[redacted] (RX DAY 266): BIOPSY OF THE OPERATING SITE WITH BACTERIOLOGICAL SAMPLES: STAPHYLOCOCCUS CAPITIS INFECTION
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	RECENT OPERATION OF A HERNIATED DISC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #5: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	SPONDYLODISCITIS
Preferred term	椎間板炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 266
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 266): WOUND NPTST105-MICROBIAL CULTURE: POSITIVE-STAPHYLOCOCCUS CAPITIS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 222): LUMBAR RACHIS MRI: RECURRENCE OF POSTEROMEDIAL AND POSTEROLATERAL LEFT L5S1 DISC HERNIATION IN CONFLICT WITH THE EMERGENCE OF THE LEFT S1 ROOT.; [redacted]20[redacted] (RX DAY 266): BIOPSY OF THE OPERATING SITE WITH BACTERIOLOGICAL SAMPLES: STAPHYLOCOCCUS CAPITIS INFECTION
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はフランスの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，脊椎椎間板炎，坐骨神経痛及び腰痛，炎症性椎間板ヘルニアの手術とその瘢痕を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー

性皮膚炎及び腰痛症であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は坐骨神経痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腰痛及び炎症性椎間板ヘルニアの手術とその瘢痕を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脊椎椎間板炎を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腰痛のため入院した。症状及び徴候として椎間板ヘルニアがあった。被験者は後方アプローチで第 5 腰椎／仙骨間椎間板（以下，「L5-S1」）のヘルニア治療を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，退院以降持続していた腰痛，椎間板ヘルニアの瘢痕の炎症，その朝から続く発熱のため，被験者は再入院した。治療のため鎮痛薬の用量を変更し，筋弛緩薬及び抗不安薬を追加した。治験責任医師は，リスク因子として直近の椎間板ヘルニア（L5-S1）治療を挙げた。20[redacted] 年 [redacted] 月 [redacted] 日，核磁気共鳴画像検査で椎間板ヘルニア（L5-S1）の再発及び左第 1 仙骨神経根の炎症が確認された。

20[redacted] 年 [redacted] 月 [redacted] 日，L5-S1 に脊椎椎間板炎が認められた。感染性疾患が認められ，被験者は 6 ヵ月間の治験治療中断を勧められた。このため，脊椎椎間板炎のため治験薬の投与は中断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

全情報を本報告に統合したため，AER 19P-056-3169091-00 は論理的に削除された。

メトカルバモール，thiocolchicoside，アルプラゾラム，スルファメトキサゾール／トリメトプリム，ケトプロフェン，paracetamol，levofloxacin，リファンピシン，及び morphine sulfate が投与された。

The patient's past medications include:

METHOTREXATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLIXIMAB for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MYCOPHENOLATE MOFETIL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CYCLOSPORIN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CLOBETASOL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DIFLUCORTOLONE VALERATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CHLORURE BENZALKONIUM for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Spondylodiscitis (10062691) (Intervertebral discitis (10060738)) [v.23.0] [10062691]

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

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

Dechallenge: No

2) Sciatica (10039674) (Sciatica (10039674)) [v.23.0] [10039674]

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

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

Dechallenge: Not Applicable

3) Low back pain (10024891) (Back pain (10003988)) [v.23.0] [10024891]

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

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

Dechallenge: No

4) Surgical scar (10057060) (Scar (10039580)) [v.23.0] [10057060]

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

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

Dechallenge: No

5) Intervertebral disc herniation (10048856) (Intervertebral disc protrusion (10050296)) [v.23.0] [10048856]

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 SPONDYLODISCITIS

- Investigator: Not applicable

- AbbVie: Risk factor includes previous surgery for lumbar disc herniation with biopsy of operating site showing Staphylococcus capitis. Published data shows that Staphylococci infection account for up to 39% of reported spondylodiscitis.

Event of SCIATICA

- Investigator: Discal hernia L5-S1.

- AbbVie: Etiology of the event is not consistent with the study drug's mechanism of action. Pre-existing lumbago is an additional risk factor.

Event of LOW BACK PAIN; SCAR FROM SURGERY OF INFLAMMATORY DISC HERNIATION

- Investigator: Recent operation of a herniated disc.

- AbbVie: Events of low back pain and scar are more likely related torecent lumbar spine surgery and pre-existing lumbago. Event of disc herniation is not consistent with study drug's mechanism of action.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BIOPSY OF THE OPERATING SITE WITH BACTERIOLOGICAL SAMPLES: Staphylococcus capitis infection

[redacted] 20[redacted] LUMBAR RACHIS MRI: Recurrence of posteromedial and posterolateral left L5-S1 disc herniation in conflict with the emergence of the left S1 root.

[redacted] 20[redacted] WOUND MICROBIAL CULTURE: Positive - Staphylococcus capitis

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	5[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
CHRONIC L4 CRURALGIE	20[redacted]
HERNIATED DISC L4-L5	20[redacted]
MYELEMIA	20[redacted]
HEADACHE	NOT REPORTED
INSOMNIA	NOT REPORTED
OBESITY	NOT REPORTED
SMOKER	NOT REPORTED
SORE THROAT	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: EPIDURAL INFILTRATION OF HYDROCORTANCYL	20[redacted]
PRIOR PROCEDURES: PERI-RADICULAR INFILTRATION L4 RIGHT WITH CORTIVAZOL	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	10 CIGARETTE	37	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted] / 1	[redacted] / 112	112
UPA	15 MG	ORAL	QD	[redacted] / 113	[redacted] / 225	113

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[redacted]
PIROXICAM	20 mg	PRN	Y-M: 20[redacted]
ALPHA-AMYLASE SWINE PANCREAS	3000 OTHER: U CEIP	PRN	Y: 20[redacted]
IBUPROFEN	400 mg	PRN	Y: 20[redacted]
ZOLPIDEM	10 mg	PRN	Y: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	2.4 OTHER: MJOULES	OTHER: 17 SESSION	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	40.5 OTHER: MJOULES	OTHER: 17 SESSION	Y-M: 20[redacted]
BETAMETHASONE	15 mg	QD	Y-M: 20[redacted] / -327
METHOTREXATE	15 mg	QD	Y-M: 20[redacted] / -319
LIPIKAR	NA OTHER: UNK	BID	Y-M: 20[redacted] / -7

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
PIROXICAM	20 mg	PRN	Y-M: 20[redacted]	ONGOING
ALPHA-AMYLASE SWINE PANCREAS	3000 OTHER: U CEIP	PRN	Y: 20[redacted]	ONGOING
IBUPROFEN	400 mg	PRN	Y: 20[redacted]	ONGOING
ZOLPIDEM	10 mg	PRN	Y: 20[redacted]	ONGOING
LIPIKAR	NA OTHER: UNK	BID	Y-M: 20[redacted] / -7	ONGOING
CICAPLAST	ONCE PER DAY OTHER: APPLYING	QD	Y-M: 20[redacted] / 1	ONGOING

Event #1: Serious Adverse Event

Event Description	THORACIC PAIN
Preferred term	胸痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 43
Age at AE Onset	5[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 57): NPTST053-D DIMER: 623 [NOT REPORTED - 500] ng/mL; NPTST092-LIPASES: 47 [13 - 60] IU/L; NPTST151-TROPONIN TC HS: 13 [0 - 14] UNIT NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 57): ANGIOSCANNER: NEGATIVE RESULT, NO SIGN OF RECENT PULMONARY EMBOLISM; ECG: NORMAL RESULT; [redacted]20[redacted] (RX DAY 58): VENOUS DOPPLER ULTRASOUND OF THE LOWER LIMBS: ABSENCE OF DEEP OR SUPERFICIAL VENOUS THROMBOSIS OF THE LOWER LIMBS
AE Stopped Rx Day	59
Duration of AE	17 DAYS
Toxicity Grade	2
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はフランスの 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を投与され，胸郭痛を発現した。被験者は喫煙者（紙巻タバコ 10 本／日，37 年間）かつ飲酒者（2～4 杯／日）であり，関連する病歴はアトピー性皮膚炎及び慢性下肢神経痛（第 4 腰神経），椎間板ヘルニア（第 4／第 5 腰椎）及びコレステロール高値であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸郭痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胸郭痛は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，胸痛の強さが 15 日間にわたって変化したため，被験者は入院した。特に治療することなく胸痛は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

METHOTREXATE for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINB (Blinded)

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1) Thoracic pain (10043471) (Chest pain (10008479)) [v.22.0] [10043471]

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 UPADACITINB (Blinded)

Event of THORACIC PAIN

- Investigator: Not applicable

- AbbVie: Non-specific reported event; risk factors for most common reported etiologies in gender and age group are obesity (BMI 30), current smoker, and alcohol use.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ANGIOSCANNER:** NEGATIVE RESULT, NO SIGN OF RECENT PULMONARY EMBOLISM

[redacted] **BMI:** 30 kg/m2

[redacted] **D DIMER:** 623 NG/ML (normal <500)

[redacted] **ECG:** Normal

[redacted] **LIPASE:** 47.0 IU/L (normal 13 to 60)

[redacted] **TROPONIN:** 13 ng/L (normal 0 to 14)

[redacted] **VENOUS DOPPLER ULTRASOUND OF THE LOWER LIMBS:** ABSENCE OF DEEP OR SUPERFICIAL VENOUS THROMBOSIS OF THE LOWER LIMBS

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	1[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	20[redacted]
ALLERGIC RHINITIS	20[redacted]
DEPRESSIVE SYNDROME	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: EXERESIS	20[redacted]
PRIOR PROCEDURES: EXERESIS	20[redacted]
PRIOR PROCEDURES: EXERESIS	20[redacted]
PRIOR PROCEDURES: PUNCTURE	20[redacted]
PRIOR PROCEDURES: EXERESIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 111	111
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 112	[redacted]20[redacted] / 229	118

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: 20[redacted]
BETAMETHASONE	ONCE OTHER: APPLY	QD	Y-M: 20[redacted]
DESLORATADINE	5 mg	PRN	Y-M: 20[redacted]
SERTRALINE	50 mg	QD	Y-M: 20[redacted] / -190
DIFLUCORTOLONE	ONE OTHER: APPLY	QD	Y-M: 20[redacted] / -58
HYPOCHLOROUS ACID	NA OTHER: NA	QD	Y-M: 20[redacted] / -58
EMOLLIENTS AND PROTECTIVES	ONCE OTHER: APPLY	BID	Y-M: 20[redacted] / -8
ESCITALOPRAM	5 mg	QD	Y-M: 20[redacted] / -1
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / -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 / RX Day	Stop Year-Month / RX Day
EMOLLIENTS AND PROTECTIVES	ONCE OTHER: APPLY	BID	Y-M: 20[redacted] / -8	ONGOING
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / -1	ONGOING
ESCITALOPRAM	15 mg	QD	Y-M: 20[redacted] / 47	ONGOING
BETAMETHASONE	0.05 %	OTHER: IF NECESSARY	Y-M: 20[redacted] / 65	ONGOING
ARIPIPRAZOLE	15 mg	QD	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 251
ARIPIPRAZOLE	10 mg	QD	Y-M: 20[redacted] / 252	ONGOING

Event #1: AE Leading to Discontinuation of Study Drug

Event Description	WORSENING OF DEPRESSIVE SYNDROME
Preferred term	うつ病
AE Onset Date / Rx Day	[redacted]20[redacted] / 187
Age at AE Onset	1[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	SUICIDAL IDEATION
Preferred term	自殺念慮
AE Onset Date / Rx Day	[redacted]20[redacted] / 187
Age at AE Onset	1[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	222
Duration of AE	36 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	DEPRESSIVE SYNDROME
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はフランスの 1[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を投与され，自殺念慮を発現した。被験者は非喫煙者で禁酒しており，関連する病歴はアトピー性皮膚炎，抑うつ症候群であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は自殺念慮を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，自殺念慮は消失した。

入院前，抑うつ症候群（非重篤）が悪化し始めた。

20[redacted] 年 [redacted] 月 [redacted] 日，快感消失（喜びを感じられなくなった），無為（意思活力の低下），自己卑下，および悲観性の症状が認められ，被験者は入院した。被験者は長期入院を拒否した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師は，リスク因子として被験者の父親にうつ病の病歴があることを挙げた。

The patient's past medications include:

BETAMETHASONE DIPROPIONATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SERTRALINE for DEPRESSION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

DIFLUCORTOLONE VALERATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SODIUM HYPOCHLORITE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

RISPERIDONE for DEPRESSION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Suicidal ideation (10042458) (Suicidal ideation (10042458)) [v.23.0] [10042458]

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 SUICIDAL IDEATION

- Investigator: Depressive syndrome

- AbbVie: Event is more likely related to pre-existing depressive disorder and pre-existing atopic dermatitis.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ヘルペス性状湿疹	X	X		X

Treatment Group	Age at Study Start	Sex	Race
PLACEBO/UPA 30 MG QD	3[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
XEROSIS CUTIS	19[redacted]
CHRONIC PRURITUS	19[redacted]
ALLERGY TO CITRUS FRUITS	19[redacted]
CERVIAL SPINE PAIN	20[redacted]
ECZEMA HERPITICATUM	20[redacted]
HERPES SIMPLEX (LIP)	20[redacted]
ALLERGIC CONJUNCTIVITS	20[redacted]
HEY FEVER	20[redacted]
PNEUMONIA	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 113	113
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 114	[redacted]20[redacted] / 495	382

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MOMETASONE	1 OTHER: APPLICATION	BID	Y-M: 19[redacted]-[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: APPLICATION	OTHER: INTERMITTEND	Y: 19[redacted]
SODIUM CHLORIDE	1 OTHER: APPLICATION	OTHER: INTERMITTANT	Y: 19[redacted]
CETIRIZINE	10 mg	BID	Y: 20[redacted]
PIMECROLIMUS	1 OTHER: APPLICATION	BID	Y: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: APPLICATION	OTHER: INTERMITTEND	Y: 20[redacted]
PREDNICARBATE	1 OTHER: APPLICATION	BID	Y: 20[redacted]
LORATADINE	10 mg	BID	Y: 20[redacted]
EUCERIN	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y: 20[redacted]
DESLORATADINE	5 mg	BID	Y: 20[redacted]
TRIAMCINOLONE	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted]-[redacted]
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
FEXOFENADINE	120 mg	BID	Y: 20[redacted]
PIMECROLIMUS	1 OTHER: APPLICATION	OTHER: INTERMITTANT	Y: 20[redacted]
PREDNISOLONE	20 mg	OTHER: INTERMITTANT	Y: 20[redacted]
TACROLIMUS	1 OTHER: APPLICATION	OTHER: INTERMITTANT	Y: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: APPLICATION	OTHER: INTERMITTANT	Y-M: 20[redacted]-[redacted]
SULFUR	1 OTHER: APPLICATION	OTHER: INTERMITTANT	Y-M: 20[redacted]-[redacted]
TACROLIMUS	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
CICLOSPORIN	150 mg	BID	Y-M: 20[redacted]-[redacted]

MOMETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
CICLOSPORIN	75 mg	BID	Y-M: 20[redacted]
MOMETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
TRALOKINUMAB	300 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
PIMECROLIMUS	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -217
TACROLIMUS	1 OTHER: APPLICAITON	BID	Y-M: 20[redacted] / -217
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -158
MOMETASONE	1 OTHER: APPLICATION	OTHER: INTERMITTEND	Y-M: 20[redacted] / -158
PREDNISOLONE	20 ug	OTHER: INTERMITTEND	Y-M: 20[redacted] / -127
DECYLENE GLYCOL;LICOCHALCONE A;MENT	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -97

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
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -158	ONGOING
DECYLENE GLYCOL;LICOCHALCONE A;MENT	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -97	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 167	ONGOING
ACICLOVIR	750 mg	TID	Y-M: 20[redacted] / 496	ONGOING
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 496	ONGOING
METAMIZOLE	30 mg	QID	Y-M: 20[redacted] / 496	ONGOING
OCTENIDINE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 496	ONGOING
PRUNUS DULCIS	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 496	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections, Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zosters

Event Description	ECZEMA HERPETICUM ON SCALP
Preferred term	ヘルペス性状湿疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 496 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 497): Hematocrit: 0.36 [0.4 - 0.49] FRACTION OF 1; Hemoglobin: 123 [135 - 169] G/L; Leukocytes: 7.6 [3.9 - 10.9] 10^9/L; NPTST029-C REACTIV PROTEIN: 1.5 [NOT REPORTED - 0.5] mg/dL
Microbiology	[redacted]20[redacted] (RX DAY 497): OTHER SKIN SWAB NPTST073-HERPES SIMPLEX PCR: POSITIVE-HERPES SIMPLEX PCR TEST RESULT IS: 792000 COP/ML
SAE Supplemental Procedure	NOT REPORTED

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	2
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はドイツの 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を投与され，頭皮のヘルペス性状湿疹を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎，皮膚乾燥症，慢性そう痒症，ヘルペス性状湿疹，単純ヘルペス，アレルギー性結膜炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頭皮のヘルペス性状湿疹を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日の夜，被験者は頭皮の「重苦しい痛み」と灼熱感を自覚した。被験者はクリニックを受診し，頭皮に痂皮化した皮膚病変が認められた。耳介後部リンパ節は腫脹していた。ポリメラーゼ連鎖反応（以下「PCR」）検査のため，皮膚スワブ検体を採取した。アシクロビルによる治療がクリーム塗布とともに開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。ヘルペス性状湿疹は顔面に及び，丘疹小水疱性であると報告された。PCR 検査の結果から，原因は単純ヘルペスウイルス 1 型であると診断された。

本事象を理由に治験薬の投与は中止された。

アシクロビル，clobetasol，OCTENIDINA，NOVALGIN 及びアーモンド油が投与された。

The patient's past medications include:

ECURAL for ATOPIC DERMATITIS ([redacted] 19[redacted] - 20[redacted])

CETIRIZIN for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

ELIDEL for ATOPIC DERMATITIS (20[redacted] - 20[redacted], 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

DERMATOP for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

LORATADIN for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

ATOPIC CONTROL EUCERIN for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

BETAMETHASON for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

DESLORATADIN for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

TRIAMCINOLON for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ADTOP CREAM for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

PREDNISOLON for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PROTOPIC for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

TELFAST for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

SULFUR SOLE BATH for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VIOTOP for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

CICLOSPORIN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

MONOVO for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

TRALOKINUMAB for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Eczema herpeticum (10014197) (Eczema herpeticum (10014197)) [v.23.1] [10014197]

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 ECZEMA HERPETICUM ON SCALP

- Investigator: Not applicable

- AbbVie: Risk factor includes pre-existing history of eczema herpeticum. In addition, event is more likely a complication of pre-existing AD and eczema. Eczema herpeticum is a disseminated viral infection characterized by fever and clusters of itchy blisters or punched-out erosions. It is most often seen as a complication of atopic dermatitis and eczema.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 1.5 mg/dL (normal <0.5)

[redacted] **20[redacted] HCT:** 35.8 % (normal 40 to 49.4)

[redacted] **20[redacted] HGB:** 12.3 G/DL (normal 13.5 to 16.9)

[redacted] **20[redacted] PCR SKIN SWAB:** Positive 792000 cop/mL

[redacted] 20257 X10**3/MCL (normal 3.9 to 10.9)

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD/UPA 30 MG QD	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
ATOPIC DERMATITIS	19[redacted]
ALLERGIC RHINITIS	20[redacted]
TRUE ABSTINENCE AS CONTRACEPTION	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	6 CIGARETTE	3	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted] / 1	[redacted] / 111	111
UPA	30 MG	ORAL	QD	[redacted] / 112		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BETAMETHASONE	4 MG DAILY, DECREASING mg	QD	Y-M: [redacted]
TACROLIMUS	DAILY %	BID	Y-M: [redacted]
CLOBETASOL	DAILY %	BID	Y-M: [redacted] / -124
TRIDERM	2 APPLICATIONS/DAY OTHER: APPLICATIONS	BID	Y-M: [redacted] / -38

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
TRIDERM	2 APPLICATIONS/DAY OTHER: APPLICATIONS	BID	Y-M: [redacted] / -38	ONGOING
CEFDITOREN	1 PILL TWICE A DAY FOR 7 DAYS mg	BID	Y-M: [redacted] / 125	Y-M: [redacted] / 131
CLARITHROMYCIN	2 PILLS/DAY mg	BID	Y-M: [redacted] / 125	Y-M: [redacted] / 131
ACETYLCYSTEINE	1 PILL A DAY FOR 10 DAYS OTHER: PILL	QD	Y-M: [redacted] / 125	Y-M: [redacted] / 135
FLUNISOLIDE	1 VIAL THRICE A DAY + 1 CC SALINE OTHER: 1 VIAL A DAY	QD	Y-M: [redacted] / 125	Y-M: [redacted] / 138
PREDNISONE	1 PILL/DAY FOR 4 DAYS, 1/2 PILL FOR 4 D, 1/4 PILL FOR 6 D mg	QD	Y-M: [redacted] / 125	Y-M: [redacted] / 138

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted] / 121
Age at AE Onset	[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted] (RX DAY 123): CHEST X RAY: EXCLUSION OF PNEUMOTHORAX, AREA OF CONSOLIDATION IN THE LEFT UPPER LUNG LOBE COMPATIBLE WITH PNEUMONIA
AE Stopped Rx Day	138
Duration of AE	18 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	LOWER RESPIRATORY TRACT INFECTION

Discontinued Study Drug Due to the Event NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はイタリアの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，肺炎を発現した。被験者は喫煙者（紙巻タバコ 6 本／日，3 年間）かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は発熱及び強い左胸郭痛のため入院した。入院時に呼吸困難はなかった。左肺上葉に肺浸潤影（コンソリデーション）が認められ，炎症の経過に一致する所見であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

N-アセチルシステイン，セフジトレンピボキシル，クラリスロマイシン，DELTACORTENE 及び FLUNISOLIDE AEROSOL が投与された。

The patient's past medications include:

BETAMETHASONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

CLOBETASOL PROPIONATE for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.23.0] [10035664]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMONIA

- Investigator: Lower respiratory tract infection

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** Screening: Normal

[redacted] **20[redacted] CXR:** EXCLUSION OF PNEUMOTHORAX, AREA OF CONSOLIDATION IN THE LEFT UPPER LUNG LOBE COMPATIBLE WITH PNEUMONIA

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
アレルギー性鼻炎	X			

Treatment Group	Age at Study Start	Sex	Race
PLACEBO/UPA 15 MG QD	4[redacted]	FEMALE	MULTIPLE

Medical History	Onset Year
ALLERGIC RHINITIS	19[redacted]
ATOPIC DERMATITIS	19[redacted]
ATOPIC DERMATITIS	19[redacted]
GALLSTONES	19[redacted]
TRUE ABSTINENCE AS CONTRACEPTION	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: CHOLECYSTECTOMY	19[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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 50	50
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 130		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BETAMETHASONE	4 MG/DIE, DECREASING EACH 2 DAYS mg	QD	Y-M: 20[redacted]
BILASTINE	10 MG/DIE mg	QD	Y-M: 20[redacted]
TACROLIMUS	TWICE A DAY %	BID	Y-M: 20[redacted]
BETAMETHASONE W/FUSIDIC ACID	ONCE A DAY g	BID	Y-M: 20[redacted] / -164
METHYLPREDNISOLONE	TWICE A DAY %	BID	Y-M: 20[redacted] / -97
DEXERYL	2 APPLICATIONS A DAY OTHER: APPLICATIONS	BID	Y-M: 20[redacted] / -17

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
DEXERYL	2 APPLICATIONS A DAY OTHER: APPLICATIONS	BID	Y-M: 20[redacted] / -17	NOT REPORTED

Event #1: Serious Adverse Event

Event Description	WORSENING ALLERGIC RHINITIS
Preferred term	アレルギー性鼻炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 53
Age at AE Onset	4[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 50): Lymphocytes: 1.27 [1 - 4] 10^9/L; Lymphocytes/Leukocytes: 20.5 [20 - 45] %; [redacted]20[redacted] (RX DAY 53): NPTST128-QUANTIFERON TB GOLD TEST: 0.02 [0 - 0.34] IU/ML; [redacted]20[redacted] (RX DAY 82): NPTST128-QUANTIFERON TB GOLD TEST: 0.03 [0 - 0.34] IU/ML
Microbiology	[redacted]20[redacted] (RX DAY 53): SPUTUM NPTST142-SPUTUM CULTURE: NEGATIVE-SPECIMEN CONTAMINED BY SALIVA, STAPHYLOCOCCUS AUREUS, LEUKOCYTES >25 CELLS/FIELD, EPITHELIAL SQUAMOUS CELLS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 53): CHEST X RAY: NEGATIVE
AE Stopped Rx Day	54
Duration of AE	2 DAYS
Toxicity Grade	1
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	HOSPITALIZATION FOR EVALUATION OF SUSPECT OF TB

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

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はイタリアの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，アレルギー性鼻炎増悪を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアレルギー性鼻炎及びアトピー性皮膚炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はアレルギー性鼻炎増悪を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，アレルギー性鼻炎増悪は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は Quantiferon 検査（以下，「QTF 検査」）の結果が陽性であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は結核疑いの精査を目的に入院した。後鼻漏（非重篤）及び夜間咳嗽を発現していた。同日，QTF 検査及び胸部X線検査を行ったが，いずれも異常なしであった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は状態が改善しており，退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，当該医療機関で再度 QTF 検査が行われ，検査判定は陰性であった。2 回の QTF 検査が陰性であり，胸部X線検査及び感染症専門医の診察で異常なしと判断されたことから，潜伏結核は否定された。

関連するリスク因子として，20 年間の南米居住歴が挙げられた。

The patient's past medications include:

BETAMETHASONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BILASTINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BECLOMETASONE W/FUSIDIC ACID for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METHYLPREDNISOLONE CREAM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Allergic rhinitis (10001723) (Rhinitis allergic (10039085)) [v.22.1] [10001723]

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 ALLERGIC RHINITIS

- Investigator: Hospitalization for evaluation of suspect of TB.

- AbbVie: Reported event more likely related to pre-existing allergic rhinitis.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Company Remarks

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD; QUANTIFERON TB GOLD TEST:** Negative: 0.02 IU/ML (Reference range: 0.00-0.34)

[redacted] **20[redacted] BLOOD; QUANTIFERON TB GOLD TEST:** Negative: 0.03 IU/ML (Reference range: 0.00-0.34)

[redacted] **20[redacted] CHEST X-RAY:** Screening: Normal

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

[redacted] **20[redacted] LYMPHOCYTES %:** 20.50 % (normal 20.00 to 45.00)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 1.27 X10**3/MM**3 (normal 1.00 to 4.00)

[redacted] 20[redacted] SCREENING QUANTIFERON TB GOLD: Positive

[redacted] 20[redacted] SPUTUM CULTURE: Specimen contaminated by saliva, staphylococcus aureus, leukocytes >25 cells/field, epithelial squamous cells.

[redacted] 20[redacted] SPUTUM CULTURE FOR TB: neg. for TB mycobacterium

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
乳癌	X	X		X
結腸癌	X			X

Treatment Group	Age at Study Start	Sex	Race
PLACEBO/UPA 15 MG QD	4[redacted]	FEMALE	ASIAN

Medical History	Onset Year
ALLERGIC RHINITIS	19[redacted]
ASTHMA	19[redacted]
ATOPIC DERMATITIS	19[redacted]
FOOD ALLERGY	19[redacted]
ALLERGIC CONJUNCTIVITIS	20[redacted]
INFLUENZA	20[redacted]
TRUE SEXUAL ABSTINENCE	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: NB-UVB	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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 113	113
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 114	[redacted]20[redacted] / 535	422

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: 19[redacted]
OLOPATADINE	1 OTHER: DROP	PRN	Y: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
DEXAMETHASONE	1 mg	BID	Y-M: 20[redacted]-[redacted]
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
DEXAMETHASONE	0.5 mg	BID	Y-M: 20[redacted]-[redacted]
CICLOSPORIN	100 mg	QD	Y-M: 20[redacted]-[redacted]
TACROLIMUS	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
CICLOSPORIN	150 mg	QD	Y-M: 20[redacted]-[redacted]
CICLOSPORIN	100 mg	OTHER: EOD	Y-M: 20[redacted]-[redacted]
CICLOSPORIN	150 mg	OTHER: EOD	Y-M: 20[redacted]-[redacted]
CICLOSPORIN	100 mg	QD	Y-M: 20[redacted]-[redacted]
GUAIAZULENE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
CLOBETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
BETAMETHASONE	1 mg	QD	Y-M: 20[redacted]-[redacted]
BETAMETHASONE	0.5 mg	QD	Y-M: 20[redacted]-[redacted]
BETAMETHASONE	0.5 mg	OTHER: EOD	Y-M: 20[redacted]-[redacted]
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
GUAIAZULENE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]
DEPRODONE	1 OTHER: APTPLICATION	BID	Y-M: 20[redacted]-[redacted]
FEXOFENADINE	120 mg	BID	Y-M: 20[redacted]-[redacted] / -147
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted]-[redacted] / -83
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted] / -34
ANTIVIRALS FOR SYSTEMIC USE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -16

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
OLOPATADINE	1 OTHER: DROP	PRN	Y: 20[redacted]	NOT REPORTED
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]	NOT REPORTED

FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / - NOT REPORTED 83
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / - NOT REPORTED 34
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 30 NOT REPORTED
CLOBETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 30 NOT REPORTED
DEPRODONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 30 NOT REPORTED
BUDESONIDE W/FORMOTEROL FUMARATE	1 OTHER: PUFF	BID	Y-M: 20[redacted] / 73 NOT REPORTED
THEOPHYLLINE	100 mg	BID	Y-M: 20[redacted] / 73 NOT REPORTED
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / NOT REPORTED 169
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / NOT REPORTED 536

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Possible Malignancy, Event of Interest - Malignancy, Event of Interest - Malignancy excluding NMSC

Event Description	BREAST CANCER(LEFT)
Preferred term	乳癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 520
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 501): MAMMMOGRAM: SUSPECTED BREAST CANCER(LEFT); [redacted]20[redacted] (RX DAY 520): NEEDLE BIOPSY: BREAST CANCER(LEFT); [redacted]20[redacted] (RX DAY 620): MAMMARY ULTRASONOGRAPHY: BREAST CANCER(LEFT); [redacted]20[redacted] (RX DAY 626): MASTECTOMY: NO METASTASIS TO LIMPH NODES; NEEDLE BIOPSY: NO METASTASIS TO LYMPH NODES; [redacted]20[redacted] (RX DAY 627): X-RAY(CHEST): NO PROBLEM
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	4
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #2: Serious Adverse Event, Event of Interest - Possible Malignancy, Event of Interest - Malignancy, Event of Interest - Malignancy excluding NMSC

Event Description	CANCER OF TRANSVERSE COLON

Preferred term	結腸癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 550 (15 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 550): BIOPSY: CANCER OF TRANSVERSE COLON; COLONSCOPY: CANCER OF TRANSVERSE COLON
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	4
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, IS LIFE THREATENING

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者は日本の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，乳癌（左胸）を発現した。被験者は厳密な性的禁欲状態，非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴は喘息，アトピー性皮膚炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は乳癌（左胸）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は乳房撮影スクリーニングを受けた。20[redacted] 年 [redacted] 月 [redacted] 日，生検の結果から乳癌と診断された。治験薬の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，左胸の乳房切除術及びセンチネルリンパ節生検が行われた。リンパ節への転移は認められなかった。術後痛に対し，アセトアミノフェンの内服が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，X 線検査が行われ，問題となる異常は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師は，本事象に関連のある家族歴として，祖母の癌（詳細不明）を挙げた。

アセトアミノフェンが投与された。

The patient's past medications include:

DECADRON for ATOPIC DERMATITIS ([redacted])

NEORAL for ATOPIC DERMATITIS ([redacted])

PROTOPIC for ATOPIC DERMATITIS ([redacted])

AZUNOL for ATOPIC DERMATITIS ([redacted])

LOCOID for ATOPIC DERMATITIS ([redacted])

ANAMIDOL for ATOPIC DERMATITIS ([redacted])

RINDERON for ATOPIC DERMATITIS ([redacted])

DIFLORASON DIACETATE for ATOPIC DERMATITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Breast cancer (10006187) (Breast cancer (10006187)) [v.23.1] [10006187]

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 BREAST CANCER (LEFT)

- **Investigator:** Not applicable

- **AbbVie:** A sharp increase in the frequency of breast cancer has been noted in Japan since 19[redacted], which more likely is related to change in dietary patterns in Japanese women.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **MAMMARY ULTRASONOGRAPHY:** Breast cancer (LEFT)

[redacted] 20[redacted] **MAMMOGRAM:** Breast Cancer(LEFT)

[redacted] 20[redacted] **NEEDLE BIOPSY:** Positive - Breast Cancer (LEFT)

[redacted] 20[redacted] **NEEDLE BIOPSY:** No metastasis to lymph nodes

[redacted] 20[redacted] **X-RAY:** No problems noted

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者は日本の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，横行結腸癌を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は横行結腸癌を発現した。

本事象が診断される前，20[redacted] 年 [redacted] 月 [redacted] 日の便潜血検査で陽性と確認された。

20[redacted] 年 [redacted] 月 [redacted] 日，結腸内視鏡検査及び生検が行われ，ステージ 1 の横行結腸癌と確認された。この他，コンピュータ断層撮影，磁気共鳴画像検査及び骨シンチグラフィも行われた。胃内視鏡検査，子宮体部及び頚部の細胞学的検査，並びに X 線検査の結果に異常はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，癌に対する外科手術手技を受けるため，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，外科手術（詳細不明）が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師は，本事象に関連のある家族歴として，祖母の癌（詳細不明）を挙げた。

The patient's past medications include:

DECADRON for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

NEORAL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PROTOPIC OINTMENT FOR PEDIATRIC for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZUNOL OINTMENT for ATOPIC DERMATITIS ([redacted])

LOCOID OINTMENT for ATOPIC DERMATITIS ([redacted])

ANAMIDOL OINTMENT for ATOPIC DERMATITIS ([redacted])

RINDERON for ATOPIC DERMATITIS ([redacted])

DIFLORASONE DIACETATE OINTMENT for ATOPIC DERMATITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Cancer of transverse colon (10007118) (Colon cancer (10009944)) [v.23.1] [10007118]

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 CANCER OF TRANSVERSE COLON

- Investigator: Not applicable

- AbbVie: Colorectal cancer is the third most common cancer worldwide, and in Japan, it is estimated that about 10% of men and 8% of women will be diagnosed with colorectal cancer during their lifetime. In addition a large meta-analysis showed a two fold risk of developing colorectal cancer in women who had breast cancer diagnosed before age 50.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BIOPSY:** CANCER OF TRANSVERSE COLON

[redacted] **BONE SCINTIGRAPHY:** Not reported

[redacted] **20[redacted] COLONOSCOPY:** CANCER OF TRANSVERSE COLON

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

[redacted] **20[redacted] CYTOLOGICAL EXAMINATION:** No abnormalities were found in uterine body and cervix.

[redacted] **20[redacted] FECAL OCCULT BLOOD:** positive

[redacted] **20[redacted] GASTROFIBERSCOPY:** No abnormalities were found.

[redacted] **20[redacted] MRI:** Not reported

[redacted] **20[redacted] WOUND BIOPSY:** Positive - CANCER OF TRANSVERSE COLON

[redacted] **20[redacted] XRAY:** No abnormalities were found.

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	2[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
FOOD ALLERGYC	19[redacted]
ATOPIC DERMATITIS	19[redacted]
BRONCHIAL ASTHMA	19[redacted]
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 113	113
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 114	[redacted]20[redacted] / 373	260

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[redacted]-
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
BETAMETHASONE	2 g	BID	Y-M: 20[redacted]- / -111
DIPROBASE	2 g	BID	Y-M: 20[redacted]- / -111

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
DIPROBASE	2 g	BID	Y-M: 20[redacted] / -111	ONGOING
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 453	ONGOING
PYRAZINAMIDE	1500 mg	QD	Y-M: 20[redacted] / 453	ONGOING

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

Event Description	INFILTRATIVE TUBERCULOSIS
Preferred term	肺結核
AE Onset Date / Rx Day	[redacted] / 369
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted] (RX DAY 437): X-RAY: INFILTRATIVE TUBERCULOSIS OF THE UPPER LOBES OF BOTH LUNGS
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はロシア連邦の 2[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を投与され，浸潤性結核を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎，気管支喘息であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は浸潤性結核を発現した。

本事象の発現前，スクリーニング期間である 20[redacted] 年 [redacted] 月 [redacted] 日に受けた QuantiFERON 結核菌検査の結果は陰性であった。20[redacted] 年 [redacted] 月 [redacted] 日，再度 QuantiFERON 結核菌検査が行われ，結果は陽性であった。20[redacted] 年 [redacted] 月 [redacted] 日，胸部 X 線検査で退縮している結核腫が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は試験を中止した。

20[redacted] 年 [redacted] 月 [redacted] 日，再度胸部 X 線検査が行われ，結核と確定診断された。同日，胸部コンピュータ断層撮影が行われ，浸潤性結核が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は結核の診断により入院した。結核専門医の診察が行われ，浸潤性結核と確定診断された。本事象に関連した徴候及び症状はなかった。治療が開始された。

治験責任医師は，リスク因子としてロシアに居住していること，過去に BCG ワクチン接種を受けたことを挙げた。本事象に関連する家族歴はなかった。

ピラジナミドおよび levofloxacin が投与された。

The patient's past medications include:

BETAMETHASONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MOMETASONE for RESCUE THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Tuberculosis of lung, infiltrative (10044886) (Pulmonary tuberculosis (10037440)) [v.23.0] [10044886]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of INFILTRATIVE TUBERCULOSIS

- Investigator: Not applicable

- AbbVie: Not applicable

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Company Remarks

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST CT:** In S1 of the right lung and S2 of the left lung there are foci with destruction cavities in its structure are detected. Multiple lesions are detected perifocal and in the S3 of the right lung. Dynamics compared to [redacted] 20[redacted] is negative in terms of the infiltration growth, the size of the cavities within and foci around. Infiltrative TBC of the upper lobes of both lungs in the phase of destruction and seeding. Progression.

[redacted] **20[redacted] CHEST X-RAY:** findings: normal

[redacted] **20[redacted] CHEST X-RAY:** revealed tuberculomas with decay

[redacted] **20[redacted] CHEST X-RAY:** Infiltrative tuberculosis of the upper lobes of both lungs

[redacted] **20[redacted] COVID-19 VIRUS TEST:** PCR of Sputum. Results not reported.

[redacted] **20[redacted] QUANTIFERON TEST:** negative

[redacted] **20[redacted] QUANTIFERON TEST:** positive

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD/UPA 30 MG QD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	20[redacted]
ASTHMA	20[redacted]
ALLERGIC RHINITIS	20[redacted]
FOOD ALLERGY	20[redacted]
TRUE SEXUAL ABSTINENCE	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 111	111
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 112	[redacted]20[redacted] / 183	72

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	0.3 OTHER: J/CM2	QD	Y-M: 20[redacted] / -90
CHLOROPYRAMINE	20 mg	QD	Y-M: 20[redacted] / -90
DIPROGENT	30 g	BID	Y-M: 20[redacted] / -90
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted] / -90
MOMETASONE	100 ug	QD	Y-M: 20[redacted] / -90
METHOTREXATE	15 mg	1 TIME PER WEEK	Y-M: 20[redacted] / -85
BUTYROSPERMUM PARKII;DIMETHICONOL;DIMETICONE;	0.5 g	BID	Y-M: 20[redacted] / -77
ALCLOMETASONE	0,5 g	BID	Y-M: 20[redacted] / -37

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
BUTYROSPERMUM PARKII;DIMETHICONOL;DIMETICONE;	0.5 g	BID	Y-M: 20[redacted] / -77	Y-M: 20[redacted] / 186
UNACID	2500 mg	TID	Y-M: 20[redacted] / 185	Y-M: 20[redacted] / 187
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 187	Y-M: 20[redacted] / 196
FLUCONAZOLE	300 mg	QD	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 192
MEROPENEM	1000 mg	TID	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 196

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

Event Description COMMUNITY-ACQUIRED BILATERAL PNEUMONIA
Preferred term 肺炎
AE Onset Date / Rx Day [redacted]20[redacted] / 183

Age at AE Onset	1[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 187): Creatine Kinase: 603 [29 - 200] U/L; NPTST028-BUN: 1.3 [1.7 - 8.3] MMOL/L; NPTST046-CRP: 60.9 [0.1 - 8.2] MG/L; NPTST077-IGE: 46430 [0 - 120] IU/ML; NPTST087-LDH: 514 [125 - 450] U/L; [redacted]20[redacted] (RX DAY 188): NPTST037-CHLAMYDIA PNEUMONIA IGM: 14.3 [0 - 10] IU/ML; NPTST051-CYTOMEGALOVIRUS (GRADE ANALYSIS: POSITIVE [0 - 0] UNIT NOT REPORTED; NPTST052-CYTOMEGALOVIRUS (IGG): 16.2 [0 - 0] UNIT NOT REPORTED; NPTST074-HERPES SIMPLEX VIRUS (I+II) IGM: 191.1 [0 - 20] IU/ML; NPTST113-MYCOPLASMA PNEUMONIA IGG: 32.1 [0 - 20] IU/ML; NPTST114-MYCOPLASMA PNEUMONIA IGM: 150 [0 - 13] IU/ML; [redacted]20[redacted] (RX DAY 189): NPTST078-IGG: 14.59 [8.2 - 10.7] G/L; NPTST079-IGM: 435 [0.6 - 2] G/L; [redacted]20[redacted] (RX DAY 191): Erythrocytes: 3.3 [4.1 - 5.1] 10^12/L; Hematocrit: 0.34 [0.34 - 0.44] FRACTION OF 1; Leukocytes: 14.6 [4.5 - 13] 10^9/L; Lymphocytes/Leukocytes: 18 [30 - 46] %; Monocytes: 0.93 [0.19 - 0.72] 10^9/L; NPTST059-ESR ACCELERATION: 51 [2 - 15] MM/H; Neutrophils: 11 [1.82 - 7.47] 10^9/L; Neutrophils/Leukocytes: 77.6 [46 - 65] %; Platelets: 514 [154 - 442] 10^9/L
Microbiology	[redacted]20[redacted] (RX DAY 187): SPUTUM NPTST048-CULTURE FROM THE THROAT TO THE FLORA: POSITIVE-STREPTOCOCCUS VIRIDANS, CANDIDA ALBICANS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 183): TEMPERATURE: 40C; [redacted]20[redacted] (RX DAY 185): CHEST X-RAY: X-RAY PICTURE CORRESPONDS TO LEFT-SIDED POLYSEGMENTAL PNEUMONIA; [redacted]20[redacted] (RX DAY 188): RESPIRATORY FUNCTION: A SHARP DECREASE IN BRONCHIAL CONDUCTION ACCORDING TO THE MIXED TYPE, MAINLY DUE TO THE INFLAMMATORY COMPONENT, THE TEST WITH A BRONCHODILATOR IS NEGATIVE; [redacted]20[redacted] (RX DAY 189): CT SCAN (COMPUTED TOMOGRAPHY): CT PICTURE OF BILATERAL INTERSTITIAL PNEUMONIA; [redacted]20[redacted] (RX DAY 191): ECG: SINUS ARRHYTHMIA DISAPPEARING WITH HOLDING YOUR BREATH; [redacted]20[redacted] (RX DAY 194): T-SPOT: NEGATIVE
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はロシア連邦の1[redacted]歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，市中感染性両側性肺炎を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎，喘息，アレルギー性鼻炎及び食物アレルギーであった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は市中感染性両側性肺炎を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は高体温（最高 40°C），咳嗽及び胸郭痛のため入院した。被験者はマイコプラズマ感染とクラミジア感染を併発していると診断された（重度の市中感染性両側性肺炎，I 度の呼吸不全）。

フルコナゾール，ampicillin + sulbactam，levofloxacin 及び meropenem が投与された。

The patient's past medications include:

BETAMETHASONE W/GENTAMICIN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CHLOROPYRAMINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LEVOCETIRIZINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MOMETASONE for ALLERGIC RHINITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ALCLOMETASONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Community acquired pneumonia (10010120) (Pneumonia (10035664)) [v.23.0] [10010120]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of COMMUNITY-ACQUIRED BILATERAL PNEUMONIA

- Investigator: Not applicable.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ABSOLUTE LYMPHOCYTE COUNT:** 2.06 x10^3/uL (normal 0.95 to 5.25)

[redacted] 20[redacted] **ABSOLUTE LYMPHOCYTE COUNT:** 2.92 x10^3/uL (normal 0.95 to 5.25)

[redacted] 20[redacted] **ABSOLUTE LYMPHOCYTE COUNT:** 3.39 x10^3/uL (normal 0.95 to 5.25)

[redacted] 20[redacted] **ABSOLUTE LYMPHOCYTE COUNT:** 2.45 x10^3/uL (normal 0.95 to 5.25)

[redacted] 20[redacted] **ANC:** 2.91 x10^3/uL (normal 1.65 to 8.15)

[redacted] 20[redacted] **ANC:** 2.51 x10^3/uL (normal 1.65 to 8.15)

[redacted] 20[redacted] **ANC:** 3.68 x10^3/uL (normal 1.65 to 8.15)

[redacted] 20[redacted] **ANC:** 3.53 x10^3/uL (normal 1.65 to 8.15)

[redacted] 20[redacted] **BUN:** 1.3 MMOL/L (normal 1.7 to 8.3)

[redacted] 20[redacted] **CHEST X-RAY:** Screening: Normal

[redacted] 20[redacted] **CHEST X-RAY:** X-ray picture corresponds to left-sided polysegmental pneumonia

[redacted] 20[redacted] **CHLAMYDIA PNEUMONIA IGM:** 14.3 IU/mL (normal 0 to 10)

[redacted] 20[redacted] **CREATINE KINASE:** 603 U/L (normal 29 to 200)

[redacted] 20[redacted] **CRP:** 60.9 MG/L (normal 0.1 to 8.2)

[redacted] 20[redacted] **CT SCAN:** CT picture of bilateral interstitial pneumonia

[redacted] 20[redacted] **CYTOMEGALOVIRUS (IGG):** 16.2 AU/ml (normal 0 to 0)

[redacted] 20[redacted] **CYTOMEGALOVIRUS GRADE ANALYSIS:** Positive

[redacted] 20[redacted] **ECG:** Sinus arrhythmia disappearing with holding your breath

[redacted] 20[redacted] **ESR ACCELERATION:** 51 MM/HR (normal 2 to 15)

[redacted] 20[redacted] **HEMATOCRIT:** 33.8 % (normal 34 to 44)

[redacted] 20[redacted] **HERPES SIMPLEX VIRUS I AND II IGM:** 191.1 IU/mL (normal 0 to 20)

[redacted] 20[redacted] **IGE:** 46430 IU/mL (normal 0 to 120)

[redacted] 20[redacted] **IGG:** 14.59 G/L (normal 8.2 to 10.7)

[redacted] 20[redacted] **IGM:** 435 G/L (normal 0.6 to 2)

[redacted] 20[redacted] **LDH:** 514 U/L (normal 125 to 450)

[redacted] **20[redacted] LYMPHOCYTES %:** 18 % (normal 30 to 46)

[redacted] **20[redacted] MONOCYTES ABS:** 0.93 X10**9/L (normal 0.19 to 0.72)

[redacted] **20[redacted] MYCOPLASMA PNEUMONIA IGG:** 32.1 IU/mL (normal 0 to 20)

[redacted] **20[redacted] MYCOPLASMA PNEUMONIA IGM:** 150 IU/mL (normal 0 to 13)

[redacted] **20[redacted] NEUTROPHILS %:** 77.6 % (normal 46 to 65)

[redacted] **20[redacted] NEUTROPHILS ABS:** 11.00 X10**9/L (normal 1.82 to 7.47)

[redacted] **20[redacted] PLATELET COUNT:** 514 X10**9/L (normal 154 to 442)

[redacted] **20[redacted] PULSE:** 40C

[redacted] **20[redacted] RED BLOOD CELLS:** 3.33 X10**6/MCL (normal 4.1 to 5.1)

[redacted] **20[redacted] RESPIRATORY FUNCTION TEST:** A sharp decrease in bronchial conduction according to the mixed type, mainly due to the inflammatory component, the test with a bronchodilator is negative

[redacted] **20[redacted] SPUTUM CULTURE:** Positive: streptococcus viridans, candida albicans

[redacted] **20[redacted] T-SPOT:** Negative

[redacted] **20[redacted] TEMPERATURE:** 40 Degrees C

[redacted] **20[redacted] WBC:** 6.07 x10^3/uL (normal 4.35 to 13.15)

[redacted] **20[redacted] WBC:** 6.13 x10^3/uL (normal 4.35 to 13.15)

[redacted] **20[redacted] WBC:** 8.11 x10^3/uL (normal 4.35 to 13.15)

[redacted] **20[redacted] WBC:** 7.40 x10^3/uL (normal 4.35 to 13.15)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 14.6 X10**9/L (normal 4.5 to 13)

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
皮膚播種性帯状疱疹	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD/UPA 30 MG QD	2[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
ATOPIC DERMATITIS	19[redacted]
CHICKEN POX	19[redacted]
ALLERGIC RHINITIS AND CONJUNCTIVITIS	20[redacted]
ASTHMA BRONCHIALE	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: DESENSIBILISATION	19[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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 111	111
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 112		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ALL OTHER NON-THERAPEUTIC PRODUCTS	UNK	NOT REPORTED	Y: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
TACROLIMUS	10 g	QD	Y: 20[redacted]
MOMETASONE	1 mg	OTHER: AS NEEDED	Y-M: 20[redacted]-[redacted] / -254
MOMETASONE	30 mg	OTHER: ONCE A WEEK	Y-M: 20[redacted]-[redacted] / -233
DEXERYL	50 g	BID	Y-M: 20[redacted]-[redacted] / -50
FEXOFENADINE	120 mg	OTHER: IF NEEDED	Y-M: 20[redacted]-[redacted] / -19
PSEUDOEPHEDRINE	120 mg	OTHER: IF NEEDED	Y-M: 20[redacted]-[redacted] / -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 / RX Day	Stop Year-Month / RX Day
DEXERYL	50 g	BID	Y-M: 20[redacted]-[redacted] / -50	NOT REPORTED
DICLOFENAC	60 g	OTHER: AS NEEDED	Y-M: 20[redacted]-[redacted] / 10	NOT REPORTED
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCE	NA OTHER: NA	PRN	Y-M: 20[redacted]-[redacted] / 465	Y-M: 20[redacted]-[redacted] / 491
FEXOFENADINE	120 mg	PRN	Y-M: 20[redacted]-[redacted] / 517	NOT REPORTED
FUSIDIC ACID	20MG/1G mg	BID	Y-M: 20[redacted]-[redacted] / 517	NOT REPORTED
PANTYSON	MACROGOL-6-LAURYLETHER (30MG), HARNSTOFF (50MG) mg	PRN	Y-M: 20[redacted]-[redacted] / 517	NOT REPORTED
PARACETAMOL	500 mg	QID	Y-M: 20[redacted]-[redacted] / 517	NOT REPORTED
UNDECYLENIC ACID	30MG/1G OTHER: LOTION	OTHER: IS USED WHEN GETTING A SHOWER/ HAIRWASH	Y-M: 20[redacted]-[redacted] / 517	NOT REPORTED

SPEKTRAMOX	625 mg	TID	Y-M: 20[redacted]-20[redacted] / 517 Y-M: 20[redacted]-[redacted] / 521
ACICLOVIR	750 mg	TID	Y-M: 20[redacted]-20[redacted] / 517 Y-M: 20[redacted]-[redacted] / 522
METAMIZOLE	500 mg	PRN	Y-M: 20[redacted]-20[redacted] / 517 Y-M: 20[redacted]-[redacted] / 524
TALC;TANNIC ACID;ZINC OXIDE	TALKUM (19.5G), ZINKOXID (15G), TANNIN (1G) mL	QID	Y-M: 20[redacted]-[redacted] / 518 NOT REPORTED
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted]-20[redacted] / 519 Y-M: 20[redacted]-[redacted] / 522
CICALFATE	NA mL	PRN	Y-M: 20[redacted]-[redacted] / 520 NOT REPORTED
DALIBOUR	NA OTHER: WRAPS AROUND THE FACE	BID	Y-M: 20[redacted]-[redacted] / 520 NOT REPORTED
PREGABALIN	100 mg	BID	Y-M: 20[redacted]-[redacted] / 520 NOT REPORTED
SQUA-MED	15 MG PYRITHIONUM ZINCICUM 20 MG, DISODIUM UNDECYLENAMIDO mL	OTHER: HAIRWASH	Y-M: 20[redacted]-[redacted] / 520 NOT REPORTED
SICORTEN PLUS	HALOMETHASON-MONOHYDRAT 0.5 MG/1 G TRICLOSAN 10 MG/1 G OTHER: MG/G	BID	Y-M: 20[redacted]-20[redacted] / 522 Y-M: 20[redacted]-[redacted] / 528
MOMETASONE	1 OTHER: MG/G	QD	Y-M: 20[redacted]-[redacted] / 525 NOT REPORTED
TOSYLCHLORAMIDE	150 OTHER: G/LT	BID	Y-M: 20[redacted]-[redacted] / 528 NOT REPORTED
IMACORT	10 MG CLOTRIMAZOL,2,5 MG HEXAMIDINDIISETHIONAT,5MG PREDNISON OTHER: MG/G	BID	Y-M: 20[redacted]-20[redacted] / 528 Y-M: 20[redacted]-[redacted] / 532
SICORTEN PLUS	HALOMETHASON-MONOHYDRAT 0.5 MG/1 G TRICLOSAN 10 MG/1 G OTHER: MG/G	QD	Y-M: 20[redacted]-[redacted] / 532 NOT REPORTED

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

Event Description	DISSEMINATED HERPES ZOSTER, CUTANEOUS
Preferred term	皮膚播種性帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 513
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 518): OTHER LIP NPTST014-ANTIGENS VARICELLA ZOSTER VIRUS: POSITIVE-IT WAS DETECTED VZV DNA; WOUND NPTST160-VZV DNA: POSITIVE-IT WAS

	DETECTED VARICELLA ZOSTER DNA; [redacted]20[redacted] (RX DAY 519): WOUND NPTST107-MICROSCOPY, RESISTANCE TESTING: POSITIVE-IT WAS FOUND STAPH. AUREUS , RESISTENT TO PENICILLIN, CLINDAMYCIN, ERYTHROMYCIN.
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 517): VITALSIGNS TEMPERATURE: 38.8 ?C
AE Stopped Rx Day	534
Duration of AE	22 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はスイスの 2[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を投与され，播種性帯状疱疹（皮膚）を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎，アレルギー性鼻炎（アレルギー性鼻炎結膜炎），気管支喘息であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は播種性帯状疱疹（皮膚）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，播種性帯状疱疹（皮膚）は消失した。

本事象発現の 1 週間前，被験者は疲労を感じていた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頭痛，頚部痛，敏感肌，口の周囲から全身に広がる発疹，リンパ節腫脹及び嚥下時の疼痛を自覚し始めた。20[redacted] 年 [redacted] 月 [redacted] 日，発熱（38.8℃）とともに顔面，胸部及び両下肢の膿疱が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は発熱のない状態で入院し，スワブ検体のウイルス検査で全身性水痘帯状疱疹ウイルス感染と診断された。被験者の全身状態は改善し，発熱はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師は，被験者のリスク因子としてアトピー性皮膚炎及び治験薬のヤヌスキナーゼ阻害薬を挙げた。

CO-AMOXI，DAFALGAN，アシクロビル，FUCIDIN 2%，プレガバリン，CLEXANE，TANNO HERMAL，SQUA-MED MEDIZINAL SHAMPOO LIQ PH5，TELFAST，AQUA DALIBOURI (AQUA ZINCO-CUPRICA COMPOSITE PH)，SICORTEN PLUS，NOVALGIN 及び CICALFATE が投与された。

The patient's past medications include:

TACROLIMUSfor ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

ELOCOM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MOMETASONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MONOVO for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster cutaneous disseminated (10074297) (Herpes zoster cutaneous disseminated (10074297)) [v.23.1] [10074297]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of DISSEMINATED HERPES ZOSTER, CUTANEOUS

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ANTIGENS VARICELLA ZOSTER VIRUS:** It was detected VZV DNA.

[redacted] 20[redacted] **BODY TEMPERATURE:** 38.8 Degrees C

[redacted] 20[redacted] **DIRECT IMMUNOFLUORESCENCE:** Positive

[redacted] 20[redacted] **MICROSCOPY, RESISTANCE TESTING:** It was found Staph Aureus, resistant to penicillin, clindamycin, erythromycin.

[redacted] 20[redacted] **MICROSCOPY, RESISTANCE TESTING:** It was found Staph Aureus, resistant to penicillin, clindamycin, erythromycin.

[redacted] 20[redacted] **VIRAL SWAB:** Generalized varicella zoster infection.

[redacted] 20[redacted] **VZV DNA:** Positive, it was detected Varicella Zoster DNA.

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD/UPA 30 MG QD	3[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
ASTHMA	19[redacted]
ALLERGIC RHINITIS	20[redacted]
ALLERGY ON CAT HAIR	20[redacted]
MAMMARY GLAND SWELLING LEFT SIDE	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted] / 1	[redacted] / 112	112
UPA	30 MG	ORAL	QD	[redacted] / 113	[redacted] / 199	87

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CLOBETASOL	0.5 OTHER: MG/G	QD	Y-M: 20[redacted]
NIVEA	WHOLE BODY OTHER: APPLICATION	BID	Y-M: 20[redacted] / -248
LEVOCETIRIZINE	5 mg	PRN	Y-M: 20[redacted] / -105
PREDNISONE	50 mg	QD	Y-M: 20[redacted] / -105
PRURI-MED	WHOLE BODY OTHER: APPLICATION	QD	Y-M: 20[redacted] / -105
ALL OTHER NON-THERAPEUTIC PRODUCTS	NA OTHER: MINUTES	OTHER: 3 TIMES PER WEEK	Y-M: 20[redacted] / -104
CLOBETASOL	BLANKET THERAPY OTHER: 0.5 MG/G	OTHER: 2 TIMES PER WEEK	Y-M: 20[redacted] / -104
CLOBETASOL	0,5 OTHER: MG/G	OTHER: 2 - 3 TIMES PER WEEK	Y-M: 20[redacted] / -62
TACROLIMUS	0.1 %	OTHER: 2 TIMES DAILY	Y-M: 20[redacted] / -47
PREDNICARBATE	0.25 %	QD	Y-M: 20[redacted] / -37

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
NIVEA	WHOLE BODY OTHER: APPLICATION	BID	Y-M: 20[redacted] / -248	ONGOING
LEVOCETIRIZINE	5 mg	PRN	Y-M: 20[redacted] / -105	ONGOING
PRURI-MED	WHOLE BODY OTHER: APPLICATION	QD	Y-M: 20[redacted] / -105	ONGOING
MAGNESIUM PHOSPHATE	1 OTHER: TABLET	QID	Y-M: 20[redacted] / 198	ONGOING
ARNICA MONTANA	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 207
IBUPROFEN	400 mg	OTHER: ON DEMAND	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 207
PRUNUS SPINOSA	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 207
APIS MELLIFICA W/LEVISTICUM OFFICINALE	1 mL	QD	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 219
HOMEOPATHIC PREPARATION	1 mL	QD	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 219
PARACETAMOL	500 mg	OTHER: ON DEMAND	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 223

GENTIANA LUTEA	10 gtt	TID	Y-M: 20[redacted] / 199	ONGOING
HOMEOPATHIC PREPARATION	1 OTHER: TEASPOON	BID	Y-M: 20[redacted] / 199	ONGOING
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted] / 199	ONGOING
ROSMARINUS OFFICINALIS	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 199	ONGOING
RAMIPRIL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 199	Y-M: 20[redacted] / 207
HOMEOPATHIC PREPARATION	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 199	Y-M: 20[redacted] / 219
SICORTEN PLUS	1 OTHER: APPLICATION	OTHER: ON DEMAND	Y-M: 20[redacted] / 207	Y-M: 20[redacted] / 219
FUCICORT	20 mg	BID	Y-M: 20[redacted] / 220	ONGOING
RETINOL	1 OTHER: 0.5 CM	QD	Y-M: 20[redacted] / 231	ONGOING
OTHER OPHTHALMOLOGICALS	1 gtt	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 252
TOBRADEX	1 AND 3 OTHER: MG/ML	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 252
HERBAL OPHTHALMOLOGICALS, OTHER	1 gtt	OTHER: 3-4 TIMES DAILY	Y-M: 20[redacted] / 252	ONGOING
SALVIA OFFICINALIS	1 OTHER: APPLICATION	OTHER: EVERY SECOND DAY	Y-M: 20[redacted] / 253	ONGOING

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

Event Description	MUSCULAR PAIN UPPER LEG LEFT - CAUSE UNKNOWN
Preferred term	筋肉痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 198
Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 198): Alkaline Phosphatase: 24 [0 - 46] U/L; Aspartate Aminotransferase: 19 [0 - 40] U/L; Creatine Kinase: 190 [39 - 308] U/L; Leukocytes: 8.8 [4 - 10] 10^9/L; NPTST046-CRP: 7.8 [0 - 5] MG/L; NPTST087-LDH: 287 [135 - 225] U/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 177): MRI UPPER LEG LEFT: NORMAL
AE Stopped Rx Day	259 (60 DAYS AFTER LAST TREATMENT)
Duration of AE	62 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はスイスの 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を投与され，左大腿部筋肉痛（原因不明）を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎及び左胸乳腺の腫れであった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加し，2[redacted]9 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左大腿部筋肉痛（原因不明）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左大腿部筋肉痛（原因不明）は消失した。

20[redacted] 年 [redacted] 月，被験者は左大腿部の疼痛（非重篤）を自覚し始めた。20[redacted] 年 [redacted] 月 [redacted] 日，鎮痛薬及び理学療法による治療でも改善しなかったため被験者は入院し，この際に本事象は重篤に変更された。入院時，被験者は大腿四頭筋外側（主に大腿直筋から外側広筋にかけて）の圧痛を訴えていた。大腿部を外旋させながら屈曲する際も疼痛を訴えた。疼痛により，荷重はかなり制限されていた。血栓症，静脈炎及び浮腫の徴候はなく，核磁気共鳴画像に異常所見はなく，臨床検査値にも問題となる臨床所見はなかった。治療には，薬剤による疼痛管理，治療的オイリュトミー，律動的マッサージ，理学療法，スピノサスモモの花のオイルを使用した治療浴，アルニカ湿布及びローズマリーオイル（左大腿部の按摩に使用）が用いられた。転帰は，左大腿部の疼痛が部分的に緩和したと報告された。退院時，左脚は荷重可能に復していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。リスク因子として，被験者の体重が原因で仕事中に不適切な座位をとっていることが挙げられた。

被験者は本事象を理由に試験を中止した。

アルニカ，WELEDA ARNICA GLOBULI D6，MAGNESIUM PHOSPHORICUM D6，DAFALGAN，ROSMARINUS FOL ET FLOS 20% OIL，塩化マグネシウム，BRYONIA / STANNUM，APIS CUM LEVISTICO D3，イブプロフェン，スピノサスモモの花のオイル及び WELEDA ARNICA COMP/FORMICA UNGUENT が投与された。

The patient's past medications include:

DERMOVATE UNGUENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PREDNISON for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

UVB NB for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

DERMOVATE SCALP APPLICATION for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PROTOPIC 0.1% for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNITOP for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DEXERYL CREAM for EMOLLIENT THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinde

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1) Myalgia of lower extremities (10051587) (Myalgia (10028411)) [v.22.1] [10051587]

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 MUSCULAR PAIN UPPER LEG LEFT-CAUSE UNKNOWN

- Investigator: Not Applicable

- AbbVie: Event is common in the general population, with a wide array of possible causes. Sub-optimal sitting posture during work, because of patient's weight, is an additional risk factor (as per reporter)

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ALKALINE PHOSPHASE:** 24 U/L (normal 0 to 46)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 19 U/L (normal 0 to 40)

[redacted] 20[redacted] **BMI:** 31.0 kg/m2

[redacted] 20[redacted] **CREATINE KINASE:** 190 U/L (normal 39 to 308)

[redacted] **20[redacted] CRP:** 7.8 MG/L (normal 0 to 5)

[redacted] **20[redacted] LDH:** 287 U/L (normal 135 to 225)

[redacted] **20[redacted] MRI:** upper left leg - normal

[redacted] **20[redacted] WBC:** 8.8 G/L (normal 4 to 10)

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
全身性剥脱性皮膚炎	X	X		

Treatment Group	Age at Study Start	Sex	Race
PLACEBO	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
EGG ALERGY	19[redacted]
ASTHMA	19[redacted]
HAY FEVER	19[redacted]
NUT ALLERGY	20[redacted]
EARLY MENOPAUSE	20[redacted]
ALOPECIA	20[redacted]
LOCALISED SHINGLES	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 14	14

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MOMETASONE	1 OTHER: APPLICATION	PRN	Y: 19[redacted]
EPADERM	1 OTHER: APPLICATION	BID	Y: 20[redacted]
PROGARON	1 OTHER: APPLICATION	QD	Y: 20[redacted]
QV	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
CICLOSPORIN	75 mg	BID	Y-M: 20[redacted]
CICLOSPORIN	100 mg	BID	Y-M: 20[redacted]
DIPROBASE	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -216
ZUMESTON	10.5/2.5 mg	QD	Y-M: 20[redacted] / -67

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
EPADERM	1 OTHER: APPLICATION	BID	Y: 20[redacted]	ONGOING
PROGARON	1 OTHER: APPLICATION	QD	Y: 20[redacted]	ONGOING
QV	1 OTHER: APPLICATION	PRN	Y: 20[redacted]	ONGOING
DIPROBASE	1 OTHER: APPLICATION	PRN	Y: 20[redacted]	ONGOING
ZUMESTON	10.5/2.5 mg	QD	Y-M: 20[redacted] / -67	ONGOING
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 18
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 36

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

Event Description	ERYTHRODERMA
Preferred term	全身性剥脱性皮膚炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 14
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED

AE Stopped Rx Day	18 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者は英国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，紅皮症を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎，卵アレルギー，喘息，ナッツアレルギー，脱毛症，早発閉経及びアレルギー性鼻炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加していた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は紅皮症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，紅皮症は消失した。

本事象発現に先行し，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に湿疹のフレア（非重篤）を発現した。

入院前の直近 3 週間，被験者はステロイド外用薬を中止した事により症状が再燃しており，20[redacted] 年 [redacted] 月 [redacted] 日には症状が管理困難となっていた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は極度の疼痛，熱感及び皮膚そう痒のため入院した。被験者は診察で疼痛及び不快感を訴え，紅皮症が認められた。被験者は始めのうち頻脈であったが，心拍数は改善した。湿疹面積重症度指数のスコアは 41.1 であった。被験者は糖質コルチコイドの経口薬及び外用薬を投与され，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。本事象を理由に治験薬の投与は中止された。

プレドニゾロン及び clobetasol が投与された。

The patient's past medications include:

ELOCON for ATOPIC DERMATITIS (19[redacted] - [redacted] [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

UVB for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CICLOSPORINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Erythroderma (10015277) (Dermatitis exfoliative generalised (10012456)) [v.22.0] [10015277]

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 ERYTHRODERMA

- Investigator: Not applicable.

- AbbVie: Event is more likely related to pre-existing atopic dermatitis.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] EASI SCORE:** 23.4 no units

[redacted] **20[redacted] EASI SCORE:** 16 no units

[redacted] **20[redacted] EASI SCORE:** 41.1 no units

[redacted] **20[redacted] HEART RATE:** 114 BPM

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ヘルペス性状湿疹	X			X
ヘルペス眼感染	X			X
単純ヘルペス	X			X

Treatment Group	Age at Study Start	Sex	Race
PLACEBO/UPA 30 MG QD	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
ASTHMA	19[redacted]
LATEX ALLERGY	19[redacted]
NUT ALLERGY	19[redacted]
COLD SORES	20[redacted]
HAYFEVER	20[redacted]
LOW VITAMIN D	20[redacted]
POSITIVE PATCH TEST - IRRITANT REACTION TO COBALT CHLORIDE, IMIDAZOLODINYL UREA, DIAZOLIDINYL UREA, AMERCHOL, COCAMIDOPROPYL BETAINE	20[redacted]
POSITIVE PATCH TEST - NICKEL	20[redacted]
POSITIVE RAST TEST GRASS, MIXED TREES	20[redacted]
POSITIVE RAST TEST CAT, DOG,	20[redacted]
POSITIVE RAST TEST DUST MITE	20[redacted]
PRURIGO NODULARIS	20[redacted]
LYMPHADENOPATHY	20[redacted]
MILD SINUS ARRHYTHMIA	20[redacted]
YELLOWISH SCLERAE NOTED DURING PHYSICAL EXAM	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 109	109
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 110		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARAFFIN	TOPICAL OTHER: TOPICAL	QD	Y: 19[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
CHLORPHENAMINE	UNK mg	PRN	Y-M: 20[redacted]
CLOBETASONE	UNK OTHER: TOPICAL	BID	Y-M: 20[redacted]
HYDROCORTISONE	1 %	BID	Y-M: 20[redacted]
BECLOMETASONE	2 OTHER: PUFFS	PRN	Y: 20[redacted]
FUCICORT	0.1 %	QD	Y: 20[redacted]
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
CLOBETASONE	0.5 mg	QD	Y-M: 20[redacted]
DERMOL	TOPICAL OTHER: TOPICAL	QD	Y-M: 20[redacted]
EPADERM	TOPICAL OTHER: TOPICAL	QD	Y-M: 20[redacted]
HYDROCORTISONE	1 %	BID	Y-M: 20[redacted]
TACROLIMUS	0.1 %	BID	Y-M: 20[redacted]
FLUCLOXACILLIN	500 mg	QID	Y-M: 20[redacted]
SOFT SOAP	UNK OTHER: UNK	PRN	Y: 20[redacted]
ERGOCALCIFEROL	10,000 IU	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]
TACROLIMUS	0.03 %	OTHER: NOCTE	Y-M: 20[redacted]
PIMECROLIMUS	UNK OTHER: TOPICAL	OTHER: NOCTE	Y-M: 20[redacted]
BENZALKONIUM	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
CLOBETASOL	0.5 mg	OTHER: EVRY OTHER DAY	Y-M: 20[redacted]
HYDROXYZINE	25 mg	QD	Y: 20[redacted]
PARAFFIN	TOPICAL OTHER: TOPICAL	BID	Y-M: 20[redacted]

PREDNISOLONE	5 mg	OTHER: 6 TIMES A DAY	Y-M: 20[redacted]
PREDNISOLONE	5 mg	OTHER: 6 TIMES A DAY	Y-M: 20[redacted]
CLOBETASOL	UNK OTHER: TOPICAL	QD	Y-M: 20[redacted] / -264
AQUEOUS	2 %	PRN	Y-M: 20[redacted] / -238
ALL OTHER NON-THERAPEUTIC PRODUCTS	PHOTOTHERAPY OTHER: 18.19	OTHER: J/CM2	Y-M: 20[redacted] / -192
FLUCLOXACILLIN	500 mg	QID	Y-M: 20[redacted] / -176
PREDNISOLONE	5 mg	OTHER: 6 TIMES A DAY	Y-M: 20[redacted] / -176
BETADERMIC	0.05/2.0 %	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -174
CHLORPHENAMINE	4 mg	TID	Y-M: 20[redacted] / -76
MOMETASONE	0.1 %	QD	Y-M: 20[redacted] / -72
CHLORPHENAMINE	4 mg	TID	Y-M: 20[redacted] / -52
MUPIROCIN	2 %	BID	Y-M: 20[redacted] / -52
BETADERMIC	0.05 %	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -17
CLOBETASOL	0.05 %	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -17
CLOBETASONE	0.5 mg	QD	Y-M: 20[redacted] / -17
FUCICORT	BETAMETHASONE VALERATE 0.1% FUSIDIC ACID 2% %	BID	Y-M: 20[redacted] / -17
FUSIDIC ACID	TOPICAL OTHER: TOPICAL	BID	Y-M: 20[redacted] / -17
MOMETASONE	0.1 %	QD	Y-M: 20[redacted] / -17

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
CHLORPHENAMINE	UNK mg	PRN	Y-M: 20[redacted]	NOT REPORTED
BECLOMETASONE	2 OTHER: PUFFS	PRN	Y: 20[redacted]	NOT REPORTED
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y: 20[redacted]	NOT REPORTED
DERMOL	TOPICAL OTHER: TOPICAL	QD	Y-M: 20[redacted]	NOT REPORTED
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 244
ERGOCALCIFEROL	10,000 IU	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]	NOT REPORTED
PARAFFIN	TOPICAL OTHER: TOPICAL	BID	Y-M: 20[redacted]	NOT REPORTED
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 253
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 75	NOT REPORTED
CLOBETASONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 138	NOT REPORTED

BENZALKONIUM	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 152	NOT REPORTED
UREA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 168	NOT REPORTED
ACICLOVIR	400 mg	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 243
FLUCLOXACILLIN	500 mg	QID	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 243
ACICLOVIR	400 mg	TID	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 247
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 247
FLUCLOXACILLIN	2 g	QID	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 247
GANCICLOVIR	1 OTHER: DROP BOTH EYES	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 253
FUCIDIN H	1 OTHER: APPLICATION	TID	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 254
AQUEOUS	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 243	Y-M: 20[redacted] / 284
CETIRIZINE	10 mg	PRN	Y-M: 20[redacted] / 244	NOT REPORTED
DIPROBASE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 244	NOT REPORTED
FEXOFENADINE	120 mg	QD	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 248
CHLORPHENAMINE	4 mg	TID	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 253
TERBINAFINE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 248
ACICLOVIR	400 mg	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 247	Y-M: 20[redacted] / 253
FLUCLOXACILLIN	500 mg	QID	Y-M: 20[redacted] / 247	Y-M: 20[redacted] / 253
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 339
MOMETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 253	Y-M: 20[redacted] / 284
MOMETASONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 254	NOT REPORTED
ACICLOVIR	400 mg	BID	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 340
CLOBETASOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 340	NOT REPORTED
ACICLOVIR	400 mg	BID	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 441
ACICLOVIR	400 mg	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 441	Y-M: 20[redacted] / 446
AUGMENTIN	625 mg	TID	Y-M: 20[redacted] / 441	Y-M: 20[redacted] / 448
GANCICLOVIR	1 OTHER: APPLICATION	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 442	Y-M: 20[redacted] / 449

ACICLOVIR	400 mg	BID	Y-M: 20[redacted] / 447	Y-M: 20[redacted] / 450
CAPASAL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 448	NOT REPORTED
GANCICLOVIR	1 OTHER: APPLICATION	TID	Y-M: 20[redacted] / 450	NOT REPORTED
ACICLOVIR	400 mg	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 450	Y-M: 20[redacted] / 461

Event #1: Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zosters

Event Description	ECZEMA HERPETICUM LEFT LOWER LIP AND LEFT INNER EYEBROW INVOLVEMENT
Preferred term	ヘルペス性状湿疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 238
Age at AE Onset	2[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	243
Duration of AE	6 DAYS
Toxicity Grade	2
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 - Serious Infections, Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zosters

Event Description	WORSENING OF ECZEMA HERPETICUM
Preferred term	ヘルペス性状湿疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 243
Age at AE Onset	2[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 243): Leukocytes: 6.8 [4.2 - 10.6] UNIT NOT REPORTED; Lymphocytes: 0.8 [1.1 - 3.6] UNIT NOT REPORTED; NPTST032-C-REACTIVE PROTEIN: 32.1 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 245): Leukocytes: 3.9 [4.2 - 10.6] UNIT NOT REPORTED; Neutrophils: 1.9 [2 - 7.1] UNIT NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 243): OTHER LEFT EYE SKIN SWAB NPTST047-CULTURE: POSITIVE-CULTURE STAPHYLOCOCCUS AUREUS +++ NO ANAEROBES ISOLATED. REPORT STATUS FINAL ORGANISM STAPHYLOCOCCUS AUREUS+++; [redacted]20[redacted] (RX DAY 244): WOUND NPTST159-VIRUS SCREEN - VESICLE/ULCER PCR: NEGATIVE-ND=NOT DETECTED HSV-1AND2:ND VARICELLA ZOSTER VIRUS:ND ADENOVIRUS:ND CYTOMEGALOVIRUS:ND EPSTEIN-BARR VIRUS:ND ENTEROVIRUS:ND PARECHOVIRUS:ND HHV-6:ND. NOTE: SUBOPTIMAL SAMPLE
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	254
Duration of AE	12 DAYS
Toxicity Grade	3

Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	LEFT HERPETIC CONJUNCTIVITIS
Preferred term	ヘルペス眼感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 243
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 243): WOUND NPTST088-LEFT EYE SKIN SWAB: POSITIVE-STAPHYLOCOCCUS AUREUS +++ NO ANAEROBES ISOLATED ERYTHROMYCIN SENSITIVE CLINDAMYCIN SENSITIVE FLUCLOXACILLIN SENSITIVE
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	254
Duration of AE	12 DAYS
Toxicity Grade	2
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HSV INFECTION ON A BACKGROUND OF KNOWN COLD SORES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #4: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	RIGHT HSV PERIORBITAL INFECTION
Preferred term	単純ヘルペス
AE Onset Date / Rx Day	[redacted]20[redacted] / 440
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 441): OTHER EYE SWAB NPTST099-MCS: POSITIVE-STAPHYLOCOCCUS AUREUS +++; OTHER EYE SWAB NPTST158-VIROLOGY: POSITIVE-VIRUS SCREEN - EYE SAMPLE SITE: UNKNOWN HSV-1 : DETECTED HSV-2 : NOT DETECTED VARICELLA ZOSTER VIRUS : NOT DETECTED ADENOVIRUS : NOT DETECTED ENTEROVIRUS : NOT DETECTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 442): OPTHAMOLOGY REVIEW: RE MEDIAL CORNER OF UPPER AND LOWER LID - VESICLES AND CRUSTING SIMILAR CRUSTING LONG THE LOWER LID CONJ - MILD CONGESTION - DIFFUSE CORNEA - CLEAR, NO STAIN, ANTERIOR

	CHAMBER - DEEP AND QUIETPUPIL RTL LE EXTERNALLY AND ANT SEG NAD FUNDUS EXAM: BE NAD
AE Stopped Rx Day	448
Duration of AE	9 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #5: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	PERIORBITAL (BILATERAL) FLARE OF HSV
Preferred term	単純ヘルペス
AE Onset Date / Rx Day	[redacted]20[redacted] / 450
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	453
Duration of AE	4 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者は英国の 2[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を投与され，ヘルペス性状湿疹の悪化及びヘルペス性結膜炎（左眼）を発現した。被験者は非喫煙者かつ飲酒者（2～4 杯／日）であり，関連する病歴はアトピー性皮膚炎，口唇ヘルペス，ビタミン D 低値，結節性痒疹，リンパ節症であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年[redacted] 月[redacted] 日，被験者はヘルペス性状湿疹の悪化及びヘルペス性結膜炎（左眼）を発現した。20[redacted] 年[redacted] 月[redacted] 日，ヘルペス性状湿疹の悪化及びヘルペス性結膜炎（左眼）は消失した。

本事象発現前の 20[redacted] 年[redacted] 月，被験者は Staphylococcus aureus による感染性湿疹の増悪（非重篤）を発現した。

20[redacted] 年[redacted] 月[redacted] 日，ヘルペス性小水疱の集簇及びヘルペス性状湿疹（非重篤）が左側下唇部及び左眉毛部内側に認められた。高用量アシクロビルが経口投与された。その後 48 時間にわたって症状の悪化が認められ，被験者は入院した。20[redacted] 年[redacted] 月[redacted] 日，被験者は入院し，顔面浮腫，顔全体に広がる膿痂疹性の小水疱性皮疹，両側眼瞼の腫脹，両眼の開瞼困難，両眼結膜充血及び羞明を呈していた。アシクロビル及び抗生物質が静脈内投与された。ヘルペス性結膜炎に対し眼科外用薬のガンシクロビル及び潤滑点眼薬の投与が開始された。被験者の全身的状態は良好であった。アシクロビル及び抗生物質の静脈内投与開始から 24 時間以内に，膿痂疹の打ち抜き病変，顔面浮腫，紅斑および眼瞼腫脹の消退が始まった。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。

治験責任医師は，本事象に関連するリスク因子として被験者の病歴を挙げた。被験者の申告によれば 1[redacted] 歳の時から口唇ヘルペス（単純ヘルペスウイルス 1 型）があり，直近の発現は 20[redacted] 年であった。報告された病歴にヘルペス性状湿疹はなかった。

TERBINAFINE CREAM，ガンシクロビル，FUCIDIN H OINTMENT，アシクロビル及び flucloxacillin が投与された。

The patient's past medications include:

UNGUENTUM M PARAFFIN for ATOPIC DERMATITIS (19[redacted] - [redacted] 20[redacted])

EUMOVATE CREAM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

EPADERM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

EUMOVATE OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HYDROCORTISONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FLUCLOXACILLIN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

AQUEOUS SOAP SUBSTITUTE for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

PROTOPIC for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ELIDEL for ATOPIC DERMATITIS ([redacted] 20[redacted] - 20[redacted])

HYDROXYZINE for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

CLOBETASOL PROPIONATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DERMOVATE for ATOPIC DERMATITIS and ATOPIC DERMATITIS RESCUE THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PHOTOTHERAPY for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DIPROSALIC SCALP BETAMETHASONE/SALICYLIC ACID for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CHLORPHENAMINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MOMETASONE FUROATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BACTROBAN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DIPROSALIC SCALP for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FUCIBET CREAM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FUCIDIN H OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DERMOVATE for ATOPIC DERMATITIS RESCUE THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

HYDROCORTISONE for ATOPIC DERMATITIS RESCUE THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

ELOCON for ATOPIC DERMATITIS RESCUE THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

SYNALAR for ATOPIC DERMATITIS RESCUE THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Eczema herpeticum (10014197) (Eczema herpeticum (10014197)) [v.23.1] [10014197]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, outcome unknown

2) Herpes ophthalmic (10062004) (Herpes ophthalmic (10062004)) [v.23.1] [10062004]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF ECZEMA HERPETICUM

- Investigator: Not applicable

- AbbVie: Eczema herpeticum is a disseminated viral infection characterized by fever and clusters of itchy blisters or punched-out erosions. It is most often seen as a complication of atopic dermatitis/eczema.

Event of LEFT HERPETIC CONJUNCTIVITIS

- Investigator: HSV infection on a background of known cold sores.

- AbbVie: Event is more likely related to concurrent event of eczema Herpeticum due to HSV 1 Infection.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD ANA:** Negative by CTD screen

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 32.1 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] LEFT EYE SKIN SWAB CULTURE:** Positive - culture Staphylococcus aureus +++. No anaerobes isolated. Report status final organism staphylococcus aureus+++

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.8 X10**9/L (normal 1.1 to 3.6)

[redacted] **20[redacted] NEUTROPHILS ABS:** 1.9 X10**9/L (normal 2.0 to 7.1)

[redacted] 20[redacted] **VIRUS SCREEN-VESICLE/ULCER PCR:** Negative - ND=not detected. HSV-1and 2: ND, Varicella Zoster virus: ND, Adenovirus: ND, Cytomegalovirus: ND, Epstein-Barr virus: ND, Enterovirus: ND, Parechovirus: ND, HHV-6: ND. NOTE: SUBOPTIMAL SAMPLE

[redacted] 20[redacted] **WEIGHT:** 72.7 KG

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 6.8 X10**9/L (normal 4.2 to 10.6)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.9 X10**9/L (normal 4.2 to 10.6)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者は英国の 2[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を投与され，単純ヘルペスウイルス感染による眼窩周囲炎（右眼）及び単純ヘルペスウイルスによる眼窩周囲炎再燃（両眼）を発現した。被験者は非喫煙者かつ飲酒者（2～4 杯／日）であり，関連する病歴はアトピー性皮膚炎，喘息，口唇ヘルペス，枯草熱，結節性痒疹，リンパ節症，パッチテスト陽性（塩化コバルト，IMIDAZOLODINYL UREA，DIAZOLIDINYL UREA，AMERCHOL，COCAMIDOPROPYL BETAINE，ニッケル），放射性アレルゲン吸着検査陽性（ネコ，イヌ，家塵ダニ，イネ科草本，樹木類）であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年[redacted] 月[redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年[redacted] 月[redacted] 日，被験者は単純ヘルペスウイルス感染による眼窩周囲炎（右眼）を発現した。20[redacted] 年[redacted] 月[redacted] 日，単純ヘルペスウイルス感染による眼窩周囲炎（右眼）は消失した。20[redacted] 年[redacted] 月[redacted] 日，被験者は単純ヘルペスウイルスによる眼窩周囲炎再燃（両眼）を発現した。20[redacted] 年[redacted] 月[redacted] 日，単純ヘルペスウイルスによる眼窩周囲炎再燃（両眼）は消失した。

20[redacted] 年[redacted] 月[redacted] 日，被験者から治験スタッフに，自身の症状に関して相談があった。被験者は眼窩周囲の腫脹，疼痛及び痂皮を訴えた。被験者によれば，視力の変化，眼球そのものの疼痛，眼球可動域の減少はなかった。同日に被験者は来院し，診察を受けた。被験者の病歴を考慮し，単純ヘルペスウイルス検査及び細菌検査のためスワブ検体を採取した。アシクロビルの経験的投与が開始された（事象発現前に予防投与された）。20[redacted] 年[redacted] 月[redacted] 日，眼科チームの診察が行われた。眼科チームの見解では重篤な問題はなく，ガンシクロビルの点眼が行われた。

20[redacted] 年[redacted] 月[redacted] 日，被験者は治験実施施設に連絡を取り，眼窩周囲（両眼）の単純ヘルペスウイルス再活性化の再発を訴え，アシクロビル（400 mg を 1 日 5 回，10 日間）の投与再開及び治験薬の投与中止を勧められた。20[redacted] 年[redacted] 月[redacted] 日，被験者は治験実施施設に連絡を取って患部の新しい写真を提供し，感染が解消したことを報告した。被験者は以前も治験薬中断による継続的な再燃を経験していたため，治験薬投与の再開を強く希望した。被験者は，感染解消から 48 時間経過すれば治験薬を投与再開できるかもしれない旨を指導された。アシクロビルの治療で再発したことから，治療薬は valaciclovir に変更された。

過去にも単純ヘルペスウイルスによる眼周囲症状が発現しており，20[redacted] 年[redacted] 月の入院期間中にはヘルペス性状湿疹の発現があった。

アシクロビル，ガンシクロビル，valaciclovir および CO-AMOXICLAV が投与された。

The patient's past medications include:

UNGUENTUM M PARAFFIN for ATOPIC DERMATITIS (19[redacted] - [redacted] 20[redacted])

FUCIBET for ATOPIC DERMATITIS (20[redacted] - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CETIRIZINE for HAYFEVER ([redacted] 20[redacted] - [redacted] 20[redacted])

EPADERM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

EUMOVATE OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HYDROCORTISONE CREAM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FLUCLOXACILLIN for ATOPIC DERMATITIS and ECZEMA HERPETICUM ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PROTOPIC for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ELIDEL for ATOPIC DERMATITIS ([redacted] 20[redacted] - 20[redacted])

HYDROXYZINE for ATOPIC DERMATITIS (20[redacted] - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CLOBETASOL PROPIONATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CHLORPHENAMINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

AQUEOUS CREAM for ATOPIC DERMATITIS ([redacted] 20[redacted] - 20[redacted])

DIPROSALIC SCALP BETAMETHASONE/SALICYLIC ACID for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BACTROBAN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FUCIDEN H OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) HSV infection (10063570) (Herpes simplex (10019948)) [v.23.1] [10063570]

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

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

Dechallenge: Not Applicable

2) Herpes simplex aggravated (10048418) (Herpes simplex (10019948)) [v.23.1] [10048418]

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 HSV PERIORBITAL INFECTION

- Investigator: Not applicable

- AbbVie: Event is more likely due to pre-existing HSV infection and history of cold sores. Additional risk factor is pre-existing atopic dermatitis.

Event of PERIORBITAL (BILATERAL) FLARE OF HSV

- Investigator: Not applicable

- AbbVie: Event is more likely due to pre-existing HSV infection and history of cold sores. Additional risk factor is pre-existing atopic dermatitis.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] MCS:** EYE SWAB: Positive for Staphylococcus aureus

[redacted] **20[redacted] OPHTHAMOLOGY REVIEW:** Re medial corner of upper and lower lid - vesicles and crusting similar crusting long the lower lid; CONJ - mild congestion – diffuse; Cornea - clear, no stain; Anterior Chamber - deep and quiet; pupil RTL; LE externally and ant seg NAD; Fundus exam: be NAD

[redacted] **20[redacted] VIROLOGY:** EYE SWAB: positive; HSV-1 : DETECTED HSV-2: NOT DETECTED VARICELLA ZOSTER VIRUS: NOT DETECTED ADENOVIRUS: NOT DETECTED ENTEROVIRUS: NOT DETECTED

非重篤な有害事象

ヘルペス性状湿疹：湿疹の特徴について丘疹小水疱性である（左側下唇部及び左側眉毛部内側に及ぶ）と報告され，推定罹患面積は 2%であった。臨床検査にエラーが出たため，原因は報告されなかった。原発部位ではなかった。本事象は入院を要する重症度に悪化した。治験薬の投与は中断された。

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腎盂腎炎	X	X		X

Treatment Group	Age at Study Start	Sex	Race
PLACEBO/UPA 30 MG QD	4[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
LEFT KIDNEY LARGER THAN RIGHT	19[redacted]
ANIMAL DANDER ALLERGY	19[redacted]
ATOPIC DERMATITIS	19[redacted]
DUST MITE ALLERGY	19[redacted]
HAYFEVER	19[redacted]
ASTHMA	19[redacted]
ORAL HERPES	19[redacted]
4 MOLARS REMOVED	19[redacted]
HEADACHES	19[redacted]
WARTS	19[redacted]
DEPRESSION	20[redacted]
BILATERAL ECTROPION	20[redacted]
GASTROESOPHAGEAL REFLUX	20[redacted]
5TH METACARPAL FRACTURE	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: LEFT PYELOPLASTY	19[redacted]
PRIOR PROCEDURES: LEFT PYELOPLASTY	19[redacted]
PRIOR PROCEDURES: IMMUNOTHERAPY EVERY 4 WEEKS	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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 112	112
UPA	30 MG	ORAL	QD	[redacted] / 113	[redacted] / 321	209

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	1 g	PRN	Y: 19[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	QD	Y: 20[redacted]
MOMETASONE	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
HYDROCORTISONE	2 OTHER: APPLICATIONS	OTHER: YEARLY	Y-M: 20[redacted]-[redacted]
TACROLIMUS	1 OTHER: APPLICATION	QD	Y: 20[redacted]
METHYLPREDNISOLONE	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
EPADERM	1 OTHER: APPLICATION	BID	Y: 20[redacted]
BUDESONIDE W/FORMOTEROL FUMARATE	1 OTHER: PUFF	BID	Y-M: 20[redacted]-[redacted] / -361
CETIRIZINE	10 mg	OTHER: WEEKLY	Y-M: 20[redacted]-[redacted] / -179

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	1 g	PRN	Y: 19[redacted]	ONGOING
EPADERM	1 OTHER: APPLICATION	BID	Y: 20[redacted]	ONGOING
BUDESONIDE W/FORMOTEROL FUMARATE	1 OTHER: PUFF	BID	Y-M: 20[redacted]-[redacted] / -361	ONGOING
CETIRIZINE	10 mg	OTHER: WEEKLY	Y-M: 20[redacted]-[redacted] / -179	ONGOING
HYDROCORTISONE	1 OTHER: APPLICATION	OTHER: 3 TIMES PER WEEK	Y-M: 20[redacted]-[redacted] / 195	ONGOING
TRIAMCINOLONE	1 OTHER: APPLICATION	OTHER: 3 TIMES PER WEEK	Y-M: 20[redacted]-[redacted] / 195	ONGOING
SPEKTRAMOX	875/125 mg	BID	Y-M: 20[redacted]-[redacted] / 319	Y-M: 20[redacted]-[redacted] / 320
DEXAMETHASONE	8 mg	PRN	Y-M: 20[redacted]-[redacted] / 320	Y-M: 20[redacted]-[redacted] / 320
GENTAMICIN	2 g	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 320	Y-M: 20[redacted]-[redacted] / 320
TAPENTADOL	50 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 320	Y-M: 20[redacted]-[redacted] / 320
CEFALEXIN	2 g	TID	Y-M: 20[redacted]-[redacted] / 320	Y-M: 20[redacted]-[redacted] / 321

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

Event Description	PYELONEPHRITIS LEFT
Preferred term	腎盂腎炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 318
Age at AE Onset	4[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 319): Blood Urea Nitrogen: 5.9 [3 - 8] MMOL/L; Creatinine: 78 [60 - 110] UMOL/L; Lymphocytes: 0.73 [1 - 4] 10^9/L; NPTST056-EGFR: 90 [60 - 110] UMOL/L
Microbiology	[redacted]20[redacted] (RX DAY 319): URINE NPTST153-UMCS: POSITIVE-POSITIVE FOR BLOOD +++ LEUCOCYTES >900; URINE NPTST155-URINE CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 319): CT UROGRAM: LEFT-SIDED HYDONEHPROSIS WITH CALIBRE CHANGE AT THE PUJ, WHICH MAY BE RELATED TO THE PREVIOUS PYLEOPLASTY +/- SUBACUTE OBSTRUCTION. SOME CONTRAST IN THE URETER DISTAL TO THE PUJ. NO EVIDENCE OF A RENAL STONE.; [redacted]20[redacted] (RX DAY 320): LEFT RENAL STENT: UNCOMPLICATED INSERTION OF LEFT URETERIC STENT; [redacted]20[redacted] (RX DAY 321): BLADDER BIOPSY: WITHIN NORMAL LIMITS
AE Stopped Rx Day	329 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY

Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はオーストラリアの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，腎盂腎炎（左側）を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴は腎盂形成術（左腎），腎サイズ不同（左腎が大きい），アトピー性皮膚炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腎盂腎炎（左側）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，腎盂腎炎（左側）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は排尿困難及び左側の腹痛のため，かかりつけ医を受診した。診断のため臨床検査及び他の検査が行われた。白血球数高値及び尿中亜硝酸塩が認められ，コンピュータ断層撮影検査で水腎症及び亜急性の閉塞が確認された。治験責任医師は，関連する徴候及び症状として，鋭い疼痛，赤色尿，乳白色の陰茎分泌物，疲労感及び排尿困難を報告した。被験者は閉塞による左側腎盂腎炎と診断された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左腎のステント挿入を受けるため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者は本事象を理由に試験を中止した。

デキサメタゾン，AUGMENTIN DUO，cephalexin，tapentadol 及び gentamicin が投与された。

The patient's past medications include:

CELESTONE for ATOPIC DERMATITIS (20[redacted] - [redacted] [redacted] 20[redacted])

ELOCON for ATOPIC DERMATITIS (20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

SIGMACORT for ATOPIC DERMATITIS ([redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted])

ADVANTAN FATTY OINTMENT for ATOPIC DERMATITIS ([redacted])

ADVANTAN for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

NOVASONE for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

CORTIVAL for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

TACROLIMUS for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

ELOCON LOTION for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

NOVASONE OINTMENT for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

CELESTONE CREAM for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

PROTOPIC OINTMENT for ATOPIC DERMATITIS RESCUE THERAPY and ATOPIC DERMATITIS ([redacted])

ADVANTAN for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

TRICORTONE OINTMENT for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

HYDROCORTISONE for ATOPIC DERMATITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Pyelonephritis (10037596) (Pyelonephritis (10037596)) [v.23.0] [10037596]

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 PYELONEPHRITIS LEFT

- Investigator: Not Applicable

- AbbVie: Event more likely related to sub-acute ureteral obstruction and hydronephrosis. Additional risk factor includes prior history of two pyeloplasties.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLADDER BIOPSY:** Within normal limits

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 5.9 MMOL/L (normal 3.0 to 8.0)

[redacted] **20[redacted] CREATININE:** 78 MCMOL/L (normal 60 to 110)

[redacted] **20[redacted] CT UROGRAM:** LEFT-SIDED HYDRONEHPROSIS WITH CALIBRE CHANGE AT THE PUJ, WHICH MAY BE RELATED TO THE PREVIOUS PYLEOPLASTY +/- SUBACUTE OBSTRUCTION. SOME CONTRAST IN THE URETER DISTAL TO THE PUJ. NO EVIDENCE OF A RENAL STONE.

[redacted] **20[redacted] EGFR:** >90

[redacted] **20[redacted] UMCS:** POSITIVE FOR BLOOD +++ LEUCOCYTES >900

[redacted] **20[redacted] URINE CULTURE:** Positive - Staphylococcus aureus

[redacted] **20[redacted] WHITE BLOOD CELLS:** 0.73 X10**9/L (normal 1 to 4)

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
心雑音		X		
アトピー性皮膚炎	X			
骨髄炎	X	X		X
敗血症		X		
ブドウ球菌性敗血症	X	X		X

Treatment Group	Age at Study Start	Sex	Race
PLACEBO/UPA 30 MG QD	1[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	20[redacted]
AUTISTIC SPECTRUM DISORDER (ASPERGERS)	20[redacted]
ALLERGIC RHINITIS	20[redacted]
ASTHMA	20[redacted]
INFECTED ECZEMA	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 120	120
UPA	30 MG	ORAL	QD	[redacted] / 121	[redacted] / 243	123

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
EMOLLIENTS AND PROTECTIVES	DOSE UNKNOWN OTHER: UNITS UNKNOWN	BID	Y: 20[redacted]
QV	DOSE UNKNOWN OTHER: UNITS UNKNOWN	BID	Y: 20[redacted]
BETAMETHASONE	0.02 %	BID	Y: 20[redacted]
BETAMETHASONE	0.05 %	PRN	Y: 20[redacted]
FEXOFENADINE	360 mg	BID	Y: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
CICLOSPORIN	200 mg	QD	Y: 20[redacted]
MYCOPHENOLIC ACID	1 g	BID	Y-M: 20[redacted]
SERTRALINE	100 mg	QD	Y: 20[redacted]
TACROLIMUS	4 mg	BID	Y-M: 20[redacted] / -174
CLONIDINE	50 mg	BID	Y-M: 20[redacted] / -115
RANITIDINE	150 mg	QD	Y-M: 20[redacted] / -115

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
EMOLLIENTS AND PROTECTIVES	DOSE UNKNOWN OTHER: UNITS UNKNOWN	BID	Y: 20[redacted]	ONGOING
QV	DOSE UNKNOWN OTHER: UNITS UNKNOWN	BID	Y: 20[redacted]	ONGOING
FEXOFENADINE	360 mg	BID	Y: 20[redacted]	Y-M: 20[redacted] / 251
SERTRALINE	100 mg	QD	Y: 20[redacted]	ONGOING
CLONIDINE	50 mg	BID	Y-M: 20[redacted] / -115	ONGOING
RANITIDINE	150 mg	QD	Y-M: 20[redacted] / -115	Y-M: 20[redacted] / 251
GUANFACINE	1 mg	QD	Y-M: 20[redacted] / 9	ONGOING
TEMAZEPAM	10 mg	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 134

ALIMEMAZINE	50 mg	PRN	Y-M: 20[redacted]-[redacted] / 14 Y-M: 20[redacted]-[redacted] / 147
COAL TAR	1 %	BID	Y-M: 20[redacted]-[redacted] / 22 ONGOING
BETAMETHASONE	0.02 %	BID	Y-M: 20[redacted]-[redacted] / 30 ONGOING
BETAMETHASONE	0.05 %	BID	Y-M: 20[redacted]-[redacted] / 30 ONGOING
CEFALEXIN	500 mg	BID	Y-M: 20[redacted]-[redacted] / 43 Y-M: 20[redacted]-[redacted] / 64
LORATADINE	20 mg	PRN	Y-M: 20[redacted]-[redacted] / 57 ONGOING
MUPIROCIN	2 %	BID	Y-M: 20[redacted]-[redacted] / 57 Y-M: 20[redacted]-[redacted] / 251
FLUCLOXACILLIN	500 mg	QID	Y-M: 20[redacted]-[redacted] / 69 Y-M: 20[redacted]-[redacted] / 73
BETAMETHASONE	UNKNOWN- GIVEN IN HOSPITAL (SAE 30061002007) OTHER: UNKNOWN- GIVEN IN HOSPITAL (SAE 30061002007)	OTHER: UNKNOWN- GIVEN IN HOSPITAL (SAE 30061002007)	Y-M: 20[redacted]-[redacted] / 69 Y-M: 20[redacted]-[redacted] / 75
FLUCLOXACILLIN	250 mg	QID	Y-M: 20[redacted]-[redacted] / 74 Y-M: 20[redacted]-[redacted] / 78
CEFALEXIN	500 mg	BID	Y-M: 20[redacted]-[redacted] / 216 Y-M: 20[redacted]-[redacted] / 220
CEFAZOLIN			Y-M: 20[redacted]-[redacted] / 242 ONGOING
FLUCLOXACILLIN			Y-M: 20[redacted]-[redacted] / 242 ONGOING
CEFTRIAXONE	2 g	OTHER: STAT	Y-M: 20[redacted]-[redacted] / 244 ONGOING
CLINDAMYCIN	600 mg	OTHER: STAT	Y-M: 20[redacted]-[redacted] / 244 ONGOING
VANCOMYCIN	2 g	OTHER: STAT	Y-M: 20[redacted]-[redacted] / 244 ONGOING
MEROPENEM			Y-M: 20[redacted]-[redacted] / 260 ONGOING
CIPROFLOXACIN	750 mg	BID	Y-M: 20[redacted]-[redacted] / 267 ONGOING
CLINDAMYCIN	450 mg	TID	Y-M: 20[redacted]-[redacted] / 267 ONGOING
GABAPENTIN	300 mg	PRN	Y-M: 20[redacted]-[redacted] / 270 ONGOING
OXYCODONE	5 mg	PRN	Y-M: 20[redacted]-[redacted] / 270 ONGOING
PARACETAMOL	1 g	QID	Y-M: 20[redacted]-[redacted] / 270 ONGOING

Event #1: Serious Adverse Event

Event Description	HOSPITALISATION DUE TO EXACERBATION OF ATOPIC DERMATITIS
Preferred term	アトピー性皮膚炎

AE Onset Date / Rx Day	[redacted]20[redacted] / 68
Age at AE Onset	1[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	75
Duration of AE	8 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	EXACCERBATION OF PRE-EXISTING SEVERE ATOPIC DERMATITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: AE Leading to Discontinuation of Study Drug

Event Description	SYSTOLIC FLOW MURMUR (RELATED TO SEPSIS)
Preferred term	心雑音
AE Onset Date / Rx Day	[redacted]20[redacted] / 242
Age at AE Onset	1[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	246 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Toxicity Grade	1
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections

Event Description	MULTIFOCAL OSTEOMYELITIS
Preferred term	骨髄炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 242
Age at AE Onset	1[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 242): Alanine Aminotransferase: 25 [NOT REPORTED - NOT REPORTED] U/L; Albumin: 23 [NOT REPORTED - NOT REPORTED] g/L; Alkaline Phosphatase: 123 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 41 [NOT REPORTED - NOT REPORTED] U/L; Bicarbonate: 22 [NOT REPORTED - NOT REPORTED] mmol/L; Bilirubin: 10 [NOT REPORTED - NOT REPORTED] umol/L; Calcium: 2.23 [NOT REPORTED - NOT REPORTED] mmol/L; Chloride: 90 [NOT REPORTED - NOT REPORTED] mmol/L; Creatinine: 51 [NOT REPORTED - NOT REPORTED] umol/L; Glucose: 5.9 [NOT REPORTED - NOT REPORTED] mmol/L; Hemoglobin: 85 [NOT REPORTED - NOT REPORTED] g/L; Leukocytes: 5.9 [NOT REPORTED - NOT REPORTED] 10^9/L; NPTST030-C REACTIVE PROTEIN: 314.9 [NOT REPORTED - NOT REPORTED] mg/L; NPTST062-GAMMA GT: 24 [NOT REPORTED - NOT REPORTED] U/L; NPTST096-MAGNESIUM: 1.00 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST121-PHOSPHATE: 1.10 [NOT REPORTED - NOT REPORTED] mmol/L; Platelets: 160 [NOT REPORTED - NOT REPORTED] 10^9/L; Potassium: 2.8 [3.5 - 4.5] MMOL/L; Protein: 67 [NOT

	REPORTED - NOT REPORTED] g/L; Sodium: 134 [NOT REPORTED - NOT REPORTED] mmol/L; Urate: 6.6 [NOT REPORTED - NOT REPORTED] mmol/L; [redacted]20[redacted] (RX DAY 270): Leukocytes: 7.58 [NOT REPORTED - NOT REPORTED] 10^9/L; Neutrophils: 5.00 [NOT REPORTED - NOT REPORTED] 10^9/L
Microbiology	[redacted]20[redacted] (RX DAY 242): WOUND NPTST047-CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS ISOLATED; BLOOD NPTST050-CULTURES: POSITIVE-MRSA; URINE NPTST155-URINE CULTURE: POSITIVE-MRSA; [redacted]20[redacted] (RX DAY 245): OTHER MCS NPTST089-LEFT HIP MCS: POSITIVE-MRSA
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 237): HEART RATE: 104 BPM; SPO2: 100%; TEMPERATURE (TYMPANIC): 38.1 CELCIUS; [redacted]20[redacted] (RX DAY 243): CHEST XRAY: NORMAL; DRAINAGE OF RIGHT HIP: FRANK PUS FROM JOINT +++. VOLUME UNKNOWN; INSERTION OF PERIPHERALLY INSERTED CENTRAL CATHETER LINE: PROCEDURE WELL TOLERATED.; TEMPERATURE: 39.2 CELSIUS; [redacted]20[redacted] (RX DAY 245): LEFT HIP ASPIRATE AND BILATERAL HIP WASHOUT: LEFT HIP MCS: MRSA; MRI RIGHT HIP: RIGHT HIP JOINT EFFUSION. OSTOMYOLITIC CHANGES IN RIGHT ILIUM AND ACETABULUM, COLLECTION DEEP TO GLUTEUS MINIMUS AND OBTURATOR INTERNUS; [redacted]20[redacted] (RX DAY 246): TRANSTHORACIC ECHOCARDIOGRAM: GRADE 1-2 VIBRATORY END-SYSTOLIC MURMUR AT LOWER LEFT STERNAL EDGE WITH NIL RADIATION. NO EVIDENCE OF INFECTIVE ENDOCARDITIS; [redacted]20[redacted] (RX DAY 257): BONE SCAN: INVOLVEMENT OF RIGHT ELBOW, DISTAL RIGHT RADIUS, RIGHT TARSAL REGION, PREVIOUS AREAS STILL INVOLVED (RIGHT HIP, RIGHT SIJ, DISTAL RIGHT FEMUR, DISTAL LEFT TIBIA); [redacted]20[redacted] (RX DAY 261): WASHOUT RIGHT HIP: MCS: SCANTY GROWTH ESBL; [redacted]20[redacted] (RX DAY 262): TRANSTHORACIC ECHOCARDIOGRAM: NO EVIDENCE OF INFECTIVE ENDOCARDITIS
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	3
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	IMPACT INJURY TO RIGHT HIP FOLLOWING A FALL
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #4: AE Leading to Discontinuation of Study Drug

Event Description	SYSTOLIC FLOW MURMUR (RELATED TO SEPSIS)
Preferred term	敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 242
Age at AE Onset	1[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	246 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Toxicity Grade	1
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE

Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #5: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections

Event Description	MRSA SEPSIS
Preferred term	ブドウ球菌性敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 242
Age at AE Onset	1[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 242): Alanine Aminotransferase: 25 [NOT REPORTED - NOT REPORTED] U/L; Albumin: 23 [NOT REPORTED - NOT REPORTED] g/L; Alkaline Phosphatase: 123 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 41 [NOT REPORTED - NOT REPORTED] U/L; Bicarbonate: 22 [NOT REPORTED - NOT REPORTED] mmol/L; Bilirubin: 10 [NOT REPORTED - NOT REPORTED] umol/L; Calcium: 2.23 [NOT REPORTED - NOT REPORTED] mmol/L; Chloride: 90 [NOT REPORTED - NOT REPORTED] mmol/L; Creatinine: 51 [NOT REPORTED - NOT REPORTED] umol/L; Glucose: 5.9 [NOT REPORTED - NOT REPORTED] mmol/L; Hemoglobin: 85 [NOT REPORTED - NOT REPORTED] g/L; Leukocytes: 5.9 [NOT REPORTED - NOT REPORTED] 10^9/L; NPTST030-C REACTIVE PROTEIN: 314.9 [NOT REPORTED - NOT REPORTED] mg/L; NPTST062-GAMMA GT: 24 [NOT REPORTED - NOT REPORTED] U/L; NPTST096-MAGNESIUM: 1.00 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST121-PHOSPHATE: 1.10 [NOT REPORTED - NOT REPORTED] mmol/L; Platelets: 160 [NOT REPORTED - NOT REPORTED] 10^9/L; Potassium: 2.8 [3.5 - 4.5] MMOL/L; Protein: 67 [NOT REPORTED - NOT REPORTED] g/L; Sodium: 134 [NOT REPORTED - NOT REPORTED] mmol/L; Urate: 6.6 [NOT REPORTED - NOT REPORTED] mmol/L; [redacted]20[redacted] (RX DAY 270): Leukocytes: 7.58 [NOT REPORTED - NOT REPORTED] 10^9/L; Neutrophils: 5.00 [NOT REPORTED - NOT REPORTED] 10^9/L
Microbiology	[redacted]20[redacted] (RX DAY 242): WOUND NPTST047-CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS ISOLATED; BLOOD NPTST050-CULTURES: POSITIVE-MRSA; URINE NPTST155-URINE CULTURE: POSITIVE-MRSA; [redacted]20[redacted] (RX DAY 245): OTHER MCS NPTST089-LEFT HIP MCS: POSITIVE-MRSA
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 237): HEART RATE: 104 BPM; SPO2: 100%; TEMPERATURE (TYMPANIC): 38.1 CELCIUS; [redacted]20[redacted] (RX DAY 243): CHEST XRAY: NORMAL; DRAINAGE OF RIGHT HIP: FRANK PUS FROM JOINT +++. VOLUME UNKNOWN; INSERTION OF PERIPHERALLY INSERTED CENTRAL CATHETER LINE: PROCEDURE WELL TOLERATED.; TEMPERATURE: 39.2 CELSIUS; [redacted]20[redacted] (RX DAY 245): LEFT HIP ASPIRATE AND BILATERAL HIP WASHOUT: LEFT HIP MCS: MRSA; MRI RIGHT HIP: RIGHT HIP JOINT EFFUSION. OSTOMYOLITIC CHANGES IN RIGHT ILIUM AND ACETABULUM. COLLECTION DEEP TO GLUTEUS MINIMUS AND OBTURATOR INTERNUS; [redacted]20[redacted] (RX DAY 246): TRANSTHORACIC ECHOCARDIOGRAM: GRADE 1-2 VIBRATORY END-SYSTOLIC MURMUR AT LOWER LEFT STERNAL EDGE WITH NIL RADIATION. NO EVIDENCE OF INFECTIVE ENDOCARDITIS; [redacted]20[redacted] (RX DAY 257): BONE SCAN: INVOLVEMENT OF RIGHT ELBOW, DISTAL RIGHT RADIUS, RIGHT TARSAL REGION, PREVIOUS AREAS STILL INVOLVED (RIGHT HIP, RIGHT SIJ, DISTAL RIGHT FEMUR, DISTAL LEFT TIBIA); [redacted]20[redacted] (RX DAY 261): WASHOUT RIGHT HIP: MCS: SCANTY GROWTH ESBL; [redacted]20[redacted] (RX DAY 262): TRANSTHORACIC ECHOCARDIOGRAM: NO EVIDENCE OF INFECTIVE ENDOCARDITIS
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY

Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, IS LIFE THREATENING

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はオーストラリアの 1[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を投与され，入院に至るアトピー性皮膚炎増悪を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎，自閉症スペクトラム症（アスペルガー障害），アレルギー性鼻炎及び喘息であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院に至るアトピー性皮膚炎増悪を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，入院に至るアトピー性皮膚炎増悪は消失した。

入院前の関連情報として，被験者は本試験に組み入れられる際，治験実施計画書に従い前治療薬をウォッシュアウトした。被験者の湿疹（アトピー性皮膚炎増悪［非重篤］）はすぐに悪化し始め，11 週間悪化が続き，入院を要するまでに感染性湿疹（非重篤）を 3 回発現した。20[redacted] 年 [redacted] 月，副腎皮質ホルモンの外用薬が投与再開された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はほぼ全身に及ぶ湿疹のフレア（アトピー性皮膚炎）を理由に入院した。滲出性病変であり，登校などの活動が障害されていた。その他の症状として，そう痒の増強，疼痛及び頭部ふらふら感があった。不快感及び感染リスクがあったため，ウェットドレッシング療法を毎日行えるよう，治験責任医師は入院を勧めた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

flucloxacillin，DIPROSONE CREAM 及びスルファメトキサゾール・トリメトプリムが投与された。

The patient's past medications include:

AZATHIOPRINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CYCLOSPORIN for ATOPIC DERMATITIS (20[redacted] - [redacted]0[redacted])

MYCOPHENOLATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CEPHALEXIN for INFECTED ECZEMA ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Dermatitis atopic aggravated (10012439) (Dermatitis atopic (10012438)) [v.23.0] [10012439]

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 HOSPITALIZATION DUE TO EXACERBATION OF ATOPIC DERMATITIS

- Investigator: EXACCERBATION OF PRE-EXISTING SEVERE ATOPIC DERMATITIS

- AbbVie: Event is more likely related to pre-existing atopic dermatitis.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はオーストラリアの 1[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を投与され，メチシリン耐性黄色ブドウ球菌性敗血症（以下「MRSA 敗血症」）及び多発性骨髄炎を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎，自閉症スペクトラム症（アスペルガー障害），アレルギー性鼻炎及び喘息であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は MRSA 敗血症及び多発性骨髄炎を発現した。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加し，2[redacted]9 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は階段から転落して右股関節部を激しく打ち付けた。被験者は数日間，股関節部に疼痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は擦過傷を伴う右股関節部の疼痛及び腫脹が増強していることを自覚し，化膿した右股関節のドレナージを受けるため入院となっ

た。関節から膿を除去した（量は不明）。その後，主診断名は MRSA 敗血症及び化膿性関節炎とつけられた。右足の遠位趾節間関節及び近位趾節間関節にも腫脹が認められた。血液培養検査の結果はメチシリン耐性黄色ブドウ球菌（以下「MRSA」）陽性であり，尿検査所見はブドウ球菌陽性，血尿，蛋白尿，ケトン体陽性であった。心雑音が新規に確認され，被験者は厳密な体液バランス管理下におかれた。20[redacted] 年 [redacted] 月 [redacted] 日，末梢留置型中心静脈注射用カテーテルが挿入され，処置の忍容性は良好であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左股関節の穿刺及び両股関節部の洗浄を受けた。左股関節は MRSA 陽性であった。20[redacted] 年 [redacted] 月 [redacted] 日，右股関節に基質拡張型 β-ラクタマーゼ産生菌のわずかな増殖が確認され，右股関節部は再度洗浄された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者は本試験を中止した。

vancomycin，ceftriaxone，clindamycin，シプロフロキサシン，meropenem，oxycodone，ガバペンチン，paracetamol，CEPHAZOLIN 及び flucloxacillin が投与された。

The patient's past medications include:

AZATHIOPRINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CYCLOSPORIN for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

MYCOPHENOLATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TEMAZEPAM for ITCH DUE TO ATOPIC DERMATITIS and ITCH DUE TO ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VALLERGAN for ITCHING DUE TO ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Sepsis MRSA (10049253) (Staphylococcal sepsis (10056430)) [v.23.0] [10049253]

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

Causality as per Mfr. (Drug/Vaccine): Reasonablepossibility

Dechallenge: No

2) Osteomyelitis (10031252) (Osteomyelitis (10031252)) [v.23.0] [10031252]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of MRSA SEPSIS

- Investigator: Not Applicable

- AbbVie: Not Applicable

Event of MULTIFOCAL OSTEOMYELITIS

- Investigator: Impact injury to right hip following a fall.

- AbbVie: Not Applicable

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Company Remarks

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 25 U/L

[redacted] **20[redacted] ALBUMIN:** 23 G/L

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 123 U/L

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 41 U/L

[redacted] **20[redacted] BICARBONATE:** 22 MMOL/L

[redacted] **20[redacted] BILIRUBIN:** 10 MCMOL/L

[redacted] **20[redacted] BLOOD CULTURES:** Positive for MRSA.

[redacted] **20[redacted] BONE SCAN:** INVOLVEMENT OF RIGHT ELBOW, DISTAL RIGHT RADIUS, RIGHT TARSAL REGION, PREVIOUS AREAS STILL INVOLVED (RIGHT HIP, RIGHT SIJ, DISTAL RIGHT

FEMUR, DISTAL LEFT TIBIA)

[redacted] **20[redacted] CALCIUM:** 2.23 MMOL/L

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

[redacted] **20[redacted] CHLORIDE:** 90 MMOL/L

[redacted] **20[redacted] CREATININE:** 51 umol/L

[redacted] **20[redacted] CRP:** 314.9 MG/L

[redacted] **20[redacted] GAMMA GT:** 24 U/L

[redacted] **20[redacted] GLUCOSE:** 5.9 MMOL/L

[redacted] **20[redacted] HEMOGLOBIN:** 85 G/L

[redacted] **20[redacted] MAGNESIUM:** 1.00 MMOL/L

[redacted] **20[redacted] MRI RIGHT HIP:** RIGHT HIP JOINT EFFUSION. OSTOMYOLITIC CHANGES IN RIGHT ILIUM AND ACETABULUM, COLLECTION DEEP TO GLUTEUS MINIMUS AND OBTURATOR INTERNUS

[redacted] **20[redacted] PHOSPHATE:** 1.10 MMOL/L

[redacted] **20[redacted] PLATELET COUNT:** 160 X10**9/L

[redacted] **20[redacted] POTASSIUM:** 2.8 MMOL/L

[redacted] **20[redacted] PROTEIN:** 67 G/L

[redacted] **20[redacted] SODIUM:** 134 MMOL/L

[redacted] **20[redacted] TRANSTHORACIC ECHOCARDIOGRAM:** GRADE 1-2 VIBRATORY END-SYSTOLIC MURMUR AT LOWER LEFT STERNAL EDGE WITH NIL RADIATION. NO EVIDENCE OF INFECTIVE ENDOCARDITIS

[redacted] **20[redacted] TRANSTHORACIC ECHOCARDIOGRAM:** NO EVIDENCE OF INFECTIVE ENDOCARDITIS

[redacted] **20[redacted] URIC ACID:** 6.6 MMOL/L

[redacted] **20[redacted] URINE CULTURE:** Positive for MRSA

[redacted] **20[redacted] URINE TEST:** Hematuria, proteinuria and ketones.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.9 X10**9/L

[redacted] **20[redacted] WOUND CULTURE:** Positive: staphylococcus aureus isolated

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
咽頭膿瘍	X	X		X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD	3[redacted]	FEMALE	ASIAN

Medical History	Onset Year
RETINITIS PIGMENTOSA	19[redacted]
ALLERGIC RHINITIS	19[redacted]
ATOPIC DERMATITIS	19[redacted]
ASTHMA	19[redacted]
GESTATIONAL HYPOTHYROIDISM	20[redacted]
RECURRENT TORTICOLLIS	20[redacted]
REPETITIVE TONSILLITIS	20[redacted]
NEURALGIA LEFT ARM SECONDARY TO VERTEBRAL COLLAPSE	20[redacted]
VERTEBRAL COLLAPSE	20[redacted]
DEPRESSION	20[redacted]
ACNE	20[redacted]
ATOPIC DERMATITIS	20[redacted]
LATENTE TUBERCULOSIS	20[redacted]
LOW BACK PAIN	20[redacted]
LUMBAR SPRAIN	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED
LATENT TUBERCULOSIS	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: RETINAL IMPLANT	20[redacted]
PRIOR PROCEDURES: TONSILLECTOMY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.14 CIGARETTE	0.2	20[redacted]
CIGARS	FORMER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 1 1	[redacted]0[redacted] / 30	30

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
SERETIDE	1 OTHER: INHALATION	BID	Y: 20[redacted]
LEVONORGESTREL	1 OTHER: DEVICE	OTHER: CONTINUOUS	Y-M: 20[redacted]-[redacted]
CORTICOSTEROIDS	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
VENLAFAXINE	150 mg	QD	Y-M: 20[redacted]-[redacted]
CYCLOBENZAPRINE	10 mg	PRN	Y: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]-[redacted]
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	QD	Y: 20[redacted]
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]-[redacted]
SHAMPOOS	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / -222
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted]-[redacted] / -102
ESOMEPRAZOLE W/NAPROXEN	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted] / -71
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted] / -34
ISONIAZID	300 mg	QD	Y-M: 20[redacted]-[redacted] / -26
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / -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 / RX Day	Stop Year-Month / RX Day
SERETIDE	1 OTHER: INHALATION	BID	Y: 20[redacted]	ONGOING
LEVONORGESTREL	1 OTHER: DEVICE	OTHER: CONTINUOUS	Y-M: 20[redacted]-[redacted]	ONGOING
VENLAFAXINE	150 mg	QD	Y-M: 20[redacted]-[redacted]	ONGOING
CYCLOBENZAPRINE	10 mg	PRN	Y: 20[redacted]	ONGOING
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]-[redacted]	ONGOING
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]-[redacted]	Y-M: 20[redacted]-[redacted] / 31
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted]-[redacted] / -102	ONGOING
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted] / -34	ONGOING
ISONIAZID	300 mg	QD	Y-M: 20[redacted]-[redacted] / -26	ONGOING

EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
PARACETAMOL	2 OTHER: TABLET	TID	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 12
CLINDAMYCIN	450 mg	QID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 30
DEXAMETHASONE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 30
DEXAMETHASONE	4 mg	TID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 31
PIP/TAZO	UNK OTHER: UNK	OTHER: UNK	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 37
SERETIDE	1 OTHER: INHALATION	BID	Y-M: 20[redacted] / 32	ONGOING
PROPOFOL	20 OTHER: CC	OTHER: PER HOUR	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 35
FENTANYL	150 ug	OTHER: HOUR	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 36
DEXAMETHASONE	4 mg	TID	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 39
DALTEPARIN	5000 OTHER: UNIT	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 46
PROPOFOL	22 OTHER: CC	OTHER: PER HOUR	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 36
FENTANYL	50 ug	OTHER: HOUR	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 37
PROPOFOL	30 OTHER: CC	OTHER: HOUR	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 37
BENZYLPENICILLIN	4 OTHER: M UNIT	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 51
CLINDAMYCIN	900 mg	TID	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 51
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / 38	ONGOING
NAPROXEN	500 mg	BID	Y-M: 20[redacted] / 38	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 39	ONGOING
CLINDAMYCIN	UNK OTHER: UNK	OTHER: UNK	Y-M: 20[redacted] / 51	ONGOING

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

Event Description	RETROPHARYNGEAL ABSCESS
Preferred term	咽頭膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 27
Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 30): Leukocytes: 23.2 [4.5 - 11] 10^9/L; NPTST046-CRP: 246 [0 - 10] MG/L
Microbiology	[redacted]20[redacted] (RX DAY 29): OTHER THROAT CULTURE NPTST144-THROAT CULTURE: POSITIVE-STREPTOCOCCUS GROUP A

SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 30): CT-SCAN: 6 CM X 1.3 CM ABSCESS; [redacted]20[redacted] (RX DAY 31): ABSCESS DRAINED: DRAINED FAILED; [redacted]20[redacted] (RX DAY 33): ABSCESS DRAINED UNDER GENERAL ANESTHESIA: DRAINED FAILED; CT-SCAN: 30 MM X 22 MM X 14 MM ABSCESS WITH CONTACT WITH THE LEFT CAROTID ARTERY WHOSE CALIBER IS DECREASED; TRACHEAL INTUBATION: [redacted] 20[redacted] TO [redacted] 20[redacted]; [redacted]20[redacted] (RX DAY 35): CT-SCAN: 26MM X 13MM X 9MM ABSCESS; [redacted]20[redacted] (RX DAY 37): CT-SCAN: RESULT PENDING; [redacted]20[redacted] (RX DAY 41): CT-SCAN: 21MM X 14MM X 9MM ABSCESS; [redacted]20[redacted] (RX DAY 45): CT-SCAN: 17MM X 12MM X 4MM ABSCESS; [redacted]20[redacted] (RX DAY 51): CT SCAN: SLIGHT INCREASING OF THE SIZE OF THE ABCESS; [redacted]20[redacted] (RX DAY 64): CT SCAN: COMPLETE RESOLUTION OF RETROPHARYNGEAL ABCESS
AE Stopped Rx Day	64 (34 DAYS AFTER LAST TREATMENT)
Duration of AE	38 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はカナダの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，咽後膿瘍を発現した。被験者は元喫煙者（紙巻タバコ 0.14 本／日，0.2 年間），元葉巻喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアレルギー性鼻炎，喘息，再発性扁桃炎，うつ病及びアトピー性皮膚炎であった。扁桃摘出による治療歴があった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は咽後膿瘍を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，咽後膿瘍は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者には微熱及び左顎の疼痛があった。被験者は抗生物質を投与され，耳鼻咽喉科に紹介された。耳鼻咽喉科を受診後，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は咽後膿瘍を理由に入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は抗生物質に反応せず，膿瘍ドレナージを受けたが改善が得られなかった。皮下組織の浮腫が始まり，被験者は集中治療室に入室した。同時期の 20[redacted] 年 [redacted] 月 [redacted] 日～20[redacted] 年 [redacted] 月 [redacted] 日，被験者は気管挿管を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は抗生物質の処方を受け，退院した。

治験責任医師は，リスク因子として A 群レンサ球菌に繰り返し感染していたことを挙げた。

本事象を理由に治験薬の投与は中止された。
clindamycin，ADVAIR，TAZOCIN，PENICILLIN G 及び DECADRON が投与された。

Causality for UPADACITINIB (Blinded)

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1) Retropharyngeal abscess (10038984) (Pharyngeal abscess (10067781)) [v.23.0] [10038984]

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

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

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of RETROPHARYNGEAL ABSCESS

- Investigator: Not applicable

- AbbVie: Risk factor includes past history of tonsillectomy which has a hazard ratio of 1.87 in adolescents and adults. Pre-existing history of repetitive tonsillitis is an additional risk factor.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **CRP:** 246 MG/L (normal 0 to 10)

[redacted] **CT SCAN:** 6cm x 1.3 cm abscess

[redacted] **CT SCAN:** 30mm x 22 mm x 14 abscess with contact with the left carotid artery where caliber is decreased

[redacted] **CT SCAN:** 26MM X 13MM X 9MM ABSCESS

[redacted] **CT SCAN:** 21MM X 14MM X 9MM ABSCESS

[redacted] **CT SCAN:** 17MM X 12MM X 4MM ABSCESS

[redacted] **20[redacted] CT SCAN:** Slight increasing of the size of the abcess

[redacted] **20[redacted] CT SCAN:** Complete resolution of retropharyngeal Abcess

[redacted] **20[redacted] THROAT CULTURE:** Positive, Group A streptococcus

[redacted] **20[redacted] WHITE BLOOD CELLS:** 23.2 X10**9/L (normal 4.5 to 11.0)

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腎盂腎炎	X			X

Treatment Group	Age at Study Start	Sex	Race
PLACEBO/UPA 30 MG QD	1[redacted]	FEMALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	20[redacted]
DISLOCATED RIGHT ARM	20
MILD SITUATIONAL DEPRESSION	20
ACNE VULGARIS	20
SEASONAL ALLERGIES	20
TENSION HEADACHE	20
UPPER RESPIRATORY TRACT INFECTION	20

Prior Procedures	Procedure Year
Not reported.	

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 112	112
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 113		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
PETROLATUM	1 OTHER: APPLICATION	BID	Y: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y: 20[redacted]
TACROLIMUS	1 OTHER: APPLICATION	PRN	Y: 20[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]-[redacted]
PARACETAMOL	1000 mg	PRN	Y: 20[redacted]
PARACETAMOL	1 OTHER: TABLET	PRN	Y-M: 20[redacted]-[redacted] / -17

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	1000 mg	PRN	Y: 20[redacted]	NOT REPORTED
OTHER EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]-[redacted] / 70	NOT REPORTED
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]-[redacted] / 164	Y-M: 20[redacted]-[redacted] / 166
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted]-[redacted] / 177	Y-M: 20[redacted]-[redacted] / 177
CEFTRIAXONE	2 g	OTHER: Q8H	Y-M: 20[redacted]-[redacted] / 178	Y-M: 20[redacted]-[redacted] / 180
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted]-[redacted] / 179	Y-M: 20[redacted]-[redacted] / 180
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted]-[redacted] / 181	Y-M: 20[redacted]-[redacted] / 191

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

Event Description	PYELONEPHRITIS
Preferred term	腎盂腎炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 176
Age at AE Onset	1[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 177): Leukocytes: 9.2 [3.9 - 10.2] 10^9/L; Lymphocytes: 0.5 [1 - 3.6] 10^9/L; Neutrophils: 8.4 [1.8 - 6.8] 10^9/L; [redacted]20[redacted] (RX DAY 178): Blood: GRAM (-) E COLI [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 181): ABDOMINAL ULTRASOUND: NORMAL
AE Stopped Rx Day	181
Duration of AE	6 DAYS
Toxicity Grade	3

Relation to Study Drug by Investigator REASONABLE POSSIBILITY
Investigator Alternative Etiology NOT REPORTED
Discontinued Study Drug Due to the Event NO
SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はカナダの 1[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬を投与され，腎盂腎炎を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腎盂腎炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，腎盂腎炎は消失した。

本事象発現に先行して，被験者は 20[redacted] 年 [redacted] 月に尿路感染（非重篤）を発現し，20[redacted] 年 [redacted] 月に発熱（非重篤）を自覚した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は側腹部痛及び発熱を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は症状悪化を理由に救急治療室を受診した。被験者は抗生物質の単回投与及び血液検査を受けた後，帰宅した。20[redacted] 年 [redacted] 月 [redacted] 日，臨床検査の結果から腎盂腎炎と診断された。同日，被験者は入院し，抗生物質が静脈内投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

TYLENOL ES 及び ceftriaxone が投与された。

Causality for UPADACITINIB (Blinded)

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1) Pyelonephritis (10037596) (Pyelonephritis (10037596)) [v.22.1] [10037596]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of PYELONEPHRITIS

- Investigator: Not applicable

- AbbVie: Not applicable

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Company Remarks

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] ABDOMINAL ULTRASOUND: Normal

[redacted] 20[redacted] ABSOLUTE LYMPHOCYTES: 0.5 X10**9/L (normal 1.0 to 3.6)

[redacted] 20[redacted] ABSOLUTE NEUTROPHILS: 8.4 X10**9/L (normal 1.8 to 6.8)

[redacted] 20[redacted] BLOOD TEST: Gram (-) E. Coli

[redacted] 20[redacted] LABORATORY TESTS: Pyelonephritis

[redacted] 20[redacted] WBC: 9.5 X10**9/L (normal 3.9 to 10.2)

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
脂肪肝				X
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD/UPA 30 MG QD	3[redacted]	MALE	ASIAN

Medical History	Onset Year
ASTHMA	19[redacted]
ATOPIC DERMATITIS	20[redacted]
ATOPIC DERMATITIS	20[redacted]
HEPATIC HEMANGIOMA	20[redacted]
LATENT TB	20[redacted]
ASTHMA	NOT REPORTED
LATENT TUBERCULOSIS	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 114	114
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 115		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CAMPHOR	APPROPRIATE OTHER: NA	TID	Y-M: 20[redacted] / -59
CEFTRIAXONE	3 g	QD	Y-M: 20[redacted] / -59
DEXAMETHASONE	APPROPRIATE OTHER: NA	BID	Y-M: 20[redacted] / -59
EBASTINE	10 mg	QD	Y-M: 20[redacted] / -59
GLYCYRRHIZA GLABRA	80 mg	QD	Y-M: 20[redacted] / -59
LORATADINE	10 mg	QD	Y-M: 20[redacted] / -59
OLOPATADINE	5 mg	OTHER: QN	Y-M: 20[redacted] / -59
PINUS SYLVESTRIS	APPROPRIATE OTHER: NA	OTHER: INTERMITTENT	Y-M: 20[redacted] / -59
TACROLIMUS	APPROPRIATE OTHER: NA	OTHER: QN	Y-M: 20[redacted] / -59
TOPSYNE NEOMYCINE	APPROPRIATE OTHER: NA	QD	Y-M: 20[redacted] / -59
EMOLLIENTS AND PROTECTIVES	APPROPRIATE OTHER: NA	BID	Y-M: 20[redacted] / -27
ISONIAZID	0.2 g	QD	Y-M: 20[redacted] / -15

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
EMOLLIENTS AND PROTECTIVES	APPROPRIATE OTHER: NA	BID	Y-M: 20[redacted] / -27	NOT REPORTED
ISONIAZID	0.2 g	QD	Y-M: 20[redacted] / -15	Y-M: 20[redacted] / 171
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1.4 g	TID	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 159
AMOXICILLIN	0.5 g	TID	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 167
FAGOPYRUM ESCULENTUM	1.65 g	TID	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 167
CEFTAZIDIME	1 g	OTHER: ST	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 160
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	0.7 g	TID	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 168
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1.5 g	TID	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 168
AMBROXOL	30 mg	QD	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 167
BUDESONIDE	4 mL	QD	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 167
CEFTAZIDIME	4 g	QD	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 167
LEVOFLOXACIN LACTATE AND SODIUM CHLORIDE	0.5 g	QD	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 167
RIBAVIRIN	0.8 g	QD	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 167

UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	12 g	TID	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 168
DEXAMETHASONE	10 mg	QD	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 164
DOXOFYLLINE	0.3 g	QD	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 164
MINOXIDIL	0.5 mL	BID	Y-M: 20[redacted] / 365	NOT REPORTED

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 157
Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 158): Leukocytes: 8.1 [3.5 - 9.5] 10^9/L; Neutrophils/Leukocytes: 76.37 [40 - 75] %
Microbiology	[redacted]20[redacted] (RX DAY 158): OTHER THROAT SWAB NPTST116-NOVEL CORONAVIRUS NUCLEIC ACID TESTING: NEGATIVE
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 158): CHEST CT: 1.RIGHT LOWER PULMONARY NODULES, REGULAR REEXAMINATION IS RECOMMENDED 2.RIGHT MIDDLE LOBE BRONCHIECTASIS WITH INFECTION 3.RIGHT HORIZONTAL CRACK HYPERTROPHY ADHESION 4.FATTY LIVER DISEASE; [redacted]20[redacted] (RX DAY 159): BODY TEMPERATURE: THE MAXIMUM BODY TEMPERATURE WAS 38.2? BEFORE HOSPITALIZATION; [redacted]20[redacted] (RX DAY 161): COLOR ULTRASONOGRAPHY OF LIVER, GALLBLADDER, SPLEEN AND PANCREAS: FATTY LIVER, LIVER SLIGHTLY HYPERECHOIC LIGHT GROUP; ELECTROCARDIOGRAM: 1.SINUS RHYTHM 2.T WAVE CHANGES
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	2
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ASTHMA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Event of Interest - Hepatic Disorder

Event Description	FATTY LIVER
Preferred term	脂肪肝
AE Onset Date / Rx Day	[redacted]20[redacted] / 158
Age at AE Onset	3[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	NOT REPORTED

Duration of AE	NOT REPORTED
Toxicity Grade	1
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]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者は中国の 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を投与され，肺炎を発現した。被験者は非喫煙者で禁酒しており，関連する病歴は喘息，アトピー性皮膚炎及び潜在結核であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎を発現した。

入院前，被験者は咳嗽及び鼻閉に対し，経口薬にて対症療法を受けていた。20[redacted] 年 [redacted] 月 [redacted] 日，胸部コンピュータ断層撮影が行われ，右肺下葉の小結節及び右肺中葉の気管支拡張症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，38.2°C の発熱があった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

amoxicillin 及び LIANHUA-QINGWEN，ソバカズラ，ceftazidime，リバビリン，アンブロキソール塩酸塩，LEVOFLOXACIN LACTATE 及び塩化ナトリウム，BUDESONIDE SUSPENSION，YI QING PIAN，HANCHUAN ZUPA KELI，doxofylline 及びデキサメタゾンリン酸エステルナトリウムが投与された。

The patient's past medications include:

CEFTRIAXONE SODIUM for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

COMPOUND CAMPHOR CREAM for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

COMPOUND GLYCYRRHIZIN INJECTION for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

COMPOUND PINE DISTILLATE OINTMENT for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

DEXAMETHASONE ACETATE CREAM for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

EBASTINE TABLETS for ATOPIC DERMATITIS ([redacted])

LORATADINE for ATOPIC DERMATITIS ([redacted])

NEOMYCIN SULFATE AND FLUOCINONIDE CREAM for ATOPIC DERMATITIS ([redacted])

OLOPATADINE HYDROCHLORIDE TABLETS for ATOPIC DERMATITIS ([redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.23.1] [10035664]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMONIA

- Investigator: Asthma

- AbbVie: Non-Applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BODY TEMPERATURE:** 38.2 Degrees C

[redacted] **CHEST CT:** 1.RIGHT LOWER PULMONARY NODULES, REGULAR REEXAMINATION IS RECOMMENDED 2.RIGHT MIDDLE LOBE BRONCHIECTASIS WITH INFECTION 3.RIGHT HORIZONTAL CRACK HYPERTROPHY ADHESION 4.FATTY LIVER DISEASE

[redacted] **CHEST X-RAY:** Abnormal. 1. NO OBVIOUS ABNORMAL DENSITY SHADOW WAS OBSERVED IN THE PARENCHYMA OF BOTH LUNGS 2. LITTLE HEART SHADOW, SHARP DIAPHRAGMATIC ANGLE ON BOTH SIDES 3. LIFT LEFT DIAPHRAGM

[redacted] **20[redacted] EKG:** 1.SINUS RHYTHM 2.T WAVE CHANGES

[redacted] **20[redacted] NEUTROPHILS:** 76.37 % (normal 40.00 to 75.00)

[redacted] **20[redacted] NOVEL CORONAVIRUS NUCLEIC ACID TESTING:** Negative

[redacted] **20[redacted] ULTRASONOGRAPHY:** LIVER, GALLBLADDER, SPLEEN AND PANCREAS: FATTY LIVER, LIVER SLIGHTLY HYPERECHOIC LIGHT GROUP

[redacted] **20[redacted] WBC:** 8.09 X10**9/L (normal 3.50 to 9.50)

非重篤な有害事象

脂肪肝：無症状であり，肺炎のため行われた胸部コンピュータ断層撮影検査で偶発的に発見された。

Subject [redacted] ([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			X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	1[redacted]	MALE	MULTIPLE

Medical History	Onset Year
LACRIMAL DUCT OBTRUCTION	20[redacted]
ALLERGIC RHINITIS	20[redacted]
ATOPIC DERMATITIS	20[redacted]
ACNE	20[redacted]
OBSESSIVE COMPULSIVE DISORDER	20[redacted]
ACNE	NOT REPORTED
ALLERGIC RHINITIS	NOT REPORTED
TURBINATE HYPERTROPHY	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: DACRYOCYSTORHINOSTOMY	20[redacted]
PRIOR PROCEDURES: TURRET HYPERTROPHY SURGERY	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 112	112
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 113		

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: 20[redacted]
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
OTHER EMOLLIENTS AND PROTECTIVES 4	SUBJECT USES TWO TO THREE TIMES PER DAY g	BID	Y-M: 20[redacted]
TACROLIMUS	2 g	BID	Y-M: 20[redacted]
FLUVOXAMINE	100 mg	TID	Y-M: 20[redacted]
EMOLLIENTS AND PROTECTIVES	UNK mL	TID	Y-M: 20[redacted]
CLOBETASOL	UNK g	QD	Y-M: 20[redacted] / -324
METHYLPREDNISOLONE	UNK mg	QD	Y-M: 20[redacted] / -324
FEXOFENADINE	180 mg	QD	Y-M: 20[redacted] / -61

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
OTHER EMOLLIENTS AND PROTECTIVES 4	SUBJECT USES TWO TO THREE TIMES PER DAY g	BID	Y-M: 20[redacted]	NOT REPORTED
FLUVOXAMINE	100 mg	TID	Y-M: 20[redacted]	NOT REPORTED
BENZOYL PEROXIDE	3G A DAY ON FACE AND 5G A DAY ON SHOULDERS AND UPPER BACK g	BID	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 193
ASCORBIC ACID	500 mg	OTHER: JUST ONE TIME	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 109
PARACETAMOL	500 mg	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 116
AZELAIC ACID	3 g	QD	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 456
BENZOYL PEROXIDE	3G A DAY ON FACE AND 5G A DAY ON SHOULDERS AND UPPER BACK g	QD	Y-M: 20[redacted] / 165	NOT REPORTED
DALTEPARIN	5000 uL	QD	Y-M: 20[redacted] / 449	Y-M: 20[redacted] / 449
SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 449	Y-M: 20[redacted] / 449

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

Event Description	INCREASED LEVEL OF CK (CREATIN KINASE)
Preferred term	血中クレアチンホスホキナーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 113

Age at AE Onset	1[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	120
Duration of AE	8 DAYS
Toxicity Grade	2
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 - Creatine Phosphokinase (CPK) Elevation

Event Description	INCREASED LEVEL OF CREATINE KINASE
Preferred term	血中クレアチンホスホキナーゼ増加
AE Onset Date / Rx Day	[redacted]20[redacted] / 443
Age at AE Onset	1[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 449): Alanine Aminotransferase: 102 [17 - 59] U/L; Alkaline Phosphatase: 67 [38 - 116] U/L; Aspartate Aminotransferase: 94 [21 - 72] U/L; Bilirubin: 13 [3 - 15] UMOL/L; Creatine Kinase: 3587 [46 - 171] U/L; Creatinine: 98 [53 - 97] UMOL/L; Erythrocytes: 5.1 [4.6 - 6.2] 10^12/L; Hematocrit: 0.46 [0.39 - 0.54] FRACTION OF 1; Hemoglobin: 160 [135 - 180] G/L; Leukocytes: 4.7 [4.5 - 11] 10^9/L; NPTST001- ERYTHROSEDIMENTATION AUTOMATED: 6 [0 - 10] MM/H; NPTST002- LACTIC DEHYDROGENASE: 269 [120 - 246] U/L; NPTST003- PROTEIN C REACTIVE: 0.4 [0.4 - 1] MG/DL; NPTST004- UREIC NITROGEN: 18.7 [9 - 23] MG/DL; NPTST011-AMYLASE: 59 [25 - 125] U/L; NPTST040-COCAINE: NEGATIVE [0 - 300] ng/mL; Platelets: 188 [150 - 450] 10^9/L; Protein: NEGATIVE [0 - 10] mg/dL; [redacted]20[redacted] (RX DAY 450): Alanine Aminotransferase: 66 [17 - 59] U/L; Albumin: 36 [32 - 48] G/L; Aspartate Aminotransferase: 75 [21 - 72] U/L; Blood Urea Nitrogen: 5.9 [3.2 - 8.2] MMOL/L; Calcium: 2.05 [2.22 - 2.59] MMOL/L; Creatine Kinase: 1805 [46 - 171] U/L; Creatinine: 93 [53 - 97] UMOL/L; NPTST002- LACTIC DEHYDROGENASE: 188 [120 - 246] U/L; NPTST072-HEMOGLOBIN GLYCATE A1C: 5.6 [4 - 6] %; NPTST096-MAGNESIUM: 1.8 [1.6 - 2.6] MG/DL; NPTST139-SERICAL PHOSPHORUS: 4.2 [2.4 - 5.1] MG/DL; NPTST145-THYROID STIMULATING HORMONE (TS: 3.06 [0.55 - 4.78] IU/ML; Potassium: 3.7 [3.5 - 5.1] MMOL/L; Sodium: 140 [136 - 145] MMOL/L; Urate: 345.01 [220.09 - 547.26] UMOL/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	456
Duration of AE	14 DAYS
Toxicity Grade	4
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-045

本被験者はコロンビアの 1[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を投与され，クレアチンキナーゼ値増加を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加した。20[redacted] 年 [redacted] 月 [redacted] 日に盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はクレアチンキナーゼ値増加を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，クレアチンキナーゼ値増加は消失した。

本事象に先行した非重篤な有害事象として，20[redacted] 年 [redacted] 月にクレアチンキナーゼ値増加，20[redacted] 年 [redacted] 月に過激な運動に伴う筋肉痛及びインフルエンザウイルス感染が発現しており，20[redacted] 年 [redacted] 月にいずれの事象も消失した。

入院前である 20[redacted] 年 [redacted] 月 [redacted] 日の規定来院日，臨床検査でクレアチンキナーゼ上昇が確認された。被験者は無症状であった。

20[redacted] 年 [redacted] 月 [redacted] 日，症状を伴わないクレアチンキナーゼ値上昇のため，被験者は入院した。被験者によれば，本事象発現前に栄養サプリメントや娯楽物質の使用はなかった。運動の中止及び十分な水分補給を経て，クレアチンキナーゼ値は低下した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師は，活発な身体活動に伴い十分な水分補給を行わなかったことがクレアチンキナーゼ増加に関連していたと指摘した。

塩化ナトリウムおよび DALTEPARINE が投与された。

The patient's past medications include:

TACROLIMUS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

XERACALM for EMOLLIENT THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

CLOBETASOL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METHYLPREDNISOLONE ACEPONATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

FEXOFENADINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Creatine kinase increased (10011336) (Blood creatine phosphokinase increased (10005470)) [v.23.1] [10011336]

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 INCREASED LEVEL OF CREATINE KINASE

- Investigator: Not applicable

- AbbVie: Event more likely related to high physical activity without good hydration. CPK levels improved with exercise cessation and better hydration as noted by PI.

RISK/BENEFIT STATEMENT:

There is no change to the risk/benefit profile for this study/product as a result of this individual report/event(s).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 44 U/L (normal 6 to 43)

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 28 U/L (normal 6 to 43)

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 53 U/L (normal 6 to 43)

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 102 U/L (normal 17 to 59)

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 66 U/L (normal 17 to 59)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 86 U/L (normal 50 to 250)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 96 U/L (normal 50 to 250)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 60 U/L (normal 31 to 129)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 67 U/L (normal 38 to 116)

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 31 U/L (normal 10 to 40)

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 28 U/L (normal 10 to 40)

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 66 U/L (normal 11 to 36)

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 94 U/L (normal 21 to 72)

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 75 U/L (normal21 to 72)

[redacted] **20[redacted] BILIRUBIN:** 5 umol/L (normal 3 to 21)

[redacted] **20[redacted] BILIRUBIN:** <3 umol/L

[redacted] **20[redacted] BILIRUBIN:** 17 umol/L (normal 3 to 21)

[redacted] **20[redacted] BILIRUBIN:** 0.77 mg/dL (normal 0.2 to 0.9)

[redacted] **20[redacted] BUN:** 7.1 MMOL/L (normal 1.40 to 8.60)

[redacted] **20[redacted] BUN:** 7.1 MMOL/L (normal 1.40 to 8.60)

[redacted] **20[redacted] BUN:** 16.5 mg/dL (normal 9 to 23)

[redacted] **20[redacted] CALCIUM:** 8.2 mg/dL (normal 8.9 to 10.4)

[redacted] **20[redacted] CREATINE KINASE:** 169 U/L (normal 18 to 408)

[redacted] **20[redacted] CREATINE KINASE:** 199 U/L (normal 18 to 408)

[redacted] **20[redacted] CREATINE KINASE:** 4608 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 3529 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 1805 U/L (normal 46 to 171)

[redacted] **20[redacted] CREATININE:** 106 umol/L (normal 40 to 101)

[redacted] **20[redacted] CREATININE:** 124 umol/L (normal 40 to 101)

[redacted] **20[redacted] CREATININE:** 1.11 mg/dL (normal 0.6 to 1.1)

[redacted] **20[redacted] CREATININE:** 1.05 mg/dL (normal 0.6 to 1.1)

[redacted] **20[redacted] CRP:** <0.40 mg/dL

[redacted] 20[redacted] LACTIC DEHYDROGENASE: 269 U/L (normal 120 to 246)

[redacted] 20[redacted] LACTIC DEHYDROGENASE: 188 U/L (normal 120 to 246)

[redacted] 20[redacted] PROTEIN URINE: negative

[redacted] 20[redacted] URINE COCAINE: Negative

非重篤な有害事象

血中クレアチンホスホキナーゼ増加（1 件目）：症状として発熱，筋肉痛及び腹痛があった。運動又は活発な身体活動に関連していた。また，急性疾患に関連していた。本事象は，小児科医に評価された。

M16-047 試験（投与 16 週時）

治験の標題： 中等症から重症の青少年及び成人アトピー性皮膚炎患者におけるステロイド外用薬併用下のウパダシチニブの第 III 相，ランダム化，プラセボ対照，二重盲検試験	
治験実施施設： 22 ヵ国（オーストラリア，オーストリア，ベルギー，カナダ，中国［香港］，チェコ，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，オランダ，ニュージーランド，ノルウェー，スロバキア，スペイン，スウェーデン，英国及び米国［プエルトリコ］）の 171 施設	
治験調整医師： Prof. [redacted]	
公表文献（参考資料）： なし	
試験期間（年数）： 最初の被験者の初回来院日：2018 年 8 月 9 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日（投与 16 週時）	開発のフェーズ：III
目的： 全身療法の対象である中等症から重症の青少年及び成人アトピー性皮膚炎患者の治療において副腎皮質ステロイド外用薬併用下のウパダシチニブの有効性及び安全性を評価する。 16 週間の二重盲検投与期では，副腎皮質ステロイド外用薬併用下で，ウパダシチニブ 30 mg 及び 15 mg を 1 日 1 回（以下「QD」）投与時の安全性及び有効性をプラセボ投与時と比較する。盲検継続投与期では，二重盲検投与期を完了した中等症から重症の青少年及び成人アトピー性皮膚炎患者を対象として，副腎皮質ステロイド外用薬併用下でウパダシチニブ 30 mg 及び 15 mg QD 投与時の長期的な安全性，忍容性及び有効性を評価する。	
被験者数（計画時と解析時）： 計画時：810 名，解析時：901 名	
診断と主要な組入れ基準： 選択基準は以下のとおりであった。 1）スクリーニング来院時に 12 歳以上 75 歳以下の男性及び女性，2）12 歳以上 18 歳未満の場合，ベースライン来院時の体重が 40 kg 以上である，3）スクリーニング来院時の病歴聴取，臨床検査，身体検査，胸部 X 線検査及び 12 誘導心電図の結果に基づき，治験責任（担当）医師により全般的な健康状態が良好である（アトピー性皮膚炎を除く）と評価された，4）Hanifin & Rajka の診断基準に基づく慢性アトピー性皮膚炎であり，ベースラインの少なくとも 3 年前に発症している，5）以下の疾患活動性基準をすべて満たす：スクリーニング及びベースライン来院時に湿疹面積重症度指数（以下「EASI」）スコア 16 以上，スクリーニング及びベースライン来院時にバリデートされた治験責任医師による包括的評価-アトピー性皮膚炎（以下「vIGA-AD」）スコア 3 以上，スクリーニング及びベースライン来院時にアトピー性皮膚炎病変の体表面積 10%以上，及び毎日の最悪のかゆみの数値評価尺度（以下「NRS」）のベースライン来院時の週平均値 4 以上，6）副腎皮質ステロイド外用薬又はカルシニューリン阻害外用薬が効果不十分であったことを示す記録がある（ベースライン来院前 6 ヵ月以内），又はアトピー性皮膚炎に対するベースライン来院前 6 ヵ月以内の全身療法の記録がある，7）ベースライン来院前の少なくとも連続する 7 日間，外用エモリエント（保湿剤）を 1 日 2 回使用している。	
治験方法： 本試験は，主試験（青少年及び成人を対象）及び青少年サブスタディ（青少年を対象）で構成された。主試験及び青少年サブスタディのいずれも，35 日間のスクリーニング期間，16 週間の二重盲検投与期（主要解析は投与 16 週完了時に実施）及び最長で投与 136 週までの盲検継続投与期から構成され，治験薬の最終投与から約 30 日後に追跡調査来院を行った。主試験の適格性基準を満たした被験者を，3 つの治験薬投与群（ウパダシチニブ	

15 mg 群，ウパダシチニブ 30 mg 群又はプラセボ群）のいずれかに 1:1:1 の割合でランダム化し，副腎皮質ステロイド外用薬併用下で QD 経口投与した。主試験への目標例数（810 名）の登録が完了後，引き続き追加試験（青少年サブスタディ）への青少年被験者の登録を行い，青少年被験者の登録数が試験全体（主試験 + 青少年サブスタディ）で計 180 名になるまで継続することとした。本項では，主試験の中間解析の結果（主要解析［投与 16 週完了時に実施］の結果及びデータカットオフ日までに得られた結果）を示す。 主試験では，ベースライン疾患重症度，年齢及び地理的地域による層別ランダム化を行った。二重盲検投与期終了時に，プラセボ群の被験者を 1:1 の割合で盲検継続投与期におけるウパダシチニブ 30 mg 又は 15 mg の QD 経口投与に再度割り付け（EASI 50 レスポンダー，地理的地域及び年齢による層別ランダム化を行った），136 週時来院まで継続することとした。初めにウパダシチニブ群にランダム化された被験者には，盲検継続投与期も継続して同じ用量のウパダシチニブを投与することとした。投与 4～24 週時の間の直近 2 回の規定来院時に EASI スコアのベースラインからの 50%以上の低下（以下「EASI 50」）未満となった被験者に対し，医学的に必要な場合，レスキュー治療を行うことができることとした。投与 24 週後は，規定来院又は規定外来院時に EASI 50 未満となった被験者に対し，医学的に必要な場合，レスキュー治療を行うことができることとした。
被験薬，用量 / 含量 / 濃度，投与法，ロット番号： ウパダシチニブ 15 mg 徐放錠（経口），バルクロット番号：[redacted] ウパダシチニブ 30 mg 徐放錠（経口），バルクロット番号：[redacted] 治療期間：二重盲検投与期：16 週間，盲検継続投与期：最長で投与 136 週まで
対照薬，用量 / 含量 / 濃度，投与法，ロット番号： ウパダシチニブに対応するプラセボ（経口），バルクロット番号：[redacted]

評価基準：

有効性：

共主要評価項目は，投与 16 週時に EASI スコアのベースラインからの 75%以上の低下（以下「EASI 75」）を達成した被験者の割合，及び投与 16 週時の vIGA-AD スコアが 0 又は 1 であり，かつベースラインと比較して 2 グレード以上改善（低下）した被験者の割合であった。

欧州当局 / 欧州医薬品庁（以下「EMA」）及び米国当局 / 米国食品医薬品局（以下「FDA」）の両方の規制に対応する重要な副次評価項目では，他に明記されていない限り，多重性の調整の下，各用量のウパダシチニブのプラセボに対する優越性を証明することとした。

重要な副次評価項目（FDA）	重要な副次評価項目（EMA）
投与 16 週時に最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合	投与 16 週時に最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合
投与 16 週時に EASI スコアのベースラインからの 90%以上の低下（以下「EASI 90」）を達成した被験者の割合	投与 16 週時に EASI 90 を達成した被験者の割合
投与 4 週時に最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合	投与 16 週時の最悪のかゆみの NRS のベースラインからの変化率
投与 4 週時に EASI 75 を達成した被験者の割合	投与 16 週時の EASI スコアのベースラインからの変化率
投与 2 週時に EASI 75 を達成した被験者の割合	投与 4 週時に最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合
投与 4 週時に EASI 90 を達成した被験者の割合	投与 4 週時に EASI 75 を達成した被験者の割合
（30 mg 群）投与 16 週時に EASI スコアのベースラインからの 100%以上の低下（以下「EASI 100」）を達成した被験者の割合	投与 2 週時に EASI 75 を達成した被験者の割合
投与 1 週時に最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合	投与 4 週時に EASI 90 を達成した被験者の割合
	（30 mg 群）投与 16 週時に EASI 100 を達成した被験者の割合
	投与 1 週時に最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合

その他の評価項目には，投与 16 週時及び他の規定来院時に得られた EASI 75 を達成した被験者の副腎皮質ステロイド外用薬を中断した日数，EASI 75 を達成した被験者が初めてすべての副腎皮質ステロイド外用薬を中断するまでの期間，並びに健康関連の生活の質（以下「QOL」）などが含まれた。

薬物動態：

指定された医療機関の被験者より，治験薬の投与前に血液検体を採取し，ウパダシチニブの薬物動態データを評価した（投与 2，8，12，16 週時，及び早期中止来院時）。

安全性：

試験期間を通して，有害事象，バイタルサインの変動，臨床検査（血液学的検査，血液生化学検査，尿検査）及び製品苦情のデータを評価した。

統計手法：

有効性：

主試験の ITT 集団（以下「ITT_M 集団」）は，主試験のすべてのランダム化された被験者から構成され，すべての有効性解析に用いた。ITT_M 集団の被験者の解析は，実際に受けた投与に関わらず，主試験でランダム化された投与群に基づいて実施した。二重盲検投与期にプラセボ群にランダム化され，盲検継続投与期に移行しなかった被験者は，盲検継続投与期の解析に含めなかった。主要評価項目及び重要な副次評価項目は多重検定法を用いて，全体の第 I 種の過誤率を両側 0.05 に制御した。統計解析は，治験実施計画書 5.0 版に基づいて組み入れた被験者を用いて実施した。共主要評価項目の感度分析（tipping point analysis，多重補完［MI］法及び新型コロナウイルス感染症［COVID-19］による欠測値を考慮しないノンレスポンダーインピュテーション［NRI-NC］法を用いた）を実施した。また，治験実施計画書に適合した集団を対象とした感度分析では，共主要評価項目の評価に影響を及ぼす可能性のある，重大な治験実施計画書の逸脱を有する被験者を除外した。

薬物動態：

被験者ごとの血漿中ウパダシチニブ濃度を一覧表にし，適切な統計手法を用いて要約した。

安全性：

主試験の二重盲検投与期（16 週間）の安全性解析対象集団は，主試験の二重盲検投与期に治験薬投与を 1 回以上受けたすべてのランダム化された被験者から構成された。主試験の全ウパダシチニブ投与集団は，主試験でウパダシチニブ投与を 1 回以上受けたすべての被験者から構成された。主試験の盲検継続投与期の安全性解析対象集団は，主試験の盲検継続投与期に治験薬投与を 1 回以上受けたすべてのランダム化された被験者から構成された（主試験の盲検継続投与期の安全性解析対象集団は，臨床検査の評価にのみ用いた）。

安全性は，有害事象，身体検査，臨床検査及びバイタルサインにより評価した。有害事象が発現した被験者の数及び割合を，ICH 国際医薬用語集（以下「MedDRA」）の器官別大分類及び基本語を用いて投与群ごとに示した。また，重篤な有害事象の要約，並びに重症度別及び治験責任（担当）医師が評価した治験薬との因果関係別の有害事象の要約も示した。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を一覧表に示した。各来院時のバイタルサイン，身体検査及び臨床検査の変化を要約した。規定の時点での臨床検査値のベースラインからの変動を表に示した。

要約 / 結論：

有効性の結果：

中等症から重症のアトピー性皮膚炎患者を対象とした第 III 相試験である本試験では，二重盲検投与期（プラセボ対照，16 週間）における，副腎皮質ステロイド外用薬併用下でのウパダシチニブ 30 mg 及び 15 mg のプラセボに対する優越性が共主要評価項目及び副次評価項目により一貫して示された。

共主要評価項目は，投与 16 週時に EASI 75 を達成した被験者の割合，及び投与 16 週時の vIGA-AD スコアが 0 又は 1 であり，かつベースラインと比較して 2 グレード以上改善した被験者の割合であった。共主要評価項目は，ウパダシチニブ群でプラセボ群と比較して統計学的に有意に高かった。また，様々な皮膚症状の改善及びかゆみなどの反応の基準値に関する重要な副次評価項目でプラセボ群と比較して有意な差が認められた。

副腎皮質ステロイド外用薬併用下において，ウパダシチニブ 30 mg 群及びウパダシチニブ 15 mg 群では，プラセボ群と比較してかゆみが有意に減少し，投与 16 週時に最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合は，ウパダシチニブ群の方が高かった。副腎皮質ステロイド外用薬併用下で，プラセボ群と比較して，ウパダシチニブ 30 mg 群及びウパダシチニブ 15 mg 群では早期に反応が認められ，投与 2 週時に EASI 75 を達成した被験者の割合は有意に高かった。また，最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合は，投与 1 週時の時点でウパダシチニブ 30 mg 群及びウパダシチニブ 15 mg でプラセボ群と比較して有意に高かった。

プラセボ群と比較してウパダシチニブ 30 mg 群及びウパダシチニブ 15 mg 群では，投与 16 週時までの EASI 75 を達成した被験者が副腎皮質ステロイド外用薬を中断した日数は長く，EASI 75 を達成した被験者が初めてすべての副腎皮質ステロイド外用薬を中断するまでの期間も短かった。

副腎皮質ステロイド外用薬併用下で，ウパダシチニブ 30 mg 及び 15 mg のいずれの用量も有効であったが，被験者に対し，ウパダシチニブ 30 mg はウパダシチニブ 15 mg と比較してより有益であった。青少年被験者では，共主要評価項目，様々な皮膚症状の改善及び反応の基準値に関する副次評価項目，並びにかゆみ及び他の症状の評

価で，一貫した有効性が示された。

薬物動態の結果：

24 時間の投与間隔内での血漿中ウパダシチニブ濃度の平均値の範囲は，ウパダシチニブ 15 mg 群で 6.35～29.0 ng/mL，ウパダシチニブ 30 mg 群で 17.5～58.3 ng/mL であった。

安全性の結果：

副腎皮質ステロイド外用薬併用下で，ウパダシチニブは中等症から重症のアトピー性皮膚炎患者に対し，おおむね安全で，忍容性も良好であった。ウパダシチニブの他の適応症（関節リウマチ及び乾癬性関節炎）の試験と比較して，新たな重大な安全性の懸念は認められなかった。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発現割合は，二重盲検投与期（プラセボ対照期間）を通してウパダシチニブ群及びプラセボ群で類似していた。データカットオフ日までにウパダシチニブの投与を受けたすべての被験者での，曝露期間で調整した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発現率は，ウパダシチニブ 30 mg 群及びウパダシチニブ 15 mg 群で類似していた。全体として，ウパダシチニブの投与を受けた被験者で発現割合が最も高かった有害事象は，ざ瘡及び上咽頭炎であった。本試験中に死亡は認められなかった。

ざ瘡の発現割合にはウパダシチニブの用量反応関係が認められ，ざ瘡の発現割合はプラセボ群と比較してウパダシチニブ群で高かった。ざ瘡の重症度はすべて軽度又は中等度であり，ざ瘡による治験薬の投与中止は認められなかった。ほとんどのざ瘡は顔に発現し，主に炎症性丘疹，膿疱及び面皰であった。本試験のプラセボ及びウパダシチニブの投与群全体でざ瘡の既往歴を有する被験者の割合は高かった。この原因として，ざ瘡の有病率は若年層で高いため，本試験に登録されたアトピー性皮膚炎患者集団でもざ瘡の既往歴が高かった可能性がある。

データカットオフ日までに，重篤な感染症の発現率はウパダシチニブ 30 mg 群及びウパダシチニブ 15 mg 群で類似していた。報告された日和見感染は，ヘルペス性状湿疹（カポジ水痘様発疹と同義）であった。ヘルペス性状湿疹は，アトピー性皮膚炎患者集団でよく認められるウイルス性の合併症である。帯状疱疹はヤヌスキナーゼ（以下「JAK」）阻害薬では予期される有害事象であり，その発現割合はプラセボ群と比較してウパダシチニブ群で高く，ウパダシチニブ 15 mg 群と比較してウパダシチニブ 30 mg 群で高かった。大部分の帯状疱疹が単一の皮節のみに認められた。

最も多く認められた特に注目すべき有害事象（いずれかの投与群で 10 件以上発現した事象）は，クレアチンホスホキナーゼ増加，帯状疱疹及び肝障害であった。大部分の特に注目すべき有害事象は重篤ではなく，治験薬の投与中止には至らず，重症度は軽度又は中等度であった。

ウパダシチニブ 30 mg 群の心血管系合併症の既往歴を有する被験者で，判定された主要心血管事象（非致死性脳卒中）が 1 件報告され，ウパダシチニブ 15 mg 群の被験者で腎機能障害（急性腎障害）が 1 件報告された。プラセボ群の 1 名に動脈ステント血栓症が発現した。

クレアチンホスホキナーゼ増加及び貧血の発現率は，ウパダシチニブ 15 mg 群と比較してウパダシチニブ 30 mg 群で高かった。肝障害（大部分が無症候性肝酵素増加）の発現率は，ウパダシチニブ 30 mg 群と比較してウパダシチニブ 15 mg 群で高かった。好中球減少症の発現率は，投与群間で類似していた。JAK 阻害薬では，これらの臨床検査異常に対するウパダシチニブの用量依存性は予期されている。

成人及び青少年の両方で中等度の体重増加が認められた。体重増加は成長期の青少年では予期されているものであるが，成人では様々な病因が考えられた。青少年の被験者で，身長と体重に関してウパダシチニブ投与による臨床的に意味のある差は認められなかった。

本試験では，データカットオフ日までに，判定された静脈血栓塞栓症，判定された消化管穿孔，活動性結核，リンパ腫及びリンパ球減少症は報告されなかった。青少年被験者数は成人被験者数よりも少なかったが，青少年被験者集団の安全性の結果は，好中球減少症及びざ瘡の発現率が若干高かったことを除き，全体集団の結果と一貫していた。

結論：

中等症から重症のアトピー性皮膚炎患者を対象とした第 III 相試験である本試験（M16-047 試験）では，投与 16 週時までに，共主要評価項目及び副次評価項目により，皮膚での疾患活動性及びかゆみの改善が認められ，副腎皮質ステロイド外用薬併用下でのウパダシチニブ 30 mg 及び 15 mg 投与の有効性が示された。ウパダシチニブ

は，皮膚での迅速な作用発現及び効果の深さ，並びにかゆみの改善を示した。健康関連の QOL に関するその他の評価項目により，副腎皮質ステロイド外用薬節約効果及び福祉の向上に対する一貫した効果が示された。ウパダシチニブ 15 mg 及び 30 mg QD 投与は，おおむね安全で忍容性は良好であり，報告された有害事象は臨床的に管理可能であった。全体として，ウパダシチニブ 15 mg 及び 30 mg のベネフィット・リスクのプロファイルは良好と考えられた。

青少年被験者で，共主要評価項目並びに様々な皮膚症状の改善及びかゆみなどの反応の基準値に関する副次評価項目により，全被験者と一貫した有効性が示された。本試験の結果は，中等症から重症の青少年及び成人アトピー性皮膚炎患者に対し，ウパダシチニブは有効で忍容性が良好な治療の選択肢であることを支持している。

表 1. 二重盲検投与期で有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（二重盲検投与期の安全性解析対象集団）

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
Any adverse event	190 (62.7)	200 (66.7)	215 (72.4)	415 (69.5)
血液およびリンパ系障害	4 (1.3)	4 (1.3)	8 (2.7)	12 (2.0)
貧血	1 (0.3)	0	2 (0.7)	2 (0.3)
白血球増加症	0	1 (0.3)	0	1 (0.2)
白血球減少症	0	1 (0.3)	1 (0.3)	2 (0.3)
リンパ節症	1 (0.3)	2 (0.7)	1 (0.3)	3 (0.5)
リンパ球増加症	0	0	1 (0.3)	1 (0.2)
リンパ球減少症	1 (0.3)	0	0	0
好中球減少症	0	1 (0.3)	2 (0.7)	3 (0.5)
汎血球減少症	0	0	1 (0.3)	1 (0.2)
特発性血腫	1 (0.3)	0	0	0
血小板増加症	0	0	1 (0.3)	1 (0.2)
心臓障害	0	1 (0.3)	3 (1.0)	4 (0.7)
うっ血性心不全	0	0	1 (0.3)	1 (0.2)
動悸	0	1 (0.3)	1 (0.3)	2 (0.3)
洞性徐脈	0	0	1 (0.3)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
先天性、家族性および遺伝性障害	0	1 (0.3)	1 (0.3)	2 (0.3)
ジルベール症候群	0	0	1 (0.3)	1 (0.2)
色素性網膜炎	0	1 (0.3)	0	1 (0.2)
耳および迷路障害	2 (0.7)	4 (1.3)	0	4 (0.7)
耳の障害	0	1 (0.3)	0	1 (0.2)
耳痛	2 (0.7)	3 (1.0)	0	3 (0.5)
回転性めまい	0	1 (0.3)	0	1 (0.2)
内分泌障害	0	1 (0.3)	0	1 (0.2)
甲状腺機能低下症	0	1 (0.3)	0	1 (0.2)
眼障害	8 (2.6)	9 (3.0)	13 (4.4)	22 (3.7)
アトピー性角結膜炎	1 (0.3)	0	0	0
眼瞼炎	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
白内障	0	0	1 (0.3)	1 (0.2)
結膜刺激	0	0	1 (0.3)	1 (0.2)
アレルギー性結膜炎	1 (0.3)	0	2 (0.7)	2 (0.3)
ドライアイ	0	2 (0.7)	1 (0.3)	3 (0.5)
眼の炎症	0	0	1 (0.3)	1 (0.2)
眼痛	0	1 (0.3)	0	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
眼障害 (Cont.)				
眼の異常感覚	0	0	1 (0.3)	1 (0.2)
眼瞼障害	0	0	1 (0.3)	1 (0.2)
流涙増加	0	2 (0.7)	0	2 (0.3)
非感染性結膜炎	1 (0.3)	0	0	0
視神経乳頭浮腫	0	0	1 (0.3)	1 (0.2)
羞明	1 (0.3)	0	1 (0.3)	1 (0.2)
網膜動脈閉塞	1 (0.3)	0	0	0
網膜剥離	0	1 (0.3)	0	1 (0.2)
裂孔原性網膜剥離	1 (0.3)	0	0	0
閃輝暗点	1 (0.3)	0	0	0
春季カタル	0	0	1 (0.3)	1 (0.2)
霧視	1 (0.3)	3 (1.0)	1 (0.3)	4 (0.7)
硝子体剥離	0	0	1 (0.3)	1 (0.2)
胃腸障害	25 (8.3)	44 (14.7)	47 (15.8)	91 (15.2)
腹部不快感	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
腹部膨満	1 (0.3)	2 (0.7)	2 (0.7)	4 (0.7)
腹痛	0	6 (2.0)	5 (1.7)	11 (1.8)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
胃腸障害 (Cont.)				
上腹部痛	1 (0.3)	11 (3.7)	3 (1.0)	14 (2.3)
口角口唇炎	0	0	2 (0.7)	2 (0.3)
肛門直腸不快感	0	0	1 (0.3)	1 (0.2)
アフタ性潰瘍	0	0	1 (0.3)	1 (0.2)
便習慣変化	0	0	1 (0.3)	1 (0.2)
大腸炎	1 (0.3)	0	0	0
便秘	1 (0.3)	5 (1.7)	4 (1.3)	9 (1.5)
齲歯	0	2 (0.7)	2 (0.7)	4 (0.7)
下痢	7 (2.3)	11 (3.7)	12 (4.0)	23 (3.9)
口内乾燥	2 (0.7)	0	0	0
消化不良	0	6 (2.0)	4 (1.3)	10 (1.7)
嚥下障害	0	0	1 (0.3)	1 (0.2)
腸炎	1 (0.3)	0	0	0
変色便	0	1 (0.3)	0	1 (0.2)
白色便	0	1 (0.3)	0	1 (0.2)
鼓腸	2 (0.7)	0	0	0
食中毒	2 (0.7)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
胃腸障害 (Cont.)				
排便回数増加	0	0	1 (0.3)	1 (0.2)
胃炎	1 (0.3)	1 (0.3)	0	1 (0.2)
胃腸障害	0	1 (0.3)	0	1 (0.2)
胃腸粘膜障害	0	1 (0.3)	0	1 (0.2)
胃食道逆流性疾患	0	1 (0.3)	3 (1.0)	4 (0.7)
痔核	0	0	1 (0.3)	1 (0.2)
裂孔ヘルニア	0	0	1 (0.3)	1 (0.2)
過敏性腸症候群	0	0	1 (0.3)	1 (0.2)
口唇水疱	1 (0.3)	1 (0.3)	0	1 (0.2)
口腔内潰瘍形成	0	2 (0.7)	0	2 (0.3)
粘液便	1 (0.3)	0	0	0
悪心	0	8 (2.7)	6 (2.0)	14 (2.3)
口腔そう痒症	0	0	1 (0.3)	1 (0.2)
膵炎	0	1 (0.3)	0	1 (0.2)
無髄歯	0	0	1 (0.3)	1 (0.2)
レッチング	0	0	1 (0.3)	1 (0.2)
歯の障害	0	0	1 (0.3)	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
胃腸障害 (Cont.)				
埋伏歯	1 (0.3)	0	2 (0.7)	2 (0.3)
歯痛	1 (0.3)	1 (0.3)	3 (1.0)	4 (0.7)
嘔吐	3 (1.0)	2 (0.7)	3 (1.0)	5 (0.8)
一般・全身障害および投与部位の状態	13 (4.3)	23 (7.7)	21 (7.1)	44 (7.4)
胸痛	1 (0.3)	2 (0.7)	0	2 (0.3)
悪寒	1 (0.3)	1 (0.3)	0	1 (0.2)
嚢胞	0	0	1 (0.3)	1 (0.2)
顔面痛	0	2 (0.7)	0	2 (0.3)
疲労	0	3 (1.0)	4 (1.3)	7 (1.2)
熱感	0	1 (0.3)	0	1 (0.2)
治癒不良	0	0	1 (0.3)	1 (0.2)
炎症	1 (0.3)	0	0	0
インフルエンザ様疾患	4 (1.3)	4 (1.3)	6 (2.0)	10 (1.7)
非心臓性胸痛	0	0	1 (0.3)	1 (0.2)
浮腫	1 (0.3)	0	0	0
末梢性浮腫	2 (0.7)	1 (0.3)	0	1 (0.2)
疼痛	0	3 (1.0)	1 (0.3)	4 (0.7)

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
発熱	3 (1.0)	5 (1.7)	6 (2.0)	11 (1.8)
顔面腫脹	0	1 (0.3)	0	1 (0.2)
血管ステント血栓症	1 (0.3)	0	0	0
血管穿刺部位内出血	0	0	1 (0.3)	1 (0.2)
肝胆道系障害	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
胆石症	1 (0.3)	0	0	0
肝機能異常	0	1 (0.3)	1 (0.3)	2 (0.3)
免疫系障害	5 (1.7)	1 (0.3)	2 (0.7)	3 (0.5)
動物アレルギー	1 (0.3)	0	0	0
アナフィラキシー反応	1 (0.3)	0	1 (0.3)	1 (0.2)
薬物過敏症	0	1 (0.3)	0	1 (0.2)
食物アレルギー	1 (0.3)	0	0	0
過敏症	0	0	1 (0.3)	1 (0.2)
季節性アレルギー	2 (0.7)	0	0	0
感染症および寄生虫症	113 (37.3)	129 (43.0)	137 (46.1)	266 (44.6)
腹部膿瘍	1 (0.3)	0	0	0
四肢膿瘍	0	0	1 (0.3)	1 (0.2)

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感染症および寄生虫症 (Cont.)				
口腔膿瘍	0	0	1 (0.3)	1 (0.2)
ダニ皮膚炎	0	0	1 (0.3)	1 (0.2)
膿疱性ざ瘡	0	1 (0.3)	1 (0.3)	2 (0.3)
肛門膿瘍	1 (0.3)	0	0	0
虫垂炎	0	1 (0.3)	0	1 (0.2)
細菌感染	0	1 (0.3)	1 (0.3)	2 (0.3)
細菌性膣症	0	1 (0.3)	0	1 (0.2)
細菌性外陰膣炎	1 (0.3)	0	0	0
細菌尿	1 (0.3)	0	1 (0.3)	1 (0.2)
体部白癬	0	0	1 (0.3)	1 (0.2)
気管支炎	3 (1.0)	2 (0.7)	3 (1.0)	5 (0.8)
ウイルス性気管支炎	1 (0.3)	0	0	0
蜂巣炎	2 (0.7)	1 (0.3)	0	1 (0.2)
結膜炎	5 (1.7)	3 (1.0)	2 (0.7)	5 (0.8)
細菌性結膜炎	0	1 (0.3)	1 (0.3)	2 (0.3)
膀胱炎	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
感染性下痢	0	0	1 (0.3)	1 (0.2)

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感染症および寄生虫症 (Cont.)				
耳感染	1 (0.3)	1 (0.3)	0	1 (0.2)
ヘルペス性状湿疹	0	2 (0.7)	3 (1.0)	5 (0.8)
心内膜炎	1 (0.3)	0	0	0
蟯虫症	0	1 (0.3)	0	1 (0.2)
丹毒	2 (0.7)	0	0	0
眼感染	1 (0.3)	0	0	0
眼瞼感染	0	1 (0.3)	0	1 (0.2)
毛包炎	3 (1.0)	8 (2.7)	11 (3.7)	19 (3.2)
皮膚真菌感染	0	1 (0.3)	0	1 (0.2)
せつ	0	2 (0.7)	1 (0.3)	3 (0.5)
胃腸炎	6 (2.0)	6 (2.0)	1 (0.3)	7 (1.2)
ウイルス性胃腸炎	1 (0.3)	0	1 (0.3)	1 (0.2)
消化管感染	0	1 (0.3)	0	1 (0.2)
陰部ヘルペス	0	0	1 (0.3)	1 (0.2)
歯肉炎	0	1 (0.3)	1 (0.3)	2 (0.3)
ヘリコバクター性胃炎	1 (0.3)	0	0	0
ヘルペス眼感染	0	0	1 (0.3)	1 (0.2)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
感染症および寄生虫症 (Cont.)				
単純ヘルペス	1 (0.3)	6 (2.0)	6 (2.0)	12 (2.0)
帯状疱疹	3 (1.0)	3 (1.0)	5 (1.7)	8 (1.3)
麦粒腫	0	1 (0.3)	3 (1.0)	4 (0.7)
膿痂疹	2 (0.7)	1 (0.3)	2 (0.7)	3 (0.5)
インフルエンザ	2 (0.7)	11 (3.7)	7 (2.4)	18 (3.0)
カポジ水痘様発疹	0	1 (0.3)	1 (0.3)	2 (0.3)
喉頭炎	0	1 (0.3)	0	1 (0.2)
シラミ寄生	0	0	1 (0.3)	1 (0.2)
下気道感染	1 (0.3)	0	0	0
細菌性乳腺炎	0	1 (0.3)	0	1 (0.2)
鼻ヘルペス	0	0	2 (0.7)	2 (0.3)
上咽頭炎	34 (11.2)	37 (12.3)	40 (13.5)	77 (12.9)
爪真菌症	0	1 (0.3)	1 (0.3)	2 (0.3)
眼部単純ヘルペス	0	0	3 (1.0)	3 (0.5)
口腔カンジダ症	0	1 (0.3)	1 (0.3)	2 (0.3)
口腔ヘルペス	5 (1.7)	10 (3.3)	23 (7.7)	33 (5.5)
外耳炎	1 (0.3)	2 (0.7)	1 (0.3)	3 (0.5)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
感染症および寄生虫症 (Cont.)				
中耳炎	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
扁桃周囲膿瘍	0	1 (0.3)	0	1 (0.2)
咽頭炎	1 (0.3)	6 (2.0)	4 (1.3)	10 (1.7)
レンサ球菌性咽頭炎	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
肺炎	1 (0.3)	1 (0.3)	0	1 (0.2)
マイコプラズマ性肺炎	0	0	1 (0.3)	1 (0.2)
ウイルス感染後疲労症候群	0	0	1 (0.3)	1 (0.2)
歯髄炎	1 (0.3)	0	0	0
膿疱	1 (0.3)	0	2 (0.7)	2 (0.3)
気道感染	1 (0.3)	0	1 (0.3)	1 (0.2)
ウイルス性気道感染	0	1 (0.3)	0	1 (0.2)
鼻炎	1 (0.3)	3 (1.0)	0	3 (0.5)
鼻喉頭炎	0	0	1 (0.3)	1 (0.2)
副鼻腔炎	5 (1.7)	1 (0.3)	3 (1.0)	4 (0.7)
皮膚細菌感染	2 (0.7)	1 (0.3)	1 (0.3)	2 (0.3)
皮膚カンジダ	1 (0.3)	0	0	0
皮膚感染	5 (1.7)	1 (0.3)	1 (0.3)	2 (0.3)

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Total (N=597) n (%)
感染症および寄生虫症 (Cont.)				
膿性痰	0	1 (0.3)	0	1 (0.2)
ブドウ球菌感染	0	1 (0.3)	1 (0.3)	2 (0.3)
ブドウ球菌性敗血症	1 (0.3)	0	0	0
ブドウ球菌皮膚感染	3 (1.0)	1 (0.3)	2 (0.7)	3 (0.5)
重複感染	1 (0.3)	0	0	0
細菌重複感染	1 (0.3)	0	0	0
須毛瘡	1 (0.3)	0	0	0
股部白癬	0	0	1 (0.3)	1 (0.2)
白癬感染	2 (0.7)	0	0	0
足部白癬	0	1 (0.3)	1 (0.3)	2 (0.3)
癜風	1 (0.3)	0	0	0
扁桃炎	2 (0.7)	2 (0.7)	1 (0.3)	3 (0.5)
歯感染	1 (0.3)	2 (0.7)	0	2 (0.3)
気管炎	0	1 (0.3)	0	1 (0.2)
気管気管支炎	0	1 (0.3)	0	1 (0.2)
トリコフィトン感染症	0	1 (0.3)	0	1 (0.2)
上気道感染	22 (7.3)	21 (7.0)	23 (7.7)	44 (7.4)

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
感染症および寄生虫症 (Cont.)				
尿路感染	6 (2.0)	5 (1.7)	11 (3.7)	16 (2.7)
細菌性尿路感染	0	0	1 (0.3)	1 (0.2)
膣感染	0	1 (0.3)	1 (0.3)	2 (0.3)
ガードネレラ菌性膣炎	1 (0.3)	0	0	0
ウイルス感染	0	1 (0.3)	0	1 (0.2)
ウイルス性上気道感染	4 (1.3)	5 (1.7)	5 (1.7)	10 (1.7)
外陰部膣カンジダ症	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
外陰膣真菌感染	0	0	1 (0.3)	1 (0.2)
創傷感染	1 (0.3)	0	0	0
傷害、中毒および処置合併症	10 (3.3)	10 (3.3)	19 (6.4)	29 (4.9)
事故	0	0	1 (0.3)	1 (0.2)
動物咬傷	1 (0.3)	0	0	0
節足動物咬傷	1 (0.3)	0	1 (0.3)	1 (0.2)
軟骨損傷	0	0	1 (0.3)	1 (0.2)
胸部損傷	0	0	1 (0.3)	1 (0.2)
挫傷	1 (0.3)	0	3 (1.0)	3 (0.5)
角膜擦過傷	0	0	1 (0.3)	1 (0.2)

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傷害、中毒および処置合併症 (Cont.)				
転倒	1 (0.3)	1 (0.3)	2 (0.7)	3 (0.5)
頭部損傷	1 (0.3)	0	0	0
損傷	0	1 (0.3)	1 (0.3)	2 (0.3)
関節損傷	0	0	1 (0.3)	1 (0.2)
四肢損傷	0	3 (1.0)	0	3 (0.5)
半月板損傷	1 (0.3)	1 (0.3)	0	1 (0.2)
肉離れ	3 (1.0)	1 (0.3)	3 (1.0)	4 (0.7)
過量投与	0	1 (0.3)	0	1 (0.2)
処置による疼痛	0	0	1 (0.3)	1 (0.2)
橈骨骨折	0	0	1 (0.3)	1 (0.2)
肋骨骨折	0	1 (0.3)	0	1 (0.2)
交通事故	0	0	1 (0.3)	1 (0.2)
皮膚擦過傷	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
皮膚裂傷	0	1 (0.3)	0	1 (0.2)
腱損傷	0	0	1 (0.3)	1 (0.2)
歯牙破折	0	1 (0.3)	1 (0.3)	2 (0.3)
外傷性血腫	0	1 (0.3)	0	1 (0.2)

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傷害、中毒および処置合併症 (Cont.)				
創傷	0	0	1 (0.3)	1 (0.2)
臨床検査	27 (8.9)	26 (8.7)	31 (10.4)	57 (9.5)
アラニンアミノトランスフェラーゼ増加	4 (1.3)	3 (1.0)	2 (0.7)	5 (0.8)
アスパラギン酸アミノトランスフェラーゼ増加	4 (1.3)	2 (0.7)	2 (0.7)	4 (0.7)
血中重炭酸塩減少	0	0	1 (0.3)	1 (0.2)
血中ビリルビン増加	0	1 (0.3)	0	1 (0.2)
血中クロール減少	1 (0.3)	0	0	0
血中コレステロール増加	0	1 (0.3)	0	1 (0.2)
血中クレアチンホスホキナーゼ増加	7 (2.3)	13 (4.3)	18 (6.1)	31 (5.2)
血中クレアチニン増加	1 (0.3)	0	0	0
血中免疫グロブリン E 増加	2 (0.7)	1 (0.3)	0	1 (0.2)
血中リン減少	1 (0.3)	0	0	0
血圧上昇	1 (0.3)	0	0	0
血中ナトリウム減少	1 (0.3)	0	0	0
血中トリグリセリド増加	0	1 (0.3)	1 (0.3)	2 (0.3)
血中尿酸増加	0	1 (0.3)	0	1 (0.2)
体温上昇	0	0	1 (0.3)	1 (0.2)

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臨床検査 (Cont.)				
好酸球数増加	0	1 (0.3)	0	1 (0.2)
好酸球百分率増加	0	1 (0.3)	0	1 (0.2)
ヘモグロビン減少	0	0	1 (0.3)	1 (0.2)
単球数増加	0	0	1 (0.3)	1 (0.2)
好中球数減少	0	1 (0.3)	1 (0.3)	2 (0.3)
尿中亜硝酸塩陽性	1 (0.3)	0	0	0
血小板数減少	1 (0.3)	0	0	0
血小板数増加	1 (0.3)	0	0	0
尿中蛋白陽性	1 (0.3)	2 (0.7)	0	2 (0.3)
ブドウ球菌検査陽性	4 (1.3)	0	0	0
尿検査異常	1 (0.3)	0	0	0
ビタミン D 減少	0	0	1 (0.3)	1 (0.2)
体重増加	4 (1.3)	6 (2.0)	5 (1.7)	11 (1.8)
白血球数減少	0	1 (0.3)	0	1 (0.2)
白血球数増加	1 (0.3)	0	0	0
代謝および栄養障害	7 (2.3)	6 (2.0)	8 (2.7)	14 (2.3)
食欲減退	0	2 (0.7)	0	2 (0.3)

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代謝および栄養障害 (Cont.)				
糖尿病	0	0	2 (0.7)	2 (0.3)
脂質異常症	0	0	1 (0.3)	1 (0.2)
痛風	0	1 (0.3)	1 (0.3)	2 (0.3)
高血糖	1 (0.3)	0	0	0
高ホモシステイン血症	0	1 (0.3)	0	1 (0.2)
高脂血症	1 (0.3)	2 (0.7)	2 (0.7)	4 (0.7)
高尿酸血症	3 (1.0)	1 (0.3)	1 (0.3)	2 (0.3)
食欲亢進	2 (0.7)	0	2 (0.7)	2 (0.3)
筋骨格系および結合組織障害	12 (4.0)	17 (5.7)	20 (6.7)	37 (6.2)
関節痛	1 (0.3)	4 (1.3)	3 (1.0)	7 (1.2)
関節炎	0	1 (0.3)	0	1 (0.2)
背部痛	1 (0.3)	2 (0.7)	1 (0.3)	3 (0.5)
骨痛	0	0	1 (0.3)	1 (0.2)
滑液包炎	0	0	2 (0.7)	2 (0.3)
椎間板突出	0	0	1 (0.3)	1 (0.2)
関節ロック	0	0	1 (0.3)	1 (0.2)
関節腫脹	1 (0.3)	0	0	0

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筋骨格系および結合組織障害 (Cont.)				
四肢不快感	0	1 (0.3)	0	1 (0.2)
筋痙縮	2 (0.7)	1 (0.3)	4 (1.3)	5 (0.8)
筋骨格系胸痛	1 (0.3)	0	0	0
筋骨格痛	0	0	1 (0.3)	1 (0.2)
筋骨格硬直	1 (0.3)	0	1 (0.3)	1 (0.2)
筋肉痛	3 (1.0)	4 (1.3)	3 (1.0)	7 (1.2)
頚部痛	0	2 (0.7)	0	2 (0.3)
変形性関節症	1 (0.3)	0	0	0
四肢痛	1 (0.3)	2 (0.7)	3 (1.0)	5 (0.8)
滑液嚢腫	0	0	1 (0.3)	1 (0.2)
顎関節症候群	0	1 (0.3)	0	1 (0.2)
斜頚	0	1 (0.3)	0	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	4 (1.3)	2 (0.7)	5 (1.7)	7 (1.2)
結腸腺癌	0	0	1 (0.3)	1 (0.2)
肛門性器疣贅	1 (0.3)	0	1 (0.3)	1 (0.2)
良性新生物	0	0	1 (0.3)	1 (0.2)
精巣の良性新生物	0	0	1 (0.3)	1 (0.2)

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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.)				
ケラトアカントーマ	0	0	1 (0.3)	1 (0.2)
脂肪腫	1 (0.3)	0	0	0
脂漏性角化症	0	1 (0.3)	0	1 (0.2)
皮膚乳頭腫	2 (0.7)	1 (0.3)	0	1 (0.2)
神経系障害	20 (6.6)	23 (7.7)	23 (7.7)	46 (7.7)
灼熱感	1 (0.3)	0	0	0
脳梗塞	1 (0.3)	0	0	0
注意力障害	0	1 (0.3)	0	1 (0.2)
浮動性めまい	2 (0.7)	6 (2.0)	3 (1.0)	9 (1.5)
体位性めまい	1 (0.3)	0	0	0
味覚不全	0	0	1 (0.3)	1 (0.2)
頭痛	15 (5.0)	15 (5.0)	14 (4.7)	29 (4.9)
過眠症	0	0	1 (0.3)	1 (0.2)
筋緊張亢進	0	0	1 (0.3)	1 (0.2)
感覚鈍麻	0	0	1 (0.3)	1 (0.2)
片頭痛	0	1 (0.3)	1 (0.3)	2 (0.3)
錯感覚	1 (0.3)	0	1 (0.3)	1 (0.2)

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神経系障害 (Cont.)				
失神寸前の状態	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
坐骨神経痛	0	1 (0.3)	0	1 (0.2)
傾眠	0	0	1 (0.3)	1 (0.2)
失神	0	0	1 (0.3)	1 (0.2)
三叉神経痛	0	0	1 (0.3)	1 (0.2)
製品の問題	0	1 (0.3)	0	1 (0.2)
医療機器位置異常	0	1 (0.3)	0	1 (0.2)
精神障害	5 (1.7)	6 (2.0)	15 (5.1)	21 (3.5)
感情不安定	0	1 (0.3)	0	1 (0.2)
不安	1 (0.3)	0	3 (1.0)	3 (0.5)
注意欠陥多動性障害	0	0	1 (0.3)	1 (0.2)
抑うつ気分	0	0	1 (0.3)	1 (0.2)
うつ病	1 (0.3)	0	1 (0.3)	1 (0.2)
不眠症	2 (0.7)	1 (0.3)	3 (1.0)	4 (0.7)
故意の自傷行為	1 (0.3)	0	1 (0.3)	1 (0.2)
易刺激性	0	1 (0.3)	0	1 (0.2)
リビドー減退	0	0	1 (0.3)	1 (0.2)

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精神障害 (Cont.)				
リビドー亢進	0	1 (0.3)	0	1 (0.2)
精神障害	0	0	1 (0.3)	1 (0.2)
混合性不安抑うつ障害	0	0	1 (0.3)	1 (0.2)
悪夢	0	1 (0.3)	0	1 (0.2)
パニック発作	0	1 (0.3)	0	1 (0.2)
心的外傷後ストレス障害	0	0	1 (0.3)	1 (0.2)
睡眠障害	0	0	1 (0.3)	1 (0.2)
ストレス	0	0	1 (0.3)	1 (0.2)
腎および尿路障害	4 (1.3)	6 (2.0)	2 (0.7)	8 (1.3)
急性腎障害	0	1 (0.3)	0	1 (0.2)
排尿困難	0	3 (1.0)	0	3 (0.5)
血尿	0	0	1 (0.3)	1 (0.2)
水腎症	0	1 (0.3)	0	1 (0.2)
腎結石症	0	1 (0.3)	0	1 (0.2)
夜間頻尿	1 (0.3)	1 (0.3)	0	1 (0.2)
多尿	0	1 (0.3)	0	1 (0.2)
蛋白尿	2 (0.7)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
腎および尿路障害 (Cont.)				
腎仙痛	0	0	1 (0.3)	1 (0.2)
腎嚢胞	1 (0.3)	0	0	0
生殖系および乳房障害	3 (1.0)	6 (2.0)	10 (3.4)	16 (2.7)
無月経	1 (0.3)	0	1 (0.3)	1 (0.2)
萎縮性外陰腟炎	0	0	1 (0.3)	1 (0.2)
機能不全性子宮出血	1 (0.3)	0	0	0
勃起不全	0	0	3 (1.0)	3 (0.5)
女性化乳房	0	0	1 (0.3)	1 (0.2)
過少月経	0	1 (0.3)	0	1 (0.2)
月経過多	0	1 (0.3)	0	1 (0.2)
月経障害	0	1 (0.3)	0	1 (0.2)
不規則月経	0	1 (0.3)	0	1 (0.2)
精巣腫瘤	0	0	1 (0.3)	1 (0.2)
精巣痛	0	1 (0.3)	2 (0.7)	3 (0.5)
腟分泌物	0	1 (0.3)	0	1 (0.2)
腟出血	1 (0.3)	0	0	0
女性外陰部潰瘍	0	0	1 (0.3)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
生殖系および乳房障害 (Cont.)				
外陰腟乾燥	0	1 (0.3)	0	1 (0.2)
呼吸器、胸郭および縦隔障害	20 (6.6)	35 (11.7)	32 (10.8)	67 (11.2)
急性呼吸不全	1 (0.3)	0	0	0
喘息	5 (1.7)	6 (2.0)	2 (0.7)	8 (1.3)
カタル	1 (0.3)	3 (1.0)	3 (1.0)	6 (1.0)
咳嗽	4 (1.3)	13 (4.3)	11 (3.7)	24 (4.0)
呼吸困難	0	1 (0.3)	1 (0.3)	2 (0.3)
鼻出血	1 (0.3)	3 (1.0)	3 (1.0)	6 (1.0)
喀血	0	1 (0.3)	0	1 (0.2)
鼻閉	0	0	1 (0.3)	1 (0.2)
口腔咽頭痛	3 (1.0)	6 (2.0)	9 (3.0)	15 (2.5)
咽頭腫脹	0	0	1 (0.3)	1 (0.2)
胸水	0	1 (0.3)	0	1 (0.2)
湿性咳嗽	1 (0.3)	1 (0.3)	0	1 (0.2)
気道うっ血	0	0	2 (0.7)	2 (0.3)
アレルギー性鼻炎	2 (0.7)	0	2 (0.7)	2 (0.3)
鼻漏	1 (0.3)	5 (1.7)	2 (0.7)	7 (1.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
副鼻腔うっ血	2 (0.7)	1 (0.3)	2 (0.7)	3 (0.5)
喘息発作重積	0	1 (0.3)	0	1 (0.2)
咽喉刺激感	0	0	1 (0.3)	1 (0.2)
上気道うっ血	0	1 (0.3)	0	1 (0.2)
皮膚および皮下組織障害	40 (13.2)	66 (22.0)	72 (24.2)	138 (23.1)
ざ瘡	6 (2.0)	30 (10.0)	41 (13.8)	71 (11.9)
脱毛症	1 (0.3)	1 (0.3)	0	1 (0.2)
円形脱毛症	1 (0.3)	0	0	0
血管浮腫	0	0	1 (0.3)	1 (0.2)
水疱	2 (0.7)	1 (0.3)	1 (0.3)	2 (0.3)
冷汗	1 (0.3)	0	0	0
皮膚炎	0	2 (0.7)	0	2 (0.3)
ざ瘡様皮膚炎	0	2 (0.7)	3 (1.0)	5 (0.8)
アレルギー性皮膚炎	0	1 (0.3)	0	1 (0.2)
アトピー性皮膚炎	20 (6.6)	11 (3.7)	2 (0.7)	13 (2.2)
接触皮膚炎	1 (0.3)	0	1 (0.3)	1 (0.2)
全身性剥脱性皮膚炎	2 (0.7)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
皮膚および皮下組織障害 (Cont.)				
異汗性湿疹	1 (0.3)	1 (0.3)	0	1 (0.2)
斑状出血	0	0	1 (0.3)	1 (0.2)
湿疹	3 (1.0)	5 (1.7)	2 (0.7)	7 (1.2)
紅斑	1 (0.3)	0	0	0
紅皮症型アトピー性皮膚炎	1 (0.3)	0	0	0
過剰肉芽組織	0	1 (0.3)	0	1 (0.2)
毛髪成長異常	2 (0.7)	1 (0.3)	0	1 (0.2)
汗腺炎	0	0	1 (0.3)	1 (0.2)
多汗症	0	2 (0.7)	1 (0.3)	3 (0.5)
過角化	0	1 (0.3)	0	1 (0.2)
多毛症	0	1 (0.3)	1 (0.3)	2 (0.3)
網状皮斑	0	0	1 (0.3)	1 (0.2)
稗粒腫	0	0	1 (0.3)	1 (0.2)
汗疹	0	0	1 (0.3)	1 (0.2)
丘疹	1 (0.3)	0	0	0
口囲皮膚炎	0	1 (0.3)	2 (0.7)	3 (0.5)
そう痒症	6 (2.0)	2 (0.7)	0	2 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
皮膚および皮下組織障害 (Cont.)				
紫斑	0	1 (0.3)	0	1 (0.2)
発疹	1 (0.3)	3 (1.0)	0	3 (0.5)
斑状丘疹状皮疹	0	0	1 (0.3)	1 (0.2)
丘疹性皮疹	0	1 (0.3)	2 (0.7)	3 (0.5)
そう痒性皮疹	0	1 (0.3)	0	1 (0.2)
小水疱性皮疹	0	1 (0.3)	0	1 (0.2)
酒さ	0	1 (0.3)	3 (1.0)	4 (0.7)
痂皮	0	0	1 (0.3)	1 (0.2)
脂腺過形成	1 (0.3)	0	0	0
脂漏	0	1 (0.3)	1 (0.3)	2 (0.3)
脂漏性皮膚炎	0	0	1 (0.3)	1 (0.2)
敏感肌	0	1 (0.3)	0	1 (0.2)
皮膚障害	0	0	1 (0.3)	1 (0.2)
皮膚亀裂	0	0	2 (0.7)	2 (0.3)
皮膚刺激	0	2 (0.7)	0	2 (0.3)
皮膚腫瘤	0	0	1 (0.3)	1 (0.2)
皮膚腫脹	0	0	1 (0.3)	1 (0.2)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
皮膚および皮下組織障害 (Cont.)				
皮膚潰瘍	1 (0.3)	0	0	0
皮膚熱感	0	1 (0.3)	0	1 (0.2)
日光黒子	0	1 (0.3)	0	1 (0.2)
蕁麻疹	0	2 (0.7)	8 (2.7)	10 (1.7)
血管障害	5 (1.7)	5 (1.7)	6 (2.0)	11 (1.8)
血腫	1 (0.3)	1 (0.3)	0	1 (0.2)
ほてり	1 (0.3)	0	1 (0.3)	1 (0.2)
高血圧	3 (1.0)	3 (1.0)	4 (1.3)	7 (1.2)
起立性低血圧	0	1 (0.3)	0	1 (0.2)
レイノー現象	0	0	1 (0.3)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.6.1.1

表 2. 二重盲検投与期で有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（二重盲検投与期の安全性解析対象集団，青少年）

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=39) n (%)	Active UPA 15 mg QD + TCS (N=39) n (%)	Active UPA 30 mg QD + TCS (N=37) n (%)	Active Total (N=76) n (%)
Any adverse event	17 (43.6)	27 (69.2)	31 (83.8)	58 (76.3)
血液およびリンパ系障害	0	1 (2.6)	0	1 (1.3)
リンパ節症	0	1 (2.6)	0	1 (1.3)
耳および迷路障害	0	1 (2.6)	0	1 (1.3)
耳痛	0	1 (2.6)	0	1 (1.3)
眼障害	0	0	1 (2.7)	1 (1.3)
春季カタル	0	0	1 (2.7)	1 (1.3)
胃腸障害	5 (12.8)	6 (15.4)	9 (24.3)	15 (19.7)
腹痛	0	0	3 (8.1)	3 (3.9)
上腹部痛	0	2 (5.1)	1 (2.7)	3 (3.9)
便秘	0	0	1 (2.7)	1 (1.3)
下痢	3 (7.7)	1 (2.6)	3 (8.1)	4 (5.3)
消化不良	0	1 (2.6)	1 (2.7)	2 (2.6)
変色便	0	1 (2.6)	0	1 (1.3)
口唇水疱	1 (2.6)	0	0	0
悪心	0	1 (2.6)	1 (2.7)	2 (2.6)
嘔吐	1 (2.6)	1 (2.6)	3 (8.1)	4 (5.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=39) n (%)	Active UPA 15 mg QD + TCS (N=39) n (%)	Active UPA 30 mg QD + TCS (N=37) n (%)	Active Total (N=76) n (%)
一般・全身障害および投与部位の状態	0	2 (5.1)	4 (10.8)	6 (7.9)
顔面痛	0	1 (2.6)	0	1 (1.3)
インフルエンザ様疾患	0	1 (2.6)	1 (2.7)	2 (2.6)
発熱	0	0	3 (8.1)	3 (3.9)
肝胆道系障害	0	1 (2.6)	0	1 (1.3)
肝機能異常	0	1 (2.6)	0	1 (1.3)
免疫系障害	1 (2.6)	0	1 (2.7)	1 (1.3)
過敏症	0	0	1 (2.7)	1 (1.3)
季節性アレルギー	1 (2.6)	0	0	0
感染症および寄生虫症	11 (28.2)	16 (41.0)	21 (56.8)	37 (48.7)
膿疱性ざ瘡	0	1 (2.6)	1 (2.7)	2 (2.6)
細菌尿	1 (2.6)	0	0	0
気管支炎	0	1 (2.6)	0	1 (1.3)
結膜炎	0	1 (2.6)	0	1 (1.3)
耳感染	1 (2.6)	1 (2.6)	0	1 (1.3)
毛包炎	0	0	2 (5.4)	2 (2.6)
せつ	0	2 (5.1)	0	2 (2.6)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=39) n (%)	Active UPA 15 mg QD + TCS (N=39) n (%)	Active UPA 30 mg QD + TCS (N=37) n (%)	Active Total (N=76) n (%)
感染症および寄生虫症 (Cont.)				
胃腸炎	0	1 (2.6)	0	1 (1.3)
単純ヘルペス	0	1 (2.6)	0	1 (1.3)
帯状疱疹	0	0	1 (2.7)	1 (1.3)
膿痂疹	0	1 (2.6)	1 (2.7)	2 (2.6)
インフルエンザ	0	1 (2.6)	2 (5.4)	3 (3.9)
シラミ寄生	0	0	1 (2.7)	1 (1.3)
上咽頭炎	3 (7.7)	6 (15.4)	3 (8.1)	9 (11.8)
口腔ヘルペス	0	1 (2.6)	1 (2.7)	2 (2.6)
中耳炎	1 (2.6)	0	0	0
咽頭炎	0	1 (2.6)	2 (5.4)	3 (3.9)
レンサ球菌性咽頭炎	0	0	1 (2.7)	1 (1.3)
副鼻腔炎	1 (2.6)	0	0	0
皮膚感染	2 (5.1)	0	1 (2.7)	1 (1.3)
ブドウ球菌感染	0	1 (2.6)	0	1 (1.3)
ブドウ球菌皮膚感染	2 (5.1)	0	1 (2.7)	1 (1.3)
重複感染	1 (2.6)	0	0	0
白癬感染	1 (2.6)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=39) n (%)	Active UPA 15 mg QD + TCS (N=39) n (%)	Active UPA 30 mg QD + TCS (N=37) n (%)	Active Total (N=76) n (%)
感染症および寄生虫症 (Cont.)				
扁桃炎	0	0	1 (2.7)	1 (1.3)
上気道感染	1 (2.6)	1 (2.6)	4 (10.8)	5 (6.6)
尿路感染	0	0	1 (2.7)	1 (1.3)
ウイルス性上気道感染	1 (2.6)	0	2 (5.4)	2 (2.6)
傷害、中毒および処置合併症	1 (2.6)	0	1 (2.7)	1 (1.3)
事故	0	0	1 (2.7)	1 (1.3)
頭部損傷	1 (2.6)	0	0	0
損傷	0	0	1 (2.7)	1 (1.3)
橈骨骨折	0	0	1 (2.7)	1 (1.3)
臨床検査	4 (10.3)	3 (7.7)	6 (16.2)	9 (11.8)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (2.6)	0	1 (1.3)
血中コレステロール増加	0	1 (2.6)	0	1 (1.3)
血中クレアチンホスホキナーゼ増加	0	1 (2.6)	2 (5.4)	3 (3.9)
血中免疫グロブリンＥ増加	1 (2.6)	0	0	0
血中トリグリセリド増加	0	1 (2.6)	1 (2.7)	2 (2.6)
血中尿酸増加	0	1 (2.6)	0	1 (1.3)
好酸球数増加	0	1 (2.6)	0	1 (1.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=39) n (%)	Active UPA 15 mg QD + TCS (N=39) n (%)	Active UPA 30 mg QD + TCS (N=37) n (%)	Active Total (N=76) n (%)
臨床検査 (Cont.)				
好酸球百分率増加	0	1 (2.6)	0	1 (1.3)
好中球数減少	0	0	1 (2.7)	1 (1.3)
尿中蛋白陽性	0	1 (2.6)	0	1 (1.3)
ブドウ球菌検査陽性	2 (5.1)	0	0	0
体重増加	1 (2.6)	0	2 (5.4)	2 (2.6)
代謝および栄養障害	0	3 (7.7)	0	3 (3.9)
食欲減退	0	2 (5.1)	0	2 (2.6)
高脂血症	0	1 (2.6)	0	1 (1.3)
筋骨格系および結合組織障害	1 (2.6)	1 (2.6)	0	1 (1.3)
筋肉痛	1 (2.6)	0	0	0
顎関節症候群	0	1 (2.6)	0	1 (1.3)
神経系障害	3 (7.7)	4 (10.3)	4 (10.8)	8 (10.5)
頭痛	3 (7.7)	4 (10.3)	3 (8.1)	7 (9.2)
片頭痛	0	0	1 (2.7)	1 (1.3)
失神寸前の状態	0	0	1 (2.7)	1 (1.3)
精神障害	1 (2.6)	1 (2.6)	1 (2.7)	2 (2.6)
注意欠陥多動性障害	0	0	1 (2.7)	1 (1.3)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=39) n (%)	Active UPA 15 mg QD + TCS (N=39) n (%)	Active UPA 30 mg QD + TCS (N=37) n (%)	Active Total (N=76) n (%)
精神障害 (Cont.)				
不眠症	1 (2.6)	0	0	0
悪夢	0	1 (2.6)	0	1 (1.3)
呼吸器、胸郭および縦隔障害	1 (2.6)	7 (17.9)	5 (13.5)	12 (15.8)
喘息	0	0	1 (2.7)	1 (1.3)
カタル	1 (2.6)	1 (2.6)	3 (8.1)	4 (5.3)
咳嗽	0	3 (7.7)	1 (2.7)	4 (5.3)
鼻出血	0	1 (2.6)	0	1 (1.3)
口腔咽頭痛	0	1 (2.6)	1 (2.7)	2 (2.6)
鼻漏	0	2 (5.1)	1 (2.7)	3 (3.9)
副鼻腔うっ血	0	1 (2.6)	0	1 (1.3)
皮膚および皮下組織障害	3 (7.7)	11 (28.2)	7 (18.9)	18 (23.7)
ざ瘡	0	5 (12.8)	5 (13.5)	10 (13.2)
ざ瘡様皮膚炎	0	0	1 (2.7)	1 (1.3)
アトピー性皮膚炎	2 (5.1)	3 (7.7)	0	3 (3.9)
異汗性湿疹	1 (2.6)	1 (2.6)	0	1 (1.3)
湿疹	1 (2.6)	0	0	0
そう痒症	0	1 (2.6)	0	1 (1.3)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=39) n (%)	Active UPA 15 mg QD + TCS (N=39) n (%)	Active UPA 30 mg QD + TCS (N=37) n (%)	Total (N=76) n (%)
皮膚および皮下組織障害 (Cont.)				
発疹	0	1 (2.6)	0	1 (1.3)
蕁麻疹	0	0	1 (2.7)	1 (1.3)
血管障害	0	0	1 (2.7)	1 (1.3)
高血圧	0	0	1 (2.7)	1 (1.3)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.6.1.2

表 3. 二重盲検投与期で有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（二重盲検投与期の安全性解析対象集団，成人）

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
Any adverse event	173 (65.5)	173 (66.3)	184 (70.8)	357 (68.5)
血液およびリンパ系障害	4 (1.5)	3 (1.1)	8 (3.1)	11 (2.1)
貧血	1 (0.4)	0	2 (0.8)	2 (0.4)
白血球増加症	0	1 (0.4)	0	1 (0.2)
白血球減少症	0	1 (0.4)	1 (0.4)	2 (0.4)
リンパ節症	1 (0.4)	1 (0.4)	1 (0.4)	2 (0.4)
リンパ球増加症	0	0	1 (0.4)	1 (0.2)
リンパ球減少症	1 (0.4)	0	0	0
好中球減少症	0	1 (0.4)	2 (0.8)	3 (0.6)
汎血球減少症	0	0	1 (0.4)	1 (0.2)
特発性血腫	1 (0.4)	0	0	0
血小板増加症	0	0	1 (0.4)	1 (0.2)
心臓障害	0	1 (0.4)	3 (1.2)	4 (0.8)
うっ血性心不全	0	0	1 (0.4)	1 (0.2)
動悸	0	1 (0.4)	1 (0.4)	2 (0.4)
洞性徐脈	0	0	1 (0.4)	1 (0.2)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
先天性、家族性および遺伝性障害	0	1 (0.4)	1 (0.4)	2 (0.4)
ジルベール症候群	0	0	1 (0.4)	1 (0.2)
色素性網膜炎	0	1 (0.4)	0	1 (0.2)
耳および迷路障害	2 (0.8)	3 (1.1)	0	3 (0.6)
耳の障害	0	1 (0.4)	0	1 (0.2)
耳痛	2 (0.8)	2 (0.8)	0	2 (0.4)
回転性めまい	0	1 (0.4)	0	1 (0.2)
内分泌障害	0	1 (0.4)	0	1 (0.2)
甲状腺機能低下症	0	1 (0.4)	0	1 (0.2)
眼障害	8 (3.0)	9 (3.4)	12 (4.6)	21 (4.0)
アトピー性角結膜炎	1 (0.4)	0	0	0
眼瞼炎	1 (0.4)	1 (0.4)	1 (0.4)	2 (0.4)
白内障	0	0	1 (0.4)	1 (0.2)
結膜刺激	0	0	1 (0.4)	1 (0.2)
アレルギー性結膜炎	1 (0.4)	0	2 (0.8)	2 (0.4)
ドライアイ	0	2 (0.8)	1 (0.4)	3 (0.6)
眼の炎症	0	0	1 (0.4)	1 (0.2)
眼痛	0	1 (0.4)	0	1 (0.2)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
眼障害 (Cont.)				
眼の異常感覚	0	0	1 (0.4)	1 (0.2)
眼瞼障害	0	0	1 (0.4)	1 (0.2)
流涙増加	0	2 (0.8)	0	2 (0.4)
非感染性結膜炎	1 (0.4)	0	0	0
視神経乳頭浮腫	0	0	1 (0.4)	1 (0.2)
羞明	1 (0.4)	0	1 (0.4)	1 (0.2)
網膜動脈閉塞	1 (0.4)	0	0	0
網膜剥離	0	1 (0.4)	0	1 (0.2)
裂孔原性網膜剥離	1 (0.4)	0	0	0
閃輝暗点	1 (0.4)	0	0	0
霧視	1 (0.4)	3 (1.1)	1 (0.4)	4 (0.8)
硝子体剥離	0	0	1 (0.4)	1 (0.2)
胃腸障害	20 (7.6)	38 (14.6)	38 (14.6)	76 (14.6)
腹部不快感	1 (0.4)	1 (0.4)	1 (0.4)	2 (0.4)
腹部膨満	1 (0.4)	2 (0.8)	2 (0.8)	4 (0.8)
腹痛	0	6 (2.3)	2 (0.8)	8 (1.5)
上腹部痛	1 (0.4)	9 (3.4)	2 (0.8)	11 (2.1)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
胃腸障害 (Cont.)				
口角口唇炎	0	0	2 (0.8)	2 (0.4)
肛門直腸不快感	0	0	1 (0.4)	1 (0.2)
アフタ性潰瘍	0	0	1 (0.4)	1 (0.2)
便習慣変化	0	0	1 (0.4)	1 (0.2)
大腸炎	1 (0.4)	0	0	0
便秘	1 (0.4)	5 (1.9)	3 (1.2)	8 (1.5)
齲歯	0	2 (0.8)	2 (0.8)	4 (0.8)
下痢	4 (1.5)	10 (3.8)	9 (3.5)	19 (3.6)
口内乾燥	2 (0.8)	0	0	0
消化不良	0	5 (1.9)	3 (1.2)	8 (1.5)
嚥下障害	0	0	1 (0.4)	1 (0.2)
腸炎	1 (0.4)	0	0	0
白色便	0	1 (0.4)	0	1 (0.2)
鼓腸	2 (0.8)	0	0	0
食中毒	2 (0.8)	0	0	0
排便回数増加	0	0	1 (0.4)	1 (0.2)
胃炎	1 (0.4)	1 (0.4)	0	1 (0.2)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
胃腸障害 (Cont.)				
胃腸障害	0	1 (0.4)	0	1 (0.2)
胃腸粘膜障害	0	1 (0.4)	0	1 (0.2)
胃食道逆流性疾患	0	1 (0.4)	3 (1.2)	4 (0.8)
痔核	0	0	1 (0.4)	1 (0.2)
裂孔ヘルニア	0	0	1 (0.4)	1 (0.2)
過敏性腸症候群	0	0	1 (0.4)	1 (0.2)
口唇水疱	0	1 (0.4)	0	1 (0.2)
口腔内潰瘍形成	0	2 (0.8)	0	2 (0.4)
粘液便	1 (0.4)	0	0	0
悪心	0	7 (2.7)	5 (1.9)	12 (2.3)
口腔そう痒症	0	0	1 (0.4)	1 (0.2)
膵炎	0	1 (0.4)	0	1 (0.2)
無髄歯	0	0	1 (0.4)	1 (0.2)
レッチング	0	0	1 (0.4)	1 (0.2)
歯の障害	0	0	1 (0.4)	1 (0.2)
埋伏歯	1 (0.4)	0	2 (0.8)	2 (0.4)
歯痛	1 (0.4)	1 (0.4)	3 (1.2)	4 (0.8)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
胃腸障害 (Cont.)				
嘔吐	2 (0.8)	1 (0.4)	0	1 (0.2)
一般・全身障害および投与部位の状態	13 (4.9)	21 (8.0)	17 (6.5)	38 (7.3)
胸痛	1 (0.4)	2 (0.8)	0	2 (0.4)
悪寒	1 (0.4)	1 (0.4)	0	1 (0.2)
嚢胞	0	0	1 (0.4)	1 (0.2)
顔面痛	0	1 (0.4)	0	1 (0.2)
疲労	0	3 (1.1)	4 (1.5)	7 (1.3)
熱感	0	1 (0.4)	0	1 (0.2)
治癒不良	0	0	1 (0.4)	1 (0.2)
炎症	1 (0.4)	0	0	0
インフルエンザ様疾患	4 (1.5)	3 (1.1)	5 (1.9)	8 (1.5)
非心臓性胸痛	0	0	1 (0.4)	1 (0.2)
浮腫	1 (0.4)	0	0	0
末梢性浮腫	2 (0.8)	1 (0.4)	0	1 (0.2)
疼痛	0	3 (1.1)	1 (0.4)	4 (0.8)
発熱	3 (1.1)	5 (1.9)	3 (1.2)	8 (1.5)
顔面腫脹	0	1 (0.4)	0	1 (0.2)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
血管ステント血栓症	1 (0.4)	0	0	0
血管穿刺部位内出血	0	0	1 (0.4)	1 (0.2)
肝胆道系障害	1 (0.4)	0	1 (0.4)	1 (0.2)
胆石症	1 (0.4)	0	0	0
肝機能異常	0	0	1 (0.4)	1 (0.2)
免疫系障害	4 (1.5)	1 (0.4)	1 (0.4)	2 (0.4)
動物アレルギー	1 (0.4)	0	0	0
アナフィラキシー反応	1 (0.4)	0	1 (0.4)	1 (0.2)
薬物過敏症	0	1 (0.4)	0	1 (0.2)
食物アレルギー	1 (0.4)	0	0	0
季節性アレルギー	1 (0.4)	0	0	0
感染症および寄生虫症	102 (38.6)	113 (43.3)	116 (44.6)	229 (44.0)
腹部膿瘍	1 (0.4)	0	0	0
四肢膿瘍	0	0	1 (0.4)	1 (0.2)
口腔膿瘍	0	0	1 (0.4)	1 (0.2)
ダニ皮膚炎	0	0	1 (0.4)	1 (0.2)
肛門膿瘍	1 (0.4)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
感染症および寄生虫症 (Cont.)				
虫垂炎	0	1 (0.4)	0	1 (0.2)
細菌感染	0	1 (0.4)	1 (0.4)	2 (0.4)
細菌性膣症	0	1 (0.4)	0	1 (0.2)
細菌性外陰膣炎	1 (0.4)	0	0	0
細菌尿	0	0	1 (0.4)	1 (0.2)
体部白癬	0	0	1 (0.4)	1 (0.2)
気管支炎	3 (1.1)	1 (0.4)	3 (1.2)	4 (0.8)
ウイルス性気管支炎	1 (0.4)	0	0	0
蜂巣炎	2 (0.8)	1 (0.4)	0	1 (0.2)
結膜炎	5 (1.9)	2 (0.8)	2 (0.8)	4 (0.8)
細菌性結膜炎	0	1 (0.4)	1 (0.4)	2 (0.4)
膀胱炎	1 (0.4)	1 (0.4)	1 (0.4)	2 (0.4)
感染性下痢	0	0	1 (0.4)	1 (0.2)
ヘルペス性状湿疹	0	2 (0.8)	3 (1.2)	5 (1.0)
心内膜炎	1 (0.4)	0	0	0
蟯虫症	0	1 (0.4)	0	1 (0.2)
丹毒	2 (0.8)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
感染症および寄生虫症 (Cont.)				
眼感染	1 (0.4)	0	0	0
眼瞼感染	0	1 (0.4)	0	1 (0.2)
毛包炎	3 (1.1)	8 (3.1)	9 (3.5)	17 (3.3)
皮膚真菌感染	0	1 (0.4)	0	1 (0.2)
せつ	0	0	1 (0.4)	1 (0.2)
胃腸炎	6 (2.3)	5 (1.9)	1 (0.4)	6 (1.2)
ウイルス性胃腸炎	1 (0.4)	0	1 (0.4)	1 (0.2)
消化管感染	0	1 (0.4)	0	1 (0.2)
陰部ヘルペス	0	0	1 (0.4)	1 (0.2)
歯肉炎	0	1 (0.4)	1 (0.4)	2 (0.4)
ヘリコバクター性胃炎	1 (0.4)	0	0	0
ヘルペス眼感染	0	0	1 (0.4)	1 (0.2)
単純ヘルペス	1 (0.4)	5 (1.9)	6 (2.3)	11 (2.1)
帯状疱疹	3 (1.1)	3 (1.1)	4 (1.5)	7 (1.3)
麦粒腫	0	1 (0.4)	3 (1.2)	4 (0.8)
膿痂疹	2 (0.8)	0	1 (0.4)	1 (0.2)
インフルエンザ	2 (0.8)	10 (3.8)	5 (1.9)	15 (2.9)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
感染症および寄生虫症 (Cont.)				
カポジ水痘様発疹	0	1 (0.4)	1 (0.4)	2 (0.4)
喉頭炎	0	1 (0.4)	0	1 (0.2)
下気道感染	1 (0.4)	0	0	0
細菌性乳腺炎	0	1 (0.4)	0	1 (0.2)
鼻ヘルペス	0	0	2 (0.8)	2 (0.4)
上咽頭炎	31 (11.7)	31 (11.9)	37 (14.2)	68 (13.1)
爪真菌症	0	1 (0.4)	1 (0.4)	2 (0.4)
眼部単純ヘルペス	0	0	3 (1.2)	3 (0.6)
口腔カンジダ症	0	1 (0.4)	1 (0.4)	2 (0.4)
口腔ヘルペス	5 (1.9)	9 (3.4)	22 (8.5)	31 (6.0)
外耳炎	1 (0.4)	2 (0.8)	1 (0.4)	3 (0.6)
中耳炎	0	1 (0.4)	1 (0.4)	2 (0.4)
扁桃周囲膿瘍	0	1 (0.4)	0	1 (0.2)
咽頭炎	1 (0.4)	5 (1.9)	2 (0.8)	7 (1.3)
レンサ球菌性咽頭炎	1 (0.4)	1 (0.4)	0	1 (0.2)
肺炎	1 (0.4)	1 (0.4)	0	1 (0.2)
マイコプラズマ性肺炎	0	0	1 (0.4)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
感染症および寄生虫症 (Cont.)				
ウイルス感染後疲労症候群	0	0	1 (0.4)	1 (0.2)
歯髄炎	1 (0.4)	0	0	0
膿疱	1 (0.4)	0	2 (0.8)	2 (0.4)
気道感染	1 (0.4)	0	1 (0.4)	1 (0.2)
ウイルス性気道感染	0	1 (0.4)	0	1 (0.2)
鼻炎	1 (0.4)	3 (1.1)	0	3 (0.6)
鼻咽頭炎	0	0	1 (0.4)	1 (0.2)
副鼻腔炎	4 (1.5)	1 (0.4)	3 (1.2)	4 (0.8)
皮膚細菌感染	2 (0.8)	1 (0.4)	1 (0.4)	2 (0.4)
皮膚カンジダ	1 (0.4)	0	0	0
皮膚感染	3 (1.1)	1 (0.4)	0	1 (0.2)
膿性痰	0	1 (0.4)	0	1 (0.2)
ブドウ球菌感染	0	0	1 (0.4)	1 (0.2)
ブドウ球菌性敗血症	1 (0.4)	0	0	0
ブドウ球菌皮膚感染	1 (0.4)	1 (0.4)	1 (0.4)	2 (0.4)
細菌重複感染	1 (0.4)	0	0	0
須毛瘡	1 (0.4)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
感染症および寄生虫症 (Cont.)				
股部白癬	0	0	1 (0.4)	1 (0.2)
白癬感染	1 (0.4)	0	0	0
足部白癬	0	1 (0.4)	1 (0.4)	2 (0.4)
癜風	1 (0.4)	0	0	0
扁桃炎	2 (0.8)	2 (0.8)	0	2 (0.4)
歯感染	1 (0.4)	2 (0.8)	0	2 (0.4)
気管炎	0	1 (0.4)	0	1 (0.2)
気管気管支炎	0	1 (0.4)	0	1 (0.2)
トリコフィトン感染症	0	1 (0.4)	0	1 (0.2)
上気道感染	21 (8.0)	20 (7.7)	19 (7.3)	39 (7.5)
尿路感染	6 (2.3)	5 (1.9)	10 (3.8)	15 (2.9)
細菌性尿路感染	0	0	1 (0.4)	1 (0.2)
腟感染	0	1 (0.4)	1 (0.4)	2 (0.4)
ガードネレラ菌性腟炎	1 (0.4)	0	0	0
ウイルス感染	0	1 (0.4)	0	1 (0.2)
ウイルス性上気道感染	3 (1.1)	5 (1.9)	3 (1.2)	8 (1.5)
外陰部腟カンジダ症	1 (0.4)	1 (0.4)	1 (0.4)	2 (0.4)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
感染症および寄生虫症 (Cont.)				
外陰腟真菌感染	0	0	1 (0.4)	1 (0.2)
創傷感染	1 (0.4)	0	0	0
傷害、中毒および処置合併症	9 (3.4)	10 (3.8)	18 (6.9)	28 (5.4)
動物咬傷	1 (0.4)	0	0	0
節足動物咬傷	1 (0.4)	0	1 (0.4)	1 (0.2)
軟骨損傷	0	0	1 (0.4)	1 (0.2)
胸部損傷	0	0	1 (0.4)	1 (0.2)
挫傷	1 (0.4)	0	3 (1.2)	3 (0.6)
角膜擦過傷	0	0	1 (0.4)	1 (0.2)
転倒	1 (0.4)	1 (0.4)	2 (0.8)	3 (0.6)
損傷	0	1 (0.4)	0	1 (0.2)
関節損傷	0	0	1 (0.4)	1 (0.2)
四肢損傷	0	3 (1.1)	0	3 (0.6)
半月板損傷	1 (0.4)	1 (0.4)	0	1 (0.2)
肉離れ	3 (1.1)	1 (0.4)	3 (1.2)	4 (0.8)
過量投与	0	1 (0.4)	0	1 (0.2)
処置による疼痛	0	0	1 (0.4)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
傷害、中毒および処置合併症 (Cont.)				
肋骨骨折	0	1 (0.4)	0	1 (0.2)
交通事故	0	0	1 (0.4)	1 (0.2)
皮膚擦過傷	1 (0.4)	1 (0.4)	1 (0.4)	2 (0.4)
皮膚裂傷	0	1 (0.4)	0	1 (0.2)
腱損傷	0	0	1 (0.4)	1 (0.2)
歯牙破折	0	1 (0.4)	1 (0.4)	2 (0.4)
外傷性血腫	0	1 (0.4)	0	1 (0.2)
創傷	0	0	1 (0.4)	1 (0.2)
臨床検査	23 (8.7)	23 (8.8)	25 (9.6)	48 (9.2)
アラニンアミノトランスフェラーゼ増加	4 (1.5)	3 (1.1)	2 (0.8)	5 (1.0)
アスパラギン酸アミノトランスフェラーゼ増加	4 (1.5)	1 (0.4)	2 (0.8)	3 (0.6)
血中重炭酸塩減少	0	0	1 (0.4)	1 (0.2)
血中ビリルビン増加	0	1 (0.4)	0	1 (0.2)
血中クロール減少	1 (0.4)	0	0	0
血中クレアチンホスホキナーゼ増加	7 (2.7)	12 (4.6)	16 (6.2)	28 (5.4)
血中クレアチニン増加	1 (0.4)	0	0	0
血中免疫グロブリン E 増加	1 (0.4)	1 (0.4)	0	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
臨床検査 (Cont.)				
血中リン減少	1 (0.4)	0	0	0
血圧上昇	1 (0.4)	0	0	0
血中ナトリウム減少	1 (0.4)	0	0	0
体温上昇	0	0	1 (0.4)	1 (0.2)
ヘモグロビン減少	0	0	1 (0.4)	1 (0.2)
単球数増加	0	0	1 (0.4)	1 (0.2)
好中球数減少	0	1 (0.4)	0	1 (0.2)
尿中亜硝酸塩陽性	1 (0.4)	0	0	0
血小板数減少	1 (0.4)	0	0	0
血小板数増加	1 (0.4)	0	0	0
尿中蛋白陽性	1 (0.4)	1 (0.4)	0	1 (0.2)
ブドウ球菌検査陽性	2 (0.8)	0	0	0
尿検査異常	1 (0.4)	0	0	0
ビタミン D 減少	0	0	1 (0.4)	1 (0.2)
体重増加	3 (1.1)	6 (2.3)	3 (1.2)	9 (1.7)
白血球数減少	0	1 (0.4)	0	1 (0.2)
白血球数増加	1 (0.4)	0	0	0

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
代謝および栄養障害	7 (2.7)	3 (1.1)	8 (3.1)	11 (2.1)
糖尿病	0	0	2 (0.8)	2 (0.4)
脂質異常症	0	0	1 (0.4)	1 (0.2)
痛風	0	1 (0.4)	1 (0.4)	2 (0.4)
高血糖	1 (0.4)	0	0	0
高ホモシステイン血症	0	1 (0.4)	0	1 (0.2)
高脂血症	1 (0.4)	1 (0.4)	2 (0.8)	3 (0.6)
高尿酸血症	3 (1.1)	1 (0.4)	1 (0.4)	2 (0.4)
食欲亢進	2 (0.8)	0	2 (0.8)	2 (0.4)
筋骨格系および結合組織障害	11 (4.2)	16 (6.1)	20 (7.7)	36 (6.9)
関節痛	1 (0.4)	4 (1.5)	3 (1.2)	7 (1.3)
関節炎	0	1 (0.4)	0	1 (0.2)
背部痛	1 (0.4)	2 (0.8)	1 (0.4)	3 (0.6)
骨痛	0	0	1 (0.4)	1 (0.2)
滑液包炎	0	0	2 (0.8)	2 (0.4)
椎間板突出	0	0	1 (0.4)	1 (0.2)
関節ロック	0	0	1 (0.4)	1 (0.2)

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筋骨格系および結合組織障害 (Cont.)				
関節腫脹	1 (0.4)	0	0	0
四肢不快感	0	1 (0.4)	0	1 (0.2)
筋痙縮	2 (0.8)	1 (0.4)	4 (1.5)	5 (1.0)
筋骨格系胸痛	1 (0.4)	0	0	0
筋骨格痛	0	0	1 (0.4)	1 (0.2)
筋骨格硬直	1 (0.4)	0	1 (0.4)	1 (0.2)
筋肉痛	2 (0.8)	4 (1.5)	3 (1.2)	7 (1.3)
頚部痛	0	2 (0.8)	0	2 (0.4)
変形性関節症	1 (0.4)	0	0	0
四肢痛	1 (0.4)	2 (0.8)	3 (1.2)	5 (1.0)
滑液嚢腫	0	0	1 (0.4)	1 (0.2)
斜頚	0	1 (0.4)	0	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	4 (1.5)	2 (0.8)	5 (1.9)	7 (1.3)
結腸腺癌	0	0	1 (0.4)	1 (0.2)
肛門性器疣贅	1 (0.4)	0	1 (0.4)	1 (0.2)
良性新生物	0	0	1 (0.4)	1 (0.2)
精巣の良性新生物	0	0	1 (0.4)	1 (0.2)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) 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.)				
ケラトアカントーマ	0	0	1 (0.4)	1 (0.2)
脂肪腫	1 (0.4)	0	0	0
脂漏性角化症	0	1 (0.4)	0	1 (0.2)
皮膚乳頭腫	2 (0.8)	1 (0.4)	0	1 (0.2)
神経系障害	17 (6.4)	19 (7.3)	19 (7.3)	38 (7.3)
灼熱感	1 (0.4)	0	0	0
脳梗塞	1 (0.4)	0	0	0
注意力障害	0	1 (0.4)	0	1 (0.2)
浮動性めまい	2 (0.8)	6 (2.3)	3 (1.2)	9 (1.7)
体位性めまい	1 (0.4)	0	0	0
味覚不全	0	0	1 (0.4)	1 (0.2)
頭痛	12 (4.5)	11 (4.2)	11 (4.2)	22 (4.2)
過眠症	0	0	1 (0.4)	1 (0.2)
筋緊張亢進	0	0	1 (0.4)	1 (0.2)
感覚鈍麻	0	0	1 (0.4)	1 (0.2)
片頭痛	0	1 (0.4)	0	1 (0.2)
錯感覚	1 (0.4)	0	1 (0.4)	1 (0.2)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
神経系障害 (Cont.)				
失神寸前の状態	1 (0.4)	1 (0.4)	0	1 (0.2)
坐骨神経痛	0	1 (0.4)	0	1 (0.2)
傾眠	0	0	1 (0.4)	1 (0.2)
失神	0	0	1 (0.4)	1 (0.2)
三叉神経痛	0	0	1 (0.4)	1 (0.2)
製品の問題	0	1 (0.4)	0	1 (0.2)
医療機器位置異常	0	1 (0.4)	0	1 (0.2)
精神障害	4 (1.5)	5 (1.9)	14 (5.4)	19 (3.6)
感情不安定	0	1 (0.4)	0	1 (0.2)
不安	1 (0.4)	0	3 (1.2)	3 (0.6)
抑うつ気分	0	0	1 (0.4)	1 (0.2)
うつ病	1 (0.4)	0	1 (0.4)	1 (0.2)
不眠症	1 (0.4)	1 (0.4)	3 (1.2)	4 (0.8)
故意の自傷行為	1 (0.4)	0	1 (0.4)	1 (0.2)
易刺激性	0	1 (0.4)	0	1 (0.2)
リビドー減退	0	0	1 (0.4)	1 (0.2)
リビドー亢進	0	1 (0.4)	0	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
精神障害 (Cont.)				
精神障害	0	0	1 (0.4)	1 (0.2)
混合性不安抑うつ障害	0	0	1 (0.4)	1 (0.2)
パニック発作	0	1 (0.4)	0	1 (0.2)
心的外傷後ストレス障害	0	0	1 (0.4)	1 (0.2)
睡眠障害	0	0	1 (0.4)	1 (0.2)
ストレス	0	0	1 (0.4)	1 (0.2)
腎および尿路障害	4 (1.5)	6 (2.3)	2 (0.8)	8 (1.5)
急性腎障害	0	1 (0.4)	0	1 (0.2)
排尿困難	0	3 (1.1)	0	3 (0.6)
血尿	0	0	1 (0.4)	1 (0.2)
水腎症	0	1 (0.4)	0	1 (0.2)
腎結石症	0	1 (0.4)	0	1 (0.2)
夜間頻尿	1 (0.4)	1 (0.4)	0	1 (0.2)
多尿	0	1 (0.4)	0	1 (0.2)
蛋白尿	2 (0.8)	0	0	0
腎仙痛	0	0	1 (0.4)	1 (0.2)
腎嚢胞	1 (0.4)	0	0	0

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Total (N=521) n (%)
生殖系および乳房障害	3 (1.1)	6 (2.3)	10 (3.8)	16 (3.1)
無月経	1 (0.4)	0	1 (0.4)	1 (0.2)
萎縮性外陰腟炎	0	0	1 (0.4)	1 (0.2)
機能不全性子宮出血	1 (0.4)	0	0	0
勃起不全	0	0	3 (1.2)	3 (0.6)
女性化乳房	0	0	1 (0.4)	1 (0.2)
過少月経	0	1 (0.4)	0	1 (0.2)
月経過多	0	1 (0.4)	0	1 (0.2)
月経障害	0	1 (0.4)	0	1 (0.2)
不規則月経	0	1 (0.4)	0	1 (0.2)
精巣腫瘤	0	0	1 (0.4)	1 (0.2)
精巣痛	0	1 (0.4)	2 (0.8)	3 (0.6)
腟分泌物	0	1 (0.4)	0	1 (0.2)
腟出血	1 (0.4)	0	0	0
女性外陰部潰瘍	0	0	1 (0.4)	1 (0.2)
外陰腟乾燥	0	1 (0.4)	0	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
呼吸器、胸郭および縦隔障害	19 (7.2)	28 (10.7)	27 (10.4)	55 (10.6)
急性呼吸不全	1 (0.4)	0	0	0
喘息	5 (1.9)	6 (2.3)	1 (0.4)	7 (1.3)
カタル	0	2 (0.8)	0	2 (0.4)
咳嗽	4 (1.5)	10 (3.8)	10 (3.8)	20 (3.8)
呼吸困難	0	1 (0.4)	1 (0.4)	2 (0.4)
鼻出血	1 (0.4)	2 (0.8)	3 (1.2)	5 (1.0)
喀血	0	1 (0.4)	0	1 (0.2)
鼻閉	0	0	1 (0.4)	1 (0.2)
口腔咽頭痛	3 (1.1)	5 (1.9)	8 (3.1)	13 (2.5)
咽頭腫脹	0	0	1 (0.4)	1 (0.2)
胸水	0	1 (0.4)	0	1 (0.2)
湿性咳嗽	1 (0.4)	1 (0.4)	0	1 (0.2)
気道うっ血	0	0	2 (0.8)	2 (0.4)
アレルギー性鼻炎	2 (0.8)	0	2 (0.8)	2 (0.4)
鼻漏	1 (0.4)	3 (1.1)	1 (0.4)	4 (0.8)
副鼻腔うっ血	2 (0.8)	0	2 (0.8)	2 (0.4)
喘息発作重積	0	1 (0.4)	0	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
咽喉刺激感	0	0	1 (0.4)	1 (0.2)
上気道うっ血	0	1 (0.4)	0	1 (0.2)
皮膚および皮下組織障害	37 (14.0)	55 (21.1)	65 (25.0)	120 (23.0)
ざ瘡	6 (2.3)	25 (9.6)	36 (13.8)	61 (11.7)
脱毛症	1 (0.4)	1 (0.4)	0	1 (0.2)
円形脱毛症	1 (0.4)	0	0	0
血管浮腫	0	0	1 (0.4)	1 (0.2)
水疱	2 (0.8)	1 (0.4)	1 (0.4)	2 (0.4)
冷汗	1 (0.4)	0	0	0
皮膚炎	0	2 (0.8)	0	2 (0.4)
ざ瘡様皮膚炎	0	2 (0.8)	2 (0.8)	4 (0.8)
アレルギー性皮膚炎	0	1 (0.4)	0	1 (0.2)
アトピー性皮膚炎	18 (6.8)	8 (3.1)	2 (0.8)	10 (1.9)
接触皮膚炎	1 (0.4)	0	1 (0.4)	1 (0.2)
全身性剥脱性皮膚炎	2 (0.8)	0	0	0
斑状出血	0	0	1 (0.4)	1 (0.2)
湿疹	2 (0.8)	5 (1.9)	2 (0.8)	7 (1.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
皮膚および皮下組織障害 (Cont.)				
紅斑	1 (0.4)	0	0	0
紅皮症型アトピー性皮膚炎	1 (0.4)	0	0	0
過剰肉芽組織	0	1 (0.4)	0	1 (0.2)
毛髪成長異常	2 (0.8)	1 (0.4)	0	1 (0.2)
汗腺炎	0	0	1 (0.4)	1 (0.2)
多汗症	0	2 (0.8)	1 (0.4)	3 (0.6)
過角化	0	1 (0.4)	0	1 (0.2)
多毛症	0	1 (0.4)	1 (0.4)	2 (0.4)
網状皮斑	0	0	1 (0.4)	1 (0.2)
稗粒腫	0	0	1 (0.4)	1 (0.2)
汗疹	0	0	1 (0.4)	1 (0.2)
丘疹	1 (0.4)	0	0	0
口囲皮膚炎	0	1 (0.4)	2 (0.8)	3 (0.6)
そう痒症	6 (2.3)	1 (0.4)	0	1 (0.2)
紫斑	0	1 (0.4)	0	1 (0.2)
発疹	1 (0.4)	2 (0.8)	0	2 (0.4)
斑状丘疹状皮疹	0	0	1 (0.4)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
皮膚および皮下組織障害 (Cont.)				
丘疹性皮疹	0	1 (0.4)	2 (0.8)	3 (0.6)
そう痒性皮疹	0	1 (0.4)	0	1 (0.2)
小水疱性皮疹	0	1 (0.4)	0	1 (0.2)
酒さ	0	1 (0.4)	3 (1.2)	4 (0.8)
痂皮	0	0	1 (0.4)	1 (0.2)
脂腺過形成	1 (0.4)	0	0	0
脂漏	0	1 (0.4)	1 (0.4)	2 (0.4)
脂漏性皮膚炎	0	0	1 (0.4)	1 (0.2)
敏感肌	0	1 (0.4)	0	1 (0.2)
皮膚障害	0	0	1 (0.4)	1 (0.2)
皮膚亀裂	0	0	2 (0.8)	2 (0.4)
皮膚刺激	0	2 (0.8)	0	2 (0.4)
皮膚腫瘤	0	0	1 (0.4)	1 (0.2)
皮膚腫脹	0	0	1 (0.4)	1 (0.2)
皮膚潰瘍	1 (0.4)	0	0	0
皮膚熱感	0	1 (0.4)	0	1 (0.2)
日光黒子	0	1 (0.4)	0	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=264) n (%)	Active UPA 15 mg QD + TCS (N=261) n (%)	Active UPA 30 mg QD + TCS (N=260) n (%)	Active Total (N=521) n (%)
皮膚および皮下組織障害 (Cont.)				
蕁麻疹	0	2 (0.8)	7 (2.7)	9 (1.7)
血管障害	5 (1.9)	5 (1.9)	5 (1.9)	10 (1.9)
血腫	1 (0.4)	1 (0.4)	0	1 (0.2)
ほてり	1 (0.4)	0	1 (0.4)	1 (0.2)
高血圧	3 (1.1)	3 (1.1)	3 (1.2)	6 (1.2)
起立性低血圧	0	1 (0.4)	0	1 (0.2)
レイノー現象	0	0	1 (0.4)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.6.1.3

表 4. ウパダシチニブ投与期間中で有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
Any adverse event	306 (69.2)	326 (75.1)	632 (72.1)
血液およびリンパ系障害	6 (1.4)	15 (3.5)	21 (2.4)
貧血	1 (0.2)	4 (0.9)	5 (0.6)
内出血発生の増加傾向	0	2 (0.5)	2 (0.2)
鉄欠乏性貧血	0	1 (0.2)	1 (0.1)
白血球増加症	1 (0.2)	0	1 (0.1)
白血球減少症	1 (0.2)	1 (0.2)	2 (0.2)
リンパ節症	3 (0.7)	2 (0.5)	5 (0.6)
リンパ球増加症	0	1 (0.2)	1 (0.1)
単球減少症	0	1 (0.2)	1 (0.1)
好中球減少症	1 (0.2)	2 (0.5)	3 (0.3)
汎血球減少症	0	1 (0.2)	1 (0.1)
血小板増加症	0	1 (0.2)	1 (0.1)
心臓障害	2 (0.5)	6 (1.4)	8 (0.9)
徐脈	0	1 (0.2)	1 (0.1)
うっ血性心不全	0	1 (0.2)	1 (0.1)
動悸	1 (0.2)	3 (0.7)	4 (0.5)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
心臓障害 (Cont.)			
洞性徐脈	1 (0.2)	1 (0.2)	2 (0.2)
頻脈	1 (0.2)	0	1 (0.1)
先天性、家族性および遺伝性障害	1 (0.2)	1 (0.2)	2 (0.2)
ジルベール症候群	0	1 (0.2)	1 (0.1)
色素性網膜炎	1 (0.2)	0	1 (0.1)
耳および迷路障害	8 (1.8)	5 (1.2)	13 (1.5)
難聴	1 (0.2)	1 (0.2)	2 (0.2)
耳の障害	1 (0.2)	0	1 (0.1)
耳痛	3 (0.7)	2 (0.5)	5 (0.6)
耳垢分泌過多	1 (0.2)	0	1 (0.1)
聴力低下	0	1 (0.2)	1 (0.1)
耳鳴	0	1 (0.2)	1 (0.1)
回転性めまい	2 (0.5)	1 (0.2)	3 (0.3)
頭位性回転性めまい	1 (0.2)	0	1 (0.1)
内分泌障害	2 (0.5)	2 (0.5)	4 (0.5)
甲状腺機能正常症候群	0	1 (0.2)	1 (0.1)
甲状腺機能低下症	1 (0.2)	0	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
内分泌障害 (Cont.)			
甲状腺腫瘤	1 (0.2)	1 (0.2)	2 (0.2)
眼障害	17 (3.8)	23 (5.3)	40 (4.6)
眼瞼炎	1 (0.2)	2 (0.5)	3 (0.3)
白内障	0	2 (0.5)	2 (0.2)
霰粒腫	1 (0.2)	2 (0.5)	3 (0.3)
結膜沈着物	0	1 (0.2)	1 (0.1)
結膜充血	0	1 (0.2)	1 (0.1)
結膜刺激	0	1 (0.2)	1 (0.1)
アレルギー性結膜炎	2 (0.5)	3 (0.7)	5 (0.6)
ドライアイ	3 (0.7)	1 (0.2)	4 (0.5)
眼瞼紅斑	1 (0.2)	0	1 (0.1)
眼のアレルギー	0	1 (0.2)	1 (0.1)
眼の炎症	0	1 (0.2)	1 (0.1)
眼痛	1 (0.2)	1 (0.2)	2 (0.2)
眼の異常感覚	0	1 (0.2)	1 (0.1)
眼そう痒症	0	1 (0.2)	1 (0.1)
眼部腫脹	0	3 (0.7)	3 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
眼障害 (Cont.)			
眼瞼障害	0	1 (0.2)	1 (0.1)
緑内障	1 (0.2)	0	1 (0.1)
流涙増加	2 (0.5)	0	2 (0.2)
視神経乳頭浮腫	0	1 (0.2)	1 (0.1)
眼窩周囲浮腫	1 (0.2)	0	1 (0.1)
羞明	0	1 (0.2)	1 (0.1)
網膜剥離	1 (0.2)	1 (0.2)	2 (0.2)
裂孔原性網膜剥離	0	1 (0.2)	1 (0.1)
眼瞼腫脹	1 (0.2)	0	1 (0.1)
潰瘍性角膜炎	1 (0.2)	1 (0.2)	2 (0.2)
春季カタル	0	1 (0.2)	1 (0.1)
霧視	3 (0.7)	1 (0.2)	4 (0.5)
硝子体剥離	0	1 (0.2)	1 (0.1)
眼球乾燥症	1 (0.2)	0	1 (0.1)
胃腸障害	68 (15.4)	68 (15.7)	136 (15.5)
腹部不快感	2 (0.5)	1 (0.2)	3 (0.3)
腹部膨満	2 (0.5)	2 (0.5)	4 (0.5)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
胃腸障害 (Cont.)			
腹痛	8 (1.8)	9 (2.1)	17 (1.9)
上腹部痛	16 (3.6)	4 (0.9)	20 (2.3)
口角口唇炎	0	2 (0.5)	2 (0.2)
肛門直腸不快感	0	1 (0.2)	1 (0.1)
アフタ性潰瘍	1 (0.2)	1 (0.2)	2 (0.2)
便習慣変化	0	1 (0.2)	1 (0.1)
口唇のひび割れ	1 (0.2)	0	1 (0.1)
慢性胃炎	2 (0.5)	0	2 (0.2)
便秘	6 (1.4)	6 (1.4)	12 (1.4)
齲歯	4 (0.9)	5 (1.2)	9 (1.0)
下痢	12 (2.7)	15 (3.5)	27 (3.1)
口内乾燥	0	1 (0.2)	1 (0.1)
消化不良	8 (1.8)	4 (0.9)	12 (1.4)
嚥下障害	0	2 (0.5)	2 (0.2)
変色便	1 (0.2)	0	1 (0.1)
白色便	1 (0.2)	0	1 (0.1)
鼓腸	1 (0.2)	1 (0.2)	2 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
胃腸障害 (Cont.)			
排便回数増加	0	1 (0.2)	1 (0.1)
胃炎	1 (0.2)	1 (0.2)	2 (0.2)
胃腸障害	1 (0.2)	0	1 (0.1)
胃腸粘膜障害	1 (0.2)	0	1 (0.1)
胃食道逆流性疾患	1 (0.2)	6 (1.4)	7 (0.8)
舌炎	1 (0.2)	0	1 (0.1)
舌痛	0	1 (0.2)	1 (0.1)
痔核	0	1 (0.2)	1 (0.1)
裂孔ヘルニア	0	1 (0.2)	1 (0.1)
腸閉塞	1 (0.2)	0	1 (0.1)
過敏性腸症候群	0	2 (0.5)	2 (0.2)
口唇水疱	1 (0.2)	0	1 (0.1)
口腔内出血	0	1 (0.2)	1 (0.1)
口腔内潰瘍形成	2 (0.5)	0	2 (0.2)
悪心	12 (2.7)	13 (3.0)	25 (2.9)
嚥下痛	1 (0.2)	0	1 (0.1)
口腔瘻	1 (0.2)	0	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
胃腸障害 (Cont.)			
口腔そう痒症	0	1 (0.2)	1 (0.1)
膵炎	1 (0.2)	0	1 (0.1)
歯周病	1 (0.2)	0	1 (0.1)
無髄歯	0	1 (0.2)	1 (0.1)
レッチング	0	1 (0.2)	1 (0.1)
歯の障害	1 (0.2)	1 (0.2)	2 (0.2)
埋伏歯	1 (0.2)	3 (0.7)	4 (0.5)
歯痛	3 (0.7)	5 (1.2)	8 (0.9)
嘔吐	4 (0.9)	4 (0.9)	8 (0.9)
一般・全身障害および投与部位の状態	43 (9.7)	41 (9.4)	84 (9.6)
胸部不快感	1 (0.2)	1 (0.2)	2 (0.2)
胸痛	4 (0.9)	2 (0.5)	6 (0.7)
悪寒	2 (0.5)	0	2 (0.2)
嚢胞	1 (0.2)	1 (0.2)	2 (0.2)
顔面浮腫	1 (0.2)	0	1 (0.1)
顔面痛	3 (0.7)	0	3 (0.3)
疲労	9 (2.0)	6 (1.4)	15 (1.7)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
熱感	1 (0.2)	0	1 (0.1)
治癒不良	0	1 (0.2)	1 (0.1)
インフルエンザ様疾患	12 (2.7)	11 (2.5)	23 (2.6)
倦怠感	2 (0.5)	0	2 (0.2)
非心臓性胸痛	0	2 (0.5)	2 (0.2)
末梢性浮腫	2 (0.5)	0	2 (0.2)
疼痛	3 (0.7)	2 (0.5)	5 (0.6)
発熱	13 (2.9)	14 (3.2)	27 (3.1)
腫脹	1 (0.2)	1 (0.2)	2 (0.2)
顔面腫脹	2 (0.5)	1 (0.2)	3 (0.3)
血管穿刺部位内出血	0	1 (0.2)	1 (0.1)
肝胆道系障害	4 (0.9)	4 (0.9)	8 (0.9)
肝機能異常	3 (0.7)	1 (0.2)	4 (0.5)
脂肪肝	1 (0.2)	0	1 (0.1)
肝細胞損傷	0	1 (0.2)	1 (0.1)
肝腫大	0	1 (0.2)	1 (0.1)
非アルコール性脂肪性肝炎	0	1 (0.2)	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
免疫系障害	4 (0.9)	5 (1.2)	9 (1.0)
アレルギー性浮腫	1 (0.2)	0	1 (0.1)
動物アレルギー	0	1 (0.2)	1 (0.1)
アナフィラキシー反応	0	1 (0.2)	1 (0.1)
薬物過敏症	1 (0.2)	0	1 (0.1)
食物アレルギー	1 (0.2)	1 (0.2)	2 (0.2)
過敏症	2 (0.5)	2 (0.5)	4 (0.5)
感染症および寄生虫症	216 (48.9)	232 (53.5)	448 (51.1)
四肢膿瘍	0	1 (0.2)	1 (0.1)
口腔膿瘍	0	1 (0.2)	1 (0.1)
ダニ皮膚炎	0	1 (0.2)	1 (0.1)
膿疱性ざ瘡	1 (0.2)	2 (0.5)	3 (0.3)
急性副鼻腔炎	1 (0.2)	0	1 (0.1)
肛門膿瘍	1 (0.2)	0	1 (0.1)
虫垂炎	1 (0.2)	0	1 (0.1)
細菌性疾患キャリアー	1 (0.2)	1 (0.2)	2 (0.2)
細菌感染	2 (0.5)	1 (0.2)	3 (0.3)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
細菌性膣症	1 (0.2)	0	1 (0.1)
細菌尿	0	1 (0.2)	1 (0.1)
体部白癬	0	4 (0.9)	4 (0.5)
気管支炎	7 (1.6)	11 (2.5)	18 (2.1)
ウイルス性気管支炎	0	1 (0.2)	1 (0.1)
感染性滑液包炎	0	1 (0.2)	1 (0.1)
カンジダ感染	0	1 (0.2)	1 (0.1)
蜂巣炎	1 (0.2)	2 (0.5)	3 (0.3)
条虫感染	1 (0.2)	0	1 (0.1)
結膜炎	6 (1.4)	4 (0.9)	10 (1.1)
細菌性結膜炎	1 (0.2)	1 (0.2)	2 (0.2)
ウイルス性結膜炎	1 (0.2)	1 (0.2)	2 (0.2)
コロナウイルス感染	1 (0.2)	0	1 (0.1)
膀胱炎	1 (0.2)	1 (0.2)	2 (0.2)
感染性下痢	0	1 (0.2)	1 (0.1)
耳感染	3 (0.7)	1 (0.2)	4 (0.5)
ヘルペス性状湿疹	3 (0.7)	3 (0.7)	6 (0.7)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
膿痂疹性湿疹	0	1 (0.2)	1 (0.1)
感染性湿疹	0	1 (0.2)	1 (0.1)
エンテロバクター感染	1 (0.2)	0	1 (0.1)
蟯虫症	1 (0.2)	0	1 (0.1)
丹毒	1 (0.2)	0	1 (0.1)
眼瞼感染	1 (0.2)	0	1 (0.1)
糸状虫症	0	1 (0.2)	1 (0.1)
毛包炎	13 (2.9)	14 (3.2)	27 (3.1)
真菌感染	1 (0.2)	0	1 (0.1)
皮膚真菌感染	2 (0.5)	2 (0.5)	4 (0.5)
せつ	4 (0.9)	2 (0.5)	6 (0.7)
ウイルス性胃炎	1 (0.2)	0	1 (0.1)
胃腸炎	10 (2.3)	11 (2.5)	21 (2.4)
ウイルス性胃腸炎	0	6 (1.4)	6 (0.7)
消化管感染	1 (0.2)	0	1 (0.1)
陰部ヘルペス	0	1 (0.2)	1 (0.1)
陰部単純ヘルペス	0	3 (0.7)	3 (0.3)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
ジアルジア症	1 (0.2)	0	1 (0.1)
歯肉炎	1 (0.2)	1 (0.2)	2 (0.2)
ヘルペス眼感染	1 (0.2)	2 (0.5)	3 (0.3)
単純ヘルペス	18 (4.1)	15 (3.5)	33 (3.8)
帯状疱疹	6 (1.4)	11 (2.5)	17 (1.9)
皮膚播種性帯状疱疹	1 (0.2)	0	1 (0.1)
耳帯状疱疹	0	1 (0.2)	1 (0.1)
麦粒腫	5 (1.1)	3 (0.7)	8 (0.9)
膿痂疹	4 (0.9)	6 (1.4)	10 (1.1)
感染性皮膚嚢腫	0	1 (0.2)	1 (0.1)
感染	0	1 (0.2)	1 (0.1)
寄生虫感染	1 (0.2)	0	1 (0.1)
インフルエンザ	15 (3.4)	12 (2.8)	27 (3.1)
関節膿瘍	0	1 (0.2)	1 (0.1)
カポジ水痘様発疹	1 (0.2)	2 (0.5)	3 (0.3)
腎感染	1 (0.2)	0	1 (0.1)
喉頭炎	1 (0.2)	0	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
潜伏結核	0	1 (0.2)	1 (0.1)
シラミ寄生	0	1 (0.2)	1 (0.1)
マラセチア感染	1 (0.2)	1 (0.2)	2 (0.2)
細菌性乳腺炎	1 (0.2)	0	1 (0.1)
伝染性軟属腫	0	1 (0.2)	1 (0.1)
鼻ヘルペス	0	4 (0.9)	4 (0.5)
上咽頭炎	67 (15.2)	70 (16.1)	137 (15.6)
爪真菌症	2 (0.5)	3 (0.7)	5 (0.6)
眼部単純ヘルペス	1 (0.2)	7 (1.6)	8 (0.9)
口腔カンジダ症	1 (0.2)	1 (0.2)	2 (0.2)
口腔ヘルペス	20 (4.5)	32 (7.4)	52 (5.9)
外耳炎	3 (0.7)	1 (0.2)	4 (0.5)
中耳炎	1 (0.2)	1 (0.2)	2 (0.2)
急性中耳炎	1 (0.2)	1 (0.2)	2 (0.2)
爪囲炎	1 (0.2)	1 (0.2)	2 (0.2)
歯周炎	1 (0.2)	0	1 (0.1)
眼窩周囲蜂巣炎	1 (0.2)	0	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
扁桃周囲膿瘍	1 (0.2)	0	1 (0.1)
咽頭炎	9 (2.0)	11 (2.5)	20 (2.3)
レンサ球菌性咽頭炎	2 (0.5)	1 (0.2)	3 (0.3)
肺炎	3 (0.7)	3 (0.7)	6 (0.7)
マイコプラズマ性肺炎	0	1 (0.2)	1 (0.1)
ウイルス感染後疲労症候群	0	1 (0.2)	1 (0.1)
術後創感染	0	1 (0.2)	1 (0.1)
歯髄炎	0	1 (0.2)	1 (0.1)
化膿性分泌物	1 (0.2)	0	1 (0.1)
膿疱	0	3 (0.7)	3 (0.3)
腎盂腎炎	1 (0.2)	0	1 (0.1)
膿疱性皮疹	0	1 (0.2)	1 (0.1)
気道感染	3 (0.7)	1 (0.2)	4 (0.5)
ウイルス性気道感染	1 (0.2)	1 (0.2)	2 (0.2)
鼻炎	4 (0.9)	0	4 (0.5)
鼻咽頭炎	0	1 (0.2)	1 (0.1)
ライノウイルス感染	0	1 (0.2)	1 (0.1)

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感染症および寄生虫症 (Cont.)			
副鼻腔炎	3 (0.7)	5 (1.2)	8 (0.9)
皮膚細菌感染	1 (0.2)	1 (0.2)	2 (0.2)
皮膚感染	3 (0.7)	3 (0.7)	6 (0.7)
膿性痰	1 (0.2)	0	1 (0.1)
ブドウ球菌性膿瘍	1 (0.2)	0	1 (0.1)
ブドウ球菌性膿痂疹	1 (0.2)	0	1 (0.1)
ブドウ球菌感染	3 (0.7)	3 (0.7)	6 (0.7)
ブドウ球菌皮膚感染	2 (0.5)	3 (0.7)	5 (0.6)
股部白癬	0	3 (0.7)	3 (0.3)
白癬感染	0	1 (0.2)	1 (0.1)
足部白癬	4 (0.9)	6 (1.4)	10 (1.1)
癜風	0	1 (0.2)	1 (0.1)
扁桃炎	4 (0.9)	4 (0.9)	8 (0.9)
歯感染	3 (0.7)	3 (0.7)	6 (0.7)
気管炎	2 (0.5)	1 (0.2)	3 (0.3)
気管気管支炎	1 (0.2)	0	1 (0.1)
トリコモナス症	0	1 (0.2)	1 (0.1)

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感染症および寄生虫症 (Cont.)			
トリコフィトン感染症	1 (0.2)	0	1 (0.1)
上気道感染	37 (8.4)	39 (9.0)	76 (8.7)
尿道炎	1 (0.2)	0	1 (0.1)
尿路感染	9 (2.0)	16 (3.7)	25 (2.9)
細菌性尿路感染	0	1 (0.2)	1 (0.1)
腟感染	2 (0.5)	1 (0.2)	3 (0.3)
ウイルス感染	1 (0.2)	3 (0.7)	4 (0.5)
ウイルス性咽頭炎	2 (0.5)	2 (0.5)	4 (0.5)
ウイルス性上気道感染	5 (1.1)	9 (2.1)	14 (1.6)
外陰部腟カンジダ症	2 (0.5)	1 (0.2)	3 (0.3)
外陰腟真菌感染	1 (0.2)	1 (0.2)	2 (0.2)
トリコモナス外陰腟炎	1 (0.2)	0	1 (0.1)
傷害、中毒および処置合併症	24 (5.4)	30 (6.9)	54 (6.2)
事故	1 (0.2)	1 (0.2)	2 (0.2)
動物咬傷	1 (0.2)	0	1 (0.1)
節足動物咬傷	0	2 (0.5)	2 (0.2)
骨挫傷	0	1 (0.2)	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
傷害、中毒および処置合併症 (Cont.)			
軟骨損傷	0	1 (0.2)	1 (0.1)
胸部損傷	0	1 (0.2)	1 (0.1)
鎖骨骨折	0	1 (0.2)	1 (0.1)
挫傷	1 (0.2)	3 (0.7)	4 (0.5)
角膜擦過傷	0	1 (0.2)	1 (0.1)
頭蓋脳損傷	0	1 (0.2)	1 (0.1)
転倒	1 (0.2)	2 (0.5)	3 (0.3)
大腿骨骨折	0	1 (0.2)	1 (0.1)
足骨折	2 (0.5)	1 (0.2)	3 (0.3)
尾骨骨折	1 (0.2)	0	1 (0.1)
熱疲労	0	1 (0.2)	1 (0.1)
損傷	2 (0.5)	1 (0.2)	3 (0.3)
関節損傷	0	1 (0.2)	1 (0.1)
靭帯捻挫	1 (0.2)	0	1 (0.1)
四肢損傷	3 (0.7)	0	3 (0.3)
半月板損傷	1 (0.2)	0	1 (0.1)
肉離れ	2 (0.5)	5 (1.2)	7 (0.8)

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傷害、中毒および処置合併症 (Cont.)			
過量投与	1 (0.2)	0	1 (0.1)
処置による疼痛	1 (0.2)	1 (0.2)	2 (0.2)
橈骨骨折	0	1 (0.2)	1 (0.1)
肋骨骨折	2 (0.5)	1 (0.2)	3 (0.3)
交通事故	0	2 (0.5)	2 (0.2)
皮膚擦過傷	2 (0.5)	1 (0.2)	3 (0.3)
皮膚裂傷	3 (0.7)	1 (0.2)	4 (0.5)
脊椎骨折	1 (0.2)	0	1 (0.1)
スポーツ損傷	1 (0.2)	0	1 (0.1)
胸骨骨折	1 (0.2)	0	1 (0.1)
腱損傷	0	1 (0.2)	1 (0.1)
熱傷	1 (0.2)	0	1 (0.1)
歯牙破折	2 (0.5)	1 (0.2)	3 (0.3)
外傷性血腫	1 (0.2)	0	1 (0.1)
創傷	0	1 (0.2)	1 (0.1)
創部分泌	0	1 (0.2)	1 (0.1)

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臨床検査	54 (12.2)	56 (12.9)	110 (12.6)
アラニンアミノトランスフェラーゼ増加	8 (1.8)	4 (0.9)	12 (1.4)
アスパラギン酸アミノトランスフェラーゼ異常	1 (0.2)	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	5 (1.1)	3 (0.7)	8 (0.9)
血中アルカリホスファターゼ増加	1 (0.2)	0	1 (0.1)
血中重炭酸塩減少	0	1 (0.2)	1 (0.1)
血中ビリルビン増加	1 (0.2)	0	1 (0.1)
血中コレステロール増加	2 (0.5)	1 (0.2)	3 (0.3)
血中クレアチンホスホキナーゼ増加	26 (5.9)	29 (6.7)	55 (6.3)
血中クレアチニン増加	1 (0.2)	0	1 (0.1)
血中免疫グロブリンＥ増加	1 (0.2)	0	1 (0.1)
血圧上昇	1 (0.2)	1 (0.2)	2 (0.2)
血中トリグリセリド増加	1 (0.2)	3 (0.7)	4 (0.5)
血中尿酸増加	2 (0.5)	0	2 (0.2)
尿中血陽性	0	1 (0.2)	1 (0.1)
体温上昇	0	1 (0.2)	1 (0.1)
好酸球数増加	3 (0.7)	0	3 (0.3)
好酸球百分率増加	1 (0.2)	0	1 (0.1)

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臨床検査 (Cont.)			
真菌検査陽性	1 (0.2)	0	1 (0.1)
ヘモグロビン減少	0	2 (0.5)	2 (0.2)
肝酵素上昇	1 (0.2)	0	1 (0.1)
低比重リポ蛋白増加	0	1 (0.2)	1 (0.1)
単球数増加	0	1 (0.2)	1 (0.1)
結核菌群検査陽性	2 (0.5)	0	2 (0.2)
好中球数減少	4 (0.9)	2 (0.5)	6 (0.7)
好中球百分率減少	1 (0.2)	0	1 (0.1)
尿中蛋白陽性	2 (0.5)	1 (0.2)	3 (0.3)
子宮頚部スミア異常	1 (0.2)	0	1 (0.1)
ブドウ球菌検査陽性	2 (0.5)	0	2 (0.2)
トランスアミナーゼ上昇	0	1 (0.2)	1 (0.1)
トロポニン増加	0	1 (0.2)	1 (0.1)
ビタミン D 減少	0	1 (0.2)	1 (0.1)
体重増加	7 (1.6)	8 (1.8)	15 (1.7)
白血球数減少	1 (0.2)	1 (0.2)	2 (0.2)
白血球数増加	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
臨床検査 (Cont.)			
尿中白血球陽性	0	1 (0.2)	1 (0.1)
代謝および栄養障害	12 (2.7)	13 (3.0)	25 (2.9)
食欲減退	2 (0.5)	0	2 (0.2)
脱水	0	1 (0.2)	1 (0.1)
糖尿病	0	2 (0.5)	2 (0.2)
脂質異常症	0	2 (0.5)	2 (0.2)
食物不耐性	1 (0.2)	0	1 (0.1)
痛風	1 (0.2)	1 (0.2)	2 (0.2)
高コレステロール血症	1 (0.2)	2 (0.5)	3 (0.3)
高血糖	1 (0.2)	0	1 (0.1)
高ホモシステイン血症	1 (0.2)	0	1 (0.1)
高脂血症	3 (0.7)	3 (0.7)	6 (0.7)
高ナトリウム血症	1 (0.2)	0	1 (0.1)
高尿酸血症	1 (0.2)	1 (0.2)	2 (0.2)
低マグネシウム血症	1 (0.2)	0	1 (0.1)
食欲亢進	0	2 (0.5)	2 (0.2)
ビタミン B12 欠乏	1 (0.2)	0	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
筋骨格系および結合組織障害	30 (6.8)	38 (8.8)	68 (7.8)
関節痛	7 (1.6)	6 (1.4)	13 (1.5)
関節炎	2 (0.5)	2 (0.5)	4 (0.5)
背部痛	7 (1.6)	5 (1.2)	12 (1.4)
骨痛	0	1 (0.2)	1 (0.1)
滑液包炎	1 (0.2)	3 (0.7)	4 (0.5)
椎間板突出	0	2 (0.5)	2 (0.2)
関節ロック	0	1 (0.2)	1 (0.1)
関節腫脹	0	1 (0.2)	1 (0.1)
四肢不快感	1 (0.2)	0	1 (0.1)
筋痙縮	1 (0.2)	4 (0.9)	5 (0.6)
筋攣縮	0	1 (0.2)	1 (0.1)
筋骨格系胸痛	1 (0.2)	0	1 (0.1)
筋骨格痛	1 (0.2)	2 (0.5)	3 (0.3)
筋骨格硬直	0	1 (0.2)	1 (0.1)
筋肉痛	5 (1.1)	4 (0.9)	9 (1.0)
頚部腫瘤	0	1 (0.2)	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
筋骨格系および結合組織障害 (Cont.)			
頚部痛	2 (0.5)	1 (0.2)	3 (0.3)
骨減少症	0	1 (0.2)	1 (0.1)
四肢痛	2 (0.5)	6 (1.4)	8 (0.9)
足底筋膜炎	1 (0.2)	0	1 (0.1)
滑液嚢腫	0	1 (0.2)	1 (0.1)
顎関節症候群	1 (0.2)	1 (0.2)	2 (0.2)
腱炎	1 (0.2)	1 (0.2)	2 (0.2)
腱鞘炎	0	1 (0.2)	1 (0.1)
斜頚	1 (0.2)	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）	8 (1.8)	8 (1.8)	16 (1.8)
結腸腺癌	0	1 (0.2)	1 (0.1)
肛門性器疣贅	0	1 (0.2)	1 (0.1)
良性新生物	0	1 (0.2)	1 (0.1)
精巣の良性新生物	0	1 (0.2)	1 (0.1)
血管腫	1 (0.2)	1 (0.2)	2 (0.2)
ケラトアカントーマ	0	1 (0.2)	1 (0.1)
表皮内悪性黒色腫	0	1 (0.2)	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) 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.)			
結節性筋膜炎	1 (0.2)	0	1 (0.1)
脂漏性角化症	1 (0.2)	0	1 (0.1)
皮膚乳頭腫	5 (1.1)	1 (0.2)	6 (0.7)
子宮平滑筋腫	0	1 (0.2)	1 (0.1)
神経系障害	38 (8.6)	39 (9.0)	77 (8.8)
脳血管発作	0	1 (0.2)	1 (0.1)
注意力障害	1 (0.2)	0	1 (0.1)
浮動性めまい	7 (1.6)	5 (1.2)	12 (1.4)
味覚不全	0	2 (0.5)	2 (0.2)
てんかん	0	1 (0.2)	1 (0.1)
頭部不快感	0	1 (0.2)	1 (0.1)
頭痛	24 (5.4)	20 (4.6)	44 (5.0)
過眠症	0	1 (0.2)	1 (0.1)
筋緊張亢進	0	1 (0.2)	1 (0.1)
感覚鈍麻	1 (0.2)	1 (0.2)	2 (0.2)
片頭痛	4 (0.9)	3 (0.7)	7 (0.8)
多発性硬化症再発	0	1 (0.2)	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
神経系障害 (Cont.)			
神経圧迫	0	1 (0.2)	1 (0.1)
錯感覚	1 (0.2)	1 (0.2)	2 (0.2)
嗅覚錯誤	0	1 (0.2)	1 (0.1)
ヘルペス後神経痛	1 (0.2)	1 (0.2)	2 (0.2)
失神寸前の状態	1 (0.2)	1 (0.2)	2 (0.2)
坐骨神経痛	1 (0.2)	1 (0.2)	2 (0.2)
傾眠	0	1 (0.2)	1 (0.1)
失神	0	1 (0.2)	1 (0.1)
三叉神経痛	0	1 (0.2)	1 (0.1)
トンネル状視野	0	1 (0.2)	1 (0.1)
製品の問題	1 (0.2)	0	1 (0.1)
医療機器位置異常	1 (0.2)	0	1 (0.1)
精神障害	12 (2.7)	25 (5.8)	37 (4.2)
感情不安定	1 (0.2)	0	1 (0.1)
不安	3 (0.7)	3 (0.7)	6 (0.7)
注意欠陥多動性障害	0	1 (0.2)	1 (0.1)
双極性障害	0	1 (0.2)	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
精神障害 (Cont.)			
抑うつ気分	1 (0.2)	3 (0.7)	4 (0.5)
うつ病	1 (0.2)	2 (0.5)	3 (0.3)
不眠症	2 (0.5)	5 (1.2)	7 (0.8)
故意の自傷行為	0	1 (0.2)	1 (0.1)
易刺激性	1 (0.2)	0	1 (0.1)
リビドー減退	0	1 (0.2)	1 (0.1)
リビドー亢進	1 (0.2)	0	1 (0.1)
精神障害	0	1 (0.2)	1 (0.1)
混合性不安抑うつ障害	0	1 (0.2)	1 (0.1)
悪夢	1 (0.2)	0	1 (0.1)
パニック発作	1 (0.2)	1 (0.2)	2 (0.2)
心的外傷後ストレス障害	0	1 (0.2)	1 (0.1)
睡眠障害	0	2 (0.5)	2 (0.2)
ストレス	0	2 (0.5)	2 (0.2)
自殺念慮	0	1 (0.2)	1 (0.1)
腎および尿路障害	7 (1.6)	6 (1.4)	13 (1.5)
急性腎障害	1 (0.2)	0	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
腎および尿路障害 (Cont.)			
アルブミン尿	0	1 (0.2)	1 (0.1)
排尿困難	3 (0.7)	0	3 (0.3)
血尿	1 (0.2)	3 (0.7)	4 (0.5)
水腎症	1 (0.2)	0	1 (0.1)
腎結石症	1 (0.2)	0	1 (0.1)
夜間頻尿	1 (0.2)	0	1 (0.1)
多尿	1 (0.2)	0	1 (0.1)
蛋白尿	0	1 (0.2)	1 (0.1)
腎仙痛	0	1 (0.2)	1 (0.1)
生殖系および乳房障害	8 (1.8)	16 (3.7)	24 (2.7)
無月経	0	1 (0.2)	1 (0.1)
萎縮性外陰腟炎	0	1 (0.2)	1 (0.1)
乳房嚢胞	1 (0.2)	0	1 (0.1)
勃起不全	1 (0.2)	3 (0.7)	4 (0.5)
女性化乳房	0	1 (0.2)	1 (0.1)
過少月経	1 (0.2)	0	1 (0.1)
月経過多	1 (0.2)	0	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
生殖系および乳房障害 (Cont.)			
月経障害	1 (0.2)	0	1 (0.1)
不規則月経	1 (0.2)	2 (0.5)	3 (0.3)
不正子宮出血	0	1 (0.2)	1 (0.1)
多嚢胞性卵巣	0	1 (0.2)	1 (0.1)
精巣腫瘤	0	2 (0.5)	2 (0.2)
精巣痛	1 (0.2)	3 (0.7)	4 (0.5)
腟分泌物	1 (0.2)	0	1 (0.1)
腟出血	0	1 (0.2)	1 (0.1)
女性外陰部潰瘍	0	1 (0.2)	1 (0.1)
外陰腟乾燥	1 (0.2)	0	1 (0.1)
呼吸器、胸郭および縦隔障害	52 (11.8)	51 (11.8)	103 (11.8)
アレルギー性気管支炎	1 (0.2)	0	1 (0.1)
失声症	1 (0.2)	0	1 (0.1)
喘息	7 (1.6)	5 (1.2)	12 (1.4)
カタル	5 (1.1)	4 (0.9)	9 (1.0)
慢性閉塞性肺疾患	0	1 (0.2)	1 (0.1)
咳嗽	22 (5.0)	20 (4.6)	42 (4.8)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
呼吸困難	2 (0.5)	5 (1.2)	7 (0.8)
鼻出血	5 (1.1)	4 (0.9)	9 (1.0)
喀血	2 (0.5)	0	2 (0.2)
鼻閉	0	1 (0.2)	1 (0.1)
口腔咽頭痛	8 (1.8)	11 (2.5)	19 (2.2)
咽頭腫脹	0	1 (0.2)	1 (0.1)
胸水	1 (0.2)	0	1 (0.1)
湿性咳嗽	1 (0.2)	0	1 (0.1)
肺肉芽腫	0	1 (0.2)	1 (0.1)
肺腫瘤	0	1 (0.2)	1 (0.1)
気道うっ血	0	2 (0.5)	2 (0.2)
アレルギー性鼻炎	0	2 (0.5)	2 (0.2)
鼻漏	5 (1.1)	4 (0.9)	9 (1.0)
副鼻腔うっ血	1 (0.2)	2 (0.5)	3 (0.3)
くしゃみ	0	1 (0.2)	1 (0.1)
喘息発作重積	1 (0.2)	0	1 (0.1)
咽喉刺激感	0	1 (0.2)	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
上気道うっ血	1 (0.2)	0	1 (0.1)
喘鳴	1 (0.2)	0	1 (0.1)
皮膚および皮下組織障害	128 (29.0)	117 (27.0)	245 (28.0)
ざ瘡	57 (12.9)	64 (14.7)	121 (13.8)
脱毛症	1 (0.2)	0	1 (0.1)
血管浮腫	0	1 (0.2)	1 (0.1)
水疱	2 (0.5)	2 (0.5)	4 (0.5)
冷汗	0	1 (0.2)	1 (0.1)
皮膚嚢腫	2 (0.5)	1 (0.2)	3 (0.3)
皮膚炎	3 (0.7)	2 (0.5)	5 (0.6)
ざ瘡様皮膚炎	3 (0.7)	3 (0.7)	6 (0.7)
アレルギー性皮膚炎	2 (0.5)	1 (0.2)	3 (0.3)
アトピー性皮膚炎	27 (6.1)	14 (3.2)	41 (4.7)
接触皮膚炎	4 (0.9)	3 (0.7)	7 (0.8)
疱疹状皮膚炎	0	1 (0.2)	1 (0.1)
乾癬様皮膚炎	1 (0.2)	0	1 (0.1)
異汗性湿疹	2 (0.5)	0	2 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
皮膚および皮下組織障害 (Cont.)			
斑状出血	0	1 (0.2)	1 (0.1)
湿疹	7 (1.6)	5 (1.2)	12 (1.4)
小水疱性湿疹	0	1 (0.2)	1 (0.1)
紅斑	3 (0.7)	2 (0.5)	5 (0.6)
過剰肉芽組織	1 (0.2)	0	1 (0.1)
毛髪成長異常	1 (0.2)	1 (0.2)	2 (0.2)
汗腺炎	0	1 (0.2)	1 (0.1)
多汗症	3 (0.7)	1 (0.2)	4 (0.5)
過角化	2 (0.5)	1 (0.2)	3 (0.3)
多毛症	1 (0.2)	1 (0.2)	2 (0.2)
嵌入爪	0	2 (0.5)	2 (0.2)
苔癬化	0	1 (0.2)	1 (0.1)
網状皮斑	0	1 (0.2)	1 (0.1)
稗粒腫	0	1 (0.2)	1 (0.1)
汗疹	1 (0.2)	1 (0.2)	2 (0.2)
寝汗	1 (0.2)	0	1 (0.1)
口囲皮膚炎	1 (0.2)	3 (0.7)	4 (0.5)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
皮膚および皮下組織障害 (Cont.)			
光線過敏性反応	0	1 (0.2)	1 (0.1)
そう痒症	4 (0.9)	0	4 (0.5)
偽毛包炎	1 (0.2)	0	1 (0.1)
紫斑	2 (0.5)	0	2 (0.2)
発疹	3 (0.7)	2 (0.5)	5 (0.6)
斑状丘疹状皮疹	0	2 (0.5)	2 (0.2)
丘疹性皮疹	1 (0.2)	3 (0.7)	4 (0.5)
そう痒性皮疹	1 (0.2)	0	1 (0.1)
小水疱性皮疹	1 (0.2)	0	1 (0.1)
酒さ	2 (0.5)	3 (0.7)	5 (0.6)
痂皮	0	2 (0.5)	2 (0.2)
脂漏	1 (0.2)	1 (0.2)	2 (0.2)
脂漏性皮膚炎	0	1 (0.2)	1 (0.1)
敏感肌	1 (0.2)	0	1 (0.1)
皮膚変色	0	1 (0.2)	1 (0.1)
皮膚障害	0	1 (0.2)	1 (0.1)
皮膚亀裂	1 (0.2)	3 (0.7)	4 (0.5)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
皮膚および皮下組織障害 (Cont.)			
皮膚刺激	2 (0.5)	1 (0.2)	3 (0.3)
皮膚腫瘤	0	2 (0.5)	2 (0.2)
皮膚線条	2 (0.5)	0	2 (0.2)
皮膚腫脹	0	1 (0.2)	1 (0.1)
皮膚潰瘍	0	1 (0.2)	1 (0.1)
皮膚熱感	1 (0.2)	0	1 (0.1)
日光黒子	1 (0.2)	0	1 (0.1)
蕁麻疹	8 (1.8)	11 (2.5)	19 (2.2)
圧迫性蕁麻疹	0	1 (0.2)	1 (0.1)
社会環境	1 (0.2)	0	1 (0.1)
歯科補てつ物使用者	1 (0.2)	0	1 (0.1)
外科および内科処置	0	1 (0.2)	1 (0.1)
人工流産	0	1 (0.2)	1 (0.1)
血管障害	7 (1.6)	8 (1.8)	15 (1.7)
大動脈瘤	0	1 (0.2)	1 (0.1)
深部静脈血栓症	0	1 (0.2)	1 (0.1)
血腫	1 (0.2)	0	1 (0.1)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
血管障害 (Cont.)			
ほてり	0	1 (0.2)	1 (0.1)
高血圧	5 (1.1)	5 (1.2)	10 (1.1)
起立性低血圧	1 (0.2)	0	1 (0.1)
レイノー現象	0	1 (0.2)	1 (0.1)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.6.2.1

表 5. ウパダシチニブ投与期間中に有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団，青少年）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
Any adverse event	43 (74.1)	41 (75.9)	84 (75.0)
血液およびリンパ系障害	2 (3.4)	2 (3.7)	4 (3.6)
リンパ節症	2 (3.4)	1 (1.9)	3 (2.7)
単球減少症	0	1 (1.9)	1 (0.9)
耳および迷路障害	1 (1.7)	1 (1.9)	2 (1.8)
難聴	0	1 (1.9)	1 (0.9)
耳痛	1 (1.7)	0	1 (0.9)
耳鳴	0	1 (1.9)	1 (0.9)
内分泌障害	0	1 (1.9)	1 (0.9)
甲状腺機能正常症候群	0	1 (1.9)	1 (0.9)
眼障害	1 (1.7)	3 (5.6)	4 (3.6)
眼瞼炎	0	1 (1.9)	1 (0.9)
霰粒腫	1 (1.7)	0	1 (0.9)
眼痛	0	1 (1.9)	1 (0.9)
春季カタル	0	1 (1.9)	1 (0.9)
胃腸障害	10 (17.2)	11 (20.4)	21 (18.8)
腹痛	1 (1.7)	4 (7.4)	5 (4.5)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
胃腸障害 (Cont.)			
上腹部痛	2 (3.4)	1 (1.9)	3 (2.7)
便秘	0	1 (1.9)	1 (0.9)
下痢	1 (1.7)	4 (7.4)	5 (4.5)
消化不良	2 (3.4)	1 (1.9)	3 (2.7)
変色便	1 (1.7)	0	1 (0.9)
胃食道逆流性疾患	0	1 (1.9)	1 (0.9)
腸閉塞	1 (1.7)	0	1 (0.9)
悪心	2 (3.4)	2 (3.7)	4 (3.6)
歯の障害	1 (1.7)	0	1 (0.9)
嘔吐	2 (3.4)	3 (5.6)	5 (4.5)
一般・全身障害および投与部位の状態	3 (5.2)	8 (14.8)	11 (9.8)
顔面痛	1 (1.7)	0	1 (0.9)
疲労	1 (1.7)	1 (1.9)	2 (1.8)
インフルエンザ様疾患	1 (1.7)	3 (5.6)	4 (3.6)
発熱	1 (1.7)	3 (5.6)	4 (3.6)
顔面腫脹	0	1 (1.9)	1 (0.9)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
肝胆道系障害	1 (1.7)	0	1 (0.9)
肝機能異常	1 (1.7)	0	1 (0.9)
免疫系障害	2 (3.4)	1 (1.9)	3 (2.7)
アレルギー性浮腫	1 (1.7)	0	1 (0.9)
食物アレルギー	1 (1.7)	0	1 (0.9)
過敏症	0	1 (1.9)	1 (0.9)
感染症および寄生虫症	25 (43.1)	30 (55.6)	55 (49.1)
膿疱性ざ瘡	1 (1.7)	2 (3.7)	3 (2.7)
細菌性疾患キャリアー	1 (1.7)	1 (1.9)	2 (1.8)
気管支炎	1 (1.7)	0	1 (0.9)
結膜炎	1 (1.7)	0	1 (0.9)
耳感染	2 (3.4)	0	2 (1.8)
感染性湿疹	0	1 (1.9)	1 (0.9)
エンテロバクター感染	1 (1.7)	0	1 (0.9)
毛包炎	1 (1.7)	2 (3.7)	3 (2.7)
せつ	2 (3.4)	0	2 (1.8)
胃腸炎	1 (1.7)	1 (1.9)	2 (1.8)
ウイルス性胃腸炎	0	1 (1.9)	1 (0.9)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
感染症および寄生虫症 (Cont.)			
単純ヘルペス	3 (5.2)	2 (3.7)	5 (4.5)
帯状疱疹	0	2 (3.7)	2 (1.8)
膿痂疹	1 (1.7)	2 (3.7)	3 (2.7)
インフルエンザ	1 (1.7)	2 (3.7)	3 (2.7)
シラミ寄生	0	1 (1.9)	1 (0.9)
伝染性軟属腫	0	1 (1.9)	1 (0.9)
上咽頭炎	9 (15.5)	5 (9.3)	14 (12.5)
爪真菌症	1 (1.7)	0	1 (0.9)
口腔ヘルペス	1 (1.7)	1 (1.9)	2 (1.8)
咽頭炎	2 (3.4)	3 (5.6)	5 (4.5)
レンサ球菌性咽頭炎	0	1 (1.9)	1 (0.9)
肺炎	0	1 (1.9)	1 (0.9)
皮膚感染	0	1 (1.9)	1 (0.9)
ブドウ球菌性膿瘍	1 (1.7)	0	1 (0.9)
ブドウ球菌性膿痂疹	1 (1.7)	0	1 (0.9)
ブドウ球菌感染	1 (1.7)	0	1 (0.9)
ブドウ球菌皮膚感染	1 (1.7)	1 (1.9)	2 (1.8)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
感染症および寄生虫症 (Cont.)			
白癬感染	0	1 (1.9)	1 (0.9)
扁桃炎	0	1 (1.9)	1 (0.9)
上気道感染	3 (5.2)	6 (11.1)	9 (8.0)
尿路感染	0	2 (3.7)	2 (1.8)
ウイルス性咽頭炎	1 (1.7)	0	1 (0.9)
ウイルス性上気道感染	0	3 (5.6)	3 (2.7)
外陰部腟カンジダ症	1 (1.7)	0	1 (0.9)
傷害、中毒および処置合併症	2 (3.4)	2 (3.7)	4 (3.6)
事故	0	1 (1.9)	1 (0.9)
挫傷	1 (1.7)	0	1 (0.9)
足骨折	0	1 (1.9)	1 (0.9)
損傷	0	1 (1.9)	1 (0.9)
橈骨骨折	0	1 (1.9)	1 (0.9)
交通事故	0	1 (1.9)	1 (0.9)
スポーツ損傷	1 (1.7)	0	1 (0.9)
熱傷	1 (1.7)	0	1 (0.9)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
臨床検査	8 (13.8)	10 (18.5)	18 (16.1)
アスパラギン酸アミノトランスフェラーゼ増加	1 (1.7)	0	1 (0.9)
血中アルカリホスファターゼ増加	1 (1.7)	0	1 (0.9)
血中コレステロール増加	1 (1.7)	0	1 (0.9)
血中クレアチンホスホキナーゼ増加	3 (5.2)	4 (7.4)	7 (6.3)
血中トリグリセリド増加	1 (1.7)	1 (1.9)	2 (1.8)
血中尿酸増加	1 (1.7)	0	1 (0.9)
好酸球数増加	1 (1.7)	0	1 (0.9)
好酸球百分率増加	1 (1.7)	0	1 (0.9)
結核菌群検査陽性	1 (1.7)	0	1 (0.9)
好中球数減少	1 (1.7)	2 (3.7)	3 (2.7)
好中球百分率減少	1 (1.7)	0	1 (0.9)
尿中蛋白陽性	1 (1.7)	0	1 (0.9)
ブドウ球菌検査陽性	1 (1.7)	0	1 (0.9)
体重増加	0	2 (3.7)	2 (1.8)
白血球数減少	0	1 (1.9)	1 (0.9)
代謝および栄養障害	4 (6.9)	0	4 (3.6)
食欲減退	2 (3.4)	0	2 (1.8)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
代謝および栄養障害 (Cont.)			
食物不耐性	1 (1.7)	0	1 (0.9)
高脂血症	1 (1.7)	0	1 (0.9)
筋骨格系および結合組織障害	1 (1.7)	1 (1.9)	2 (1.8)
四肢痛	0	1 (1.9)	1 (0.9)
顎関節症候群	1 (1.7)	0	1 (0.9)
神経系障害	7 (12.1)	6 (11.1)	13 (11.6)
浮動性めまい	0	1 (1.9)	1 (0.9)
頭痛	7 (12.1)	3 (5.6)	10 (8.9)
片頭痛	0	2 (3.7)	2 (1.8)
失神寸前の状態	0	1 (1.9)	1 (0.9)
精神障害	2 (3.4)	3 (5.6)	5 (4.5)
注意欠陥多動性障害	0	1 (1.9)	1 (0.9)
抑うつ気分	0	1 (1.9)	1 (0.9)
うつ病	1 (1.7)	1 (1.9)	2 (1.8)
悪夢	1 (1.7)	0	1 (0.9)
呼吸器、胸郭および縦隔障害	9 (15.5)	6 (11.1)	15 (13.4)
アレルギー性気管支炎	1 (1.7)	0	1 (0.9)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
喘息	1 (1.7)	1 (1.9)	2 (1.8)
カタル	3 (5.2)	4 (7.4)	7 (6.3)
咳嗽	4 (6.9)	2 (3.7)	6 (5.4)
鼻出血	1 (1.7)	0	1 (0.9)
口腔咽頭痛	1 (1.7)	1 (1.9)	2 (1.8)
鼻漏	2 (3.4)	1 (1.9)	3 (2.7)
副鼻腔うっ血	1 (1.7)	0	1 (0.9)
皮膚および皮下組織障害	20 (34.5)	13 (24.1)	33 (29.5)
ざ瘡	9 (15.5)	10 (18.5)	19 (17.0)
皮膚炎	0	1 (1.9)	1 (0.9)
ざ瘡様皮膚炎	0	1 (1.9)	1 (0.9)
アレルギー性皮膚炎	1 (1.7)	0	1 (0.9)
アトピー性皮膚炎	4 (6.9)	1 (1.9)	5 (4.5)
接触皮膚炎	1 (1.7)	0	1 (0.9)
乾癬様皮膚炎	1 (1.7)	0	1 (0.9)
異汗性湿疹	2 (3.4)	0	2 (1.8)
紅斑	1 (1.7)	1 (1.9)	2 (1.8)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) n (%)	UPA 30 mg QD + TCS (N=54) n (%)	Total (N=112) n (%)
皮膚および皮下組織障害 (Cont.)			
過角化	1 (1.7)	0	1 (0.9)
そう痒症	2 (3.4)	0	2 (1.8)
発疹	1 (1.7)	1 (1.9)	2 (1.8)
皮膚変色	0	1 (1.9)	1 (0.9)
蕁麻疹	0	2 (3.7)	2 (1.8)
血管障害	0	1 (1.9)	1 (0.9)
高血圧	0	1 (1.9)	1 (0.9)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.6.2.2

表 6. ウパダシチニブ投与期間中に有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団，成人）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
Any adverse event	263 (68.5)	285 (75.0)	548 (71.7)
血液およびリンパ系障害	4 (1.0)	13 (3.4)	17 (2.2)
貧血	1 (0.3)	4 (1.1)	5 (0.7)
内出血発生の増加傾向	0	2 (0.5)	2 (0.3)
鉄欠乏性貧血	0	1 (0.3)	1 (0.1)
白血球増加症	1 (0.3)	0	1 (0.1)
白血球減少症	1 (0.3)	1 (0.3)	2 (0.3)
リンパ節症	1 (0.3)	1 (0.3)	2 (0.3)
リンパ球増加症	0	1 (0.3)	1 (0.1)
好中球減少症	1 (0.3)	2 (0.5)	3 (0.4)
汎血球減少症	0	1 (0.3)	1 (0.1)
血小板増加症	0	1 (0.3)	1 (0.1)
心臓障害	2 (0.5)	6 (1.6)	8 (1.0)
徐脈	0	1 (0.3)	1 (0.1)
うっ血性心不全	0	1 (0.3)	1 (0.1)
動悸	1 (0.3)	3 (0.8)	4 (0.5)
洞性徐脈	1 (0.3)	1 (0.3)	2 (0.3)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
心臓障害 (Cont.)			
頻脈	1 (0.3)	0	1 (0.1)
先天性、家族性および遺伝性障害	1 (0.3)	1 (0.3)	2 (0.3)
ジルベール症候群	0	1 (0.3)	1 (0.1)
色素性網膜炎	1 (0.3)	0	1 (0.1)
耳および迷路障害	7 (1.8)	4 (1.1)	11 (1.4)
難聴	1 (0.3)	0	1 (0.1)
耳の障害	1 (0.3)	0	1 (0.1)
耳痛	2 (0.5)	2 (0.5)	4 (0.5)
耳垢分泌過多	1 (0.3)	0	1 (0.1)
聴力低下	0	1 (0.3)	1 (0.1)
回転性めまい	2 (0.5)	1 (0.3)	3 (0.4)
頭位性回転性めまい	1 (0.3)	0	1 (0.1)
内分泌障害	2 (0.5)	1 (0.3)	3 (0.4)
甲状腺機能低下症	1 (0.3)	0	1 (0.1)
甲状腺腫瘤	1 (0.3)	1 (0.3)	2 (0.3)
眼障害	16 (4.2)	20 (5.3)	36 (4.7)
眼瞼炎	1 (0.3)	1 (0.3)	2 (0.3)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
眼障害 (Cont.)			
白内障	0	2 (0.5)	2 (0.3)
霰粒腫	0	2 (0.5)	2 (0.3)
結膜沈着物	0	1 (0.3)	1 (0.1)
結膜充血	0	1 (0.3)	1 (0.1)
結膜刺激	0	1 (0.3)	1 (0.1)
アレルギー性結膜炎	2 (0.5)	3 (0.8)	5 (0.7)
ドライアイ	3 (0.8)	1 (0.3)	4 (0.5)
眼瞼紅斑	1 (0.3)	0	1 (0.1)
眼のアレルギー	0	1 (0.3)	1 (0.1)
眼の炎症	0	1 (0.3)	1 (0.1)
眼痛	1 (0.3)	0	1 (0.1)
眼の異常感覚	0	1 (0.3)	1 (0.1)
眼そう痒症	0	1 (0.3)	1 (0.1)
眼部腫脹	0	3 (0.8)	3 (0.4)
眼瞼障害	0	1 (0.3)	1 (0.1)
緑内障	1 (0.3)	0	1 (0.1)
流涙増加	2 (0.5)	0	2 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
眼障害 (Cont.)			
視神経乳頭浮腫	0	1 (0.3)	1 (0.1)
眼窩周囲浮腫	1 (0.3)	0	1 (0.1)
羞明	0	1 (0.3)	1 (0.1)
網膜剥離	1 (0.3)	1 (0.3)	2 (0.3)
裂孔原性網膜剥離	0	1 (0.3)	1 (0.1)
眼瞼腫脹	1 (0.3)	0	1 (0.1)
潰瘍性角膜炎	1 (0.3)	1 (0.3)	2 (0.3)
霧視	3 (0.8)	1 (0.3)	4 (0.5)
硝子体剥離	0	1 (0.3)	1 (0.1)
眼球乾燥症	1 (0.3)	0	1 (0.1)
胃腸障害	58 (15.1)	57 (15.0)	115 (15.1)
腹部不快感	2 (0.5)	1 (0.3)	3 (0.4)
腹部膨満	2 (0.5)	2 (0.5)	4 (0.5)
腹痛	7 (1.8)	5 (1.3)	12 (1.6)
上腹部痛	14 (3.6)	3 (0.8)	17 (2.2)
口角口唇炎	0	2 (0.5)	2 (0.3)
肛門直腸不快感	0	1 (0.3)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
胃腸障害 (Cont.)			
アフタ性潰瘍	1 (0.3)	1 (0.3)	2 (0.3)
便習慣変化	0	1 (0.3)	1 (0.1)
口唇のひび割れ	1 (0.3)	0	1 (0.1)
慢性胃炎	2 (0.5)	0	2 (0.3)
便秘	6 (1.6)	5 (1.3)	11 (1.4)
齲歯	4 (1.0)	5 (1.3)	9 (1.2)
下痢	11 (2.9)	11 (2.9)	22 (2.9)
口内乾燥	0	1 (0.3)	1 (0.1)
消化不良	6 (1.6)	3 (0.8)	9 (1.2)
嚥下障害	0	2 (0.5)	2 (0.3)
白色便	1 (0.3)	0	1 (0.1)
鼓腸	1 (0.3)	1 (0.3)	2 (0.3)
排便回数増加	0	1 (0.3)	1 (0.1)
胃炎	1 (0.3)	1 (0.3)	2 (0.3)
胃腸障害	1 (0.3)	0	1 (0.1)
胃腸粘膜障害	1 (0.3)	0	1 (0.1)
胃食道逆流性疾患	1 (0.3)	5 (1.3)	6 (0.8)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
胃腸障害 (Cont.)			
舌炎	1 (0.3)	0	1 (0.1)
舌痛	0	1 (0.3)	1 (0.1)
痔核	0	1 (0.3)	1 (0.1)
裂孔ヘルニア	0	1 (0.3)	1 (0.1)
過敏性腸症候群	0	2 (0.5)	2 (0.3)
口唇水疱	1 (0.3)	0	1 (0.1)
口腔内出血	0	1 (0.3)	1 (0.1)
口腔内潰瘍形成	2 (0.5)	0	2 (0.3)
悪心	10 (2.6)	11 (2.9)	21 (2.7)
嚥下痛	1 (0.3)	0	1 (0.1)
口腔瘻	1 (0.3)	0	1 (0.1)
口腔そう痒症	0	1 (0.3)	1 (0.1)
膵炎	1 (0.3)	0	1 (0.1)
歯周病	1 (0.3)	0	1 (0.1)
無髄歯	0	1 (0.3)	1 (0.1)
レッチング	0	1 (0.3)	1 (0.1)
歯の障害	0	1 (0.3)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
胃腸障害 (Cont.)			
埋伏歯	1 (0.3)	3 (0.8)	4 (0.5)
歯痛	3 (0.8)	5 (1.3)	8 (1.0)
嘔吐	2 (0.5)	1 (0.3)	3 (0.4)
一般・全身障害および投与部位の状態	40 (10.4)	33 (8.7)	73 (9.6)
胸部不快感	1 (0.3)	1 (0.3)	2 (0.3)
胸痛	4 (1.0)	2 (0.5)	6 (0.8)
悪寒	2 (0.5)	0	2 (0.3)
嚢胞	1 (0.3)	1 (0.3)	2 (0.3)
顔面浮腫	1 (0.3)	0	1 (0.1)
顔面痛	2 (0.5)	0	2 (0.3)
疲労	8 (2.1)	5 (1.3)	13 (1.7)
熱感	1 (0.3)	0	1 (0.1)
治癒不良	0	1 (0.3)	1 (0.1)
インフルエンザ様疾患	11 (2.9)	8 (2.1)	19 (2.5)
倦怠感	2 (0.5)	0	2 (0.3)
非心臓性胸痛	0	2 (0.5)	2 (0.3)
末梢性浮腫	2 (0.5)	0	2 (0.3)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
疼痛	3 (0.8)	2 (0.5)	5 (0.7)
発熱	12 (3.1)	11 (2.9)	23 (3.0)
腫脹	1 (0.3)	1 (0.3)	2 (0.3)
顔面腫脹	2 (0.5)	0	2 (0.3)
血管穿刺部位内出血	0	1 (0.3)	1 (0.1)
肝胆道系障害	3 (0.8)	4 (1.1)	7 (0.9)
肝機能異常	2 (0.5)	1 (0.3)	3 (0.4)
脂肪肝	1 (0.3)	0	1 (0.1)
肝細胞損傷	0	1 (0.3)	1 (0.1)
肝腫大	0	1 (0.3)	1 (0.1)
非アルコール性脂肪性肝炎	0	1 (0.3)	1 (0.1)
免疫系障害	2 (0.5)	4 (1.1)	6 (0.8)
動物アレルギー	0	1 (0.3)	1 (0.1)
アナフィラキシー反応	0	1 (0.3)	1 (0.1)
薬物過敏症	1 (0.3)	0	1 (0.1)
食物アレルギー	0	1 (0.3)	1 (0.1)
過敏症	2 (0.5)	1 (0.3)	3 (0.4)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
感染症および寄生虫症	191 (49.7)	202 (53.2)	393 (51.4)
四肢膿瘍	0	1 (0.3)	1 (0.1)
口腔膿瘍	0	1 (0.3)	1 (0.1)
ダニ皮膚炎	0	1 (0.3)	1 (0.1)
急性副鼻腔炎	1 (0.3)	0	1 (0.1)
肛門膿瘍	1 (0.3)	0	1 (0.1)
虫垂炎	1 (0.3)	0	1 (0.1)
細菌感染	2 (0.5)	1 (0.3)	3 (0.4)
細菌性膣症	1 (0.3)	0	1 (0.1)
細菌尿	0	1 (0.3)	1 (0.1)
体部白癬	0	4 (1.1)	4 (0.5)
気管支炎	6 (1.6)	11 (2.9)	17 (2.2)
ウイルス性気管支炎	0	1 (0.3)	1 (0.1)
感染性滑液包炎	0	1 (0.3)	1 (0.1)
カンジダ感染	0	1 (0.3)	1 (0.1)
蜂巣炎	1 (0.3)	2 (0.5)	3 (0.4)
条虫感染	1 (0.3)	0	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
感染症および寄生虫症 (Cont.)			
結膜炎	5 (1.3)	4 (1.1)	9 (1.2)
細菌性結膜炎	1 (0.3)	1 (0.3)	2 (0.3)
ウイルス性結膜炎	1 (0.3)	1 (0.3)	2 (0.3)
コロナウイルス感染	1 (0.3)	0	1 (0.1)
膀胱炎	1 (0.3)	1 (0.3)	2 (0.3)
感染性下痢	0	1 (0.3)	1 (0.1)
耳感染	1 (0.3)	1 (0.3)	2 (0.3)
ヘルペス性状湿疹	3 (0.8)	3 (0.8)	6 (0.8)
膿痂疹性湿疹	0	1 (0.3)	1 (0.1)
蟯虫症	1 (0.3)	0	1 (0.1)
丹毒	1 (0.3)	0	1 (0.1)
眼瞼感染	1 (0.3)	0	1 (0.1)
糸状虫症	0	1 (0.3)	1 (0.1)
毛包炎	12 (3.1)	12 (3.2)	24 (3.1)
真菌感染	1 (0.3)	0	1 (0.1)
皮膚真菌感染	2 (0.5)	2 (0.5)	4 (0.5)
せつ	2 (0.5)	2 (0.5)	4 (0.5)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
感染症および寄生虫症 (Cont.)			
ウイルス性胃炎	1 (0.3)	0	1 (0.1)
胃腸炎	9 (2.3)	10 (2.6)	19 (2.5)
ウイルス性胃腸炎	0	5 (1.3)	5 (0.7)
消化管感染	1 (0.3)	0	1 (0.1)
陰部ヘルペス	0	1 (0.3)	1 (0.1)
陰部単純ヘルペス	0	3 (0.8)	3 (0.4)
ジアルジア症	1 (0.3)	0	1 (0.1)
歯肉炎	1 (0.3)	1 (0.3)	2 (0.3)
ヘルペス眼感染	1 (0.3)	2 (0.5)	3 (0.4)
単純ヘルペス	15 (3.9)	13 (3.4)	28 (3.7)
帯状疱疹	6 (1.6)	9 (2.4)	15 (2.0)
皮膚播種性帯状疱疹	1 (0.3)	0	1 (0.1)
耳帯状疱疹	0	1 (0.3)	1 (0.1)
麦粒腫	5 (1.3)	3 (0.8)	8 (1.0)
膿痂疹	3 (0.8)	4 (1.1)	7 (0.9)
感染性皮膚嚢腫	0	1 (0.3)	1 (0.1)
感染	0	1 (0.3)	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
感染症および寄生虫症 (Cont.)			
寄生虫感染	1 (0.3)	0	1 (0.1)
インフルエンザ	14 (3.6)	10 (2.6)	24 (3.1)
関節膿瘍	0	1 (0.3)	1 (0.1)
カポジ水痘様発疹	1 (0.3)	2 (0.5)	3 (0.4)
腎感染	1 (0.3)	0	1 (0.1)
喉頭炎	1 (0.3)	0	1 (0.1)
潜伏結核	0	1 (0.3)	1 (0.1)
マラセチア感染	1 (0.3)	1 (0.3)	2 (0.3)
細菌性乳腺炎	1 (0.3)	0	1 (0.1)
鼻ヘルペス	0	4 (1.1)	4 (0.5)
上咽頭炎	58 (15.1)	65 (17.1)	123 (16.1)
爪真菌症	1 (0.3)	3 (0.8)	4 (0.5)
眼部単純ヘルペス	1 (0.3)	7 (1.8)	8 (1.0)
口腔カンジダ症	1 (0.3)	1 (0.3)	2 (0.3)
口腔ヘルペス	19 (4.9)	31 (8.2)	50 (6.5)
外耳炎	3 (0.8)	1 (0.3)	4 (0.5)
中耳炎	1 (0.3)	1 (0.3)	2 (0.3)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
感染症および寄生虫症 (Cont.)			
急性中耳炎	1 (0.3)	1 (0.3)	2 (0.3)
爪囲炎	1 (0.3)	1 (0.3)	2 (0.3)
歯周炎	1 (0.3)	0	1 (0.1)
眼窩周囲蜂巣炎	1 (0.3)	0	1 (0.1)
扁桃周囲膿瘍	1 (0.3)	0	1 (0.1)
咽頭炎	7 (1.8)	8 (2.1)	15 (2.0)
レンサ球菌性咽頭炎	2 (0.5)	0	2 (0.3)
肺炎	3 (0.8)	2 (0.5)	5 (0.7)
マイコプラズマ性肺炎	0	1 (0.3)	1 (0.1)
ウイルス感染後疲労症候群	0	1 (0.3)	1 (0.1)
術後創感染	0	1 (0.3)	1 (0.1)
歯髄炎	0	1 (0.3)	1 (0.1)
化膿性分泌物	1 (0.3)	0	1 (0.1)
膿疱	0	3 (0.8)	3 (0.4)
腎盂腎炎	1 (0.3)	0	1 (0.1)
膿疱性皮疹	0	1 (0.3)	1 (0.1)
気道感染	3 (0.8)	1 (0.3)	4 (0.5)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
感染症および寄生虫症 (Cont.)			
ウイルス性気道感染	1 (0.3)	1 (0.3)	2 (0.3)
鼻炎	4 (1.0)	0	4 (0.5)
鼻咽頭炎	0	1 (0.3)	1 (0.1)
ライノウイルス感染	0	1 (0.3)	1 (0.1)
副鼻腔炎	3 (0.8)	5 (1.3)	8 (1.0)
皮膚細菌感染	1 (0.3)	1 (0.3)	2 (0.3)
皮膚感染	3 (0.8)	2 (0.5)	5 (0.7)
膿性痰	1 (0.3)	0	1 (0.1)
ブドウ球菌感染	2 (0.5)	3 (0.8)	5 (0.7)
ブドウ球菌皮膚感染	1 (0.3)	2 (0.5)	3 (0.4)
股部白癬	0	3 (0.8)	3 (0.4)
足部白癬	4 (1.0)	6 (1.6)	10 (1.3)
癜風	0	1 (0.3)	1 (0.1)
扁桃炎	4 (1.0)	3 (0.8)	7 (0.9)
歯感染	3 (0.8)	3 (0.8)	6 (0.8)
気管炎	2 (0.5)	1 (0.3)	3 (0.4)
気管気管支炎	1 (0.3)	0	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
感染症および寄生虫症 (Cont.)			
トリコモナス症	0	1 (0.3)	1 (0.1)
トリコフィトン感染症	1 (0.3)	0	1 (0.1)
上気道感染	34 (8.9)	33 (8.7)	67 (8.8)
尿道炎	1 (0.3)	0	1 (0.1)
尿路感染	9 (2.3)	14 (3.7)	23 (3.0)
細菌性尿路感染	0	1 (0.3)	1 (0.1)
腟感染	2 (0.5)	1 (0.3)	3 (0.4)
ウイルス感染	1 (0.3)	3 (0.8)	4 (0.5)
ウイルス性咽頭炎	1 (0.3)	2 (0.5)	3 (0.4)
ウイルス性上気道感染	5 (1.3)	6 (1.6)	11 (1.4)
外陰部腟カンジダ症	1 (0.3)	1 (0.3)	2 (0.3)
外陰腟真菌感染	1 (0.3)	1 (0.3)	2 (0.3)
トリコモナス外陰腟炎	1 (0.3)	0	1 (0.1)
傷害、中毒および処置合併症	22 (5.7)	28 (7.4)	50 (6.5)
事故	1 (0.3)	0	1 (0.1)
動物咬傷	1 (0.3)	0	1 (0.1)
節足動物咬傷	0	2 (0.5)	2 (0.3)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
傷害、中毒および処置合併症 (Cont.)			
骨挫傷	0	1 (0.3)	1 (0.1)
軟骨損傷	0	1 (0.3)	1 (0.1)
胸部損傷	0	1 (0.3)	1 (0.1)
鎖骨骨折	0	1 (0.3)	1 (0.1)
挫傷	0	3 (0.8)	3 (0.4)
角膜擦過傷	0	1 (0.3)	1 (0.1)
頭蓋脳損傷	0	1 (0.3)	1 (0.1)
転倒	1 (0.3)	2 (0.5)	3 (0.4)
大腿骨骨折	0	1 (0.3)	1 (0.1)
足骨折	2 (0.5)	0	2 (0.3)
尾骨骨折	1 (0.3)	0	1 (0.1)
熱疲労	0	1 (0.3)	1 (0.1)
損傷	2 (0.5)	0	2 (0.3)
関節損傷	0	1 (0.3)	1 (0.1)
靭帯捻挫	1 (0.3)	0	1 (0.1)
四肢損傷	3 (0.8)	0	3 (0.4)
半月板損傷	1 (0.3)	0	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
傷害、中毒および処置合併症 (Cont.)			
肉離れ	2 (0.5)	5 (1.3)	7 (0.9)
過量投与	1 (0.3)	0	1 (0.1)
処置による疼痛	1 (0.3)	1 (0.3)	2 (0.3)
肋骨骨折	2 (0.5)	1 (0.3)	3 (0.4)
交通事故	0	1 (0.3)	1 (0.1)
皮膚擦過傷	2 (0.5)	1 (0.3)	3 (0.4)
皮膚裂傷	3 (0.8)	1 (0.3)	4 (0.5)
脊椎骨折	1 (0.3)	0	1 (0.1)
胸骨骨折	1 (0.3)	0	1 (0.1)
腱損傷	0	1 (0.3)	1 (0.1)
歯牙破折	2 (0.5)	1 (0.3)	3 (0.4)
外傷性血腫	1 (0.3)	0	1 (0.1)
創傷	0	1 (0.3)	1 (0.1)
創部分泌	0	1 (0.3)	1 (0.1)
臨床検査	46 (12.0)	46 (12.1)	92 (12.0)
アラニンアミノトランスフェラーゼ増加	8 (2.1)	4 (1.1)	12 (1.6)
アスパラギン酸アミノトランスフェラーゼ異常	1 (0.3)	0	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
臨床検査 (Cont.)			
アスパラギン酸アミノトランスフェラーゼ増加	4 (1.0)	3 (0.8)	7 (0.9)
血中重炭酸塩減少	0	1 (0.3)	1 (0.1)
血中ビリルビン増加	1 (0.3)	0	1 (0.1)
血中コレステロール増加	1 (0.3)	1 (0.3)	2 (0.3)
血中クレアチンホスホキナーゼ増加	23 (6.0)	25 (6.6)	48 (6.3)
血中クレアチニン増加	1 (0.3)	0	1 (0.1)
血中免疫グロブリンＥ増加	1 (0.3)	0	1 (0.1)
血圧上昇	1 (0.3)	1 (0.3)	2 (0.3)
血中トリグリセリド増加	0	2 (0.5)	2 (0.3)
血中尿酸増加	1 (0.3)	0	1 (0.1)
尿中血陽性	0	1 (0.3)	1 (0.1)
体温上昇	0	1 (0.3)	1 (0.1)
好酸球数増加	2 (0.5)	0	2 (0.3)
真菌検査陽性	1 (0.3)	0	1 (0.1)
ヘモグロビン減少	0	2 (0.5)	2 (0.3)
肝酵素上昇	1 (0.3)	0	1 (0.1)
低比重リポ蛋白増加	0	1 (0.3)	1 (0.1)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
臨床検査 (Cont.)			
単球数増加	0	1 (0.3)	1 (0.1)
結核菌群検査陽性	1 (0.3)	0	1 (0.1)
好中球数減少	3 (0.8)	0	3 (0.4)
尿中蛋白陽性	1 (0.3)	1 (0.3)	2 (0.3)
子宮頚部スミア異常	1 (0.3)	0	1 (0.1)
ブドウ球菌検査陽性	1 (0.3)	0	1 (0.1)
トランスアミナーゼ上昇	0	1 (0.3)	1 (0.1)
トロポニン増加	0	1 (0.3)	1 (0.1)
ビタミン D 減少	0	1 (0.3)	1 (0.1)
体重増加	7 (1.8)	6 (1.6)	13 (1.7)
白血球数減少	1 (0.3)	0	1 (0.1)
白血球数増加	0	1 (0.3)	1 (0.1)
尿中白血球陽性	0	1 (0.3)	1 (0.1)
代謝および栄養障害	8 (2.1)	13 (3.4)	21 (2.7)
脱水	0	1 (0.3)	1 (0.1)
糖尿病	0	2 (0.5)	2 (0.3)
脂質異常症	0	2 (0.5)	2 (0.3)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
代謝および栄養障害 (Cont.)			
痛風	1 (0.3)	1 (0.3)	2 (0.3)
高コレステロール血症	1 (0.3)	2 (0.5)	3 (0.4)
高血糖	1 (0.3)	0	1 (0.1)
高ホモシステイン血症	1 (0.3)	0	1 (0.1)
高脂血症	2 (0.5)	3 (0.8)	5 (0.7)
高ナトリウム血症	1 (0.3)	0	1 (0.1)
高尿酸血症	1 (0.3)	1 (0.3)	2 (0.3)
低マグネシウム血症	1 (0.3)	0	1 (0.1)
食欲亢進	0	2 (0.5)	2 (0.3)
ビタミン B12 欠乏	1 (0.3)	0	1 (0.1)
筋骨格系および結合組織障害	29 (7.6)	37 (9.7)	66 (8.6)
関節痛	7 (1.8)	6 (1.6)	13 (1.7)
関節炎	2 (0.5)	2 (0.5)	4 (0.5)
背部痛	7 (1.8)	5 (1.3)	12 (1.6)
骨痛	0	1 (0.3)	1 (0.1)
滑液包炎	1 (0.3)	3 (0.8)	4 (0.5)
椎間板突出	0	2 (0.5)	2 (0.3)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
筋骨格系および結合組織障害 (Cont.)			
関節ロック	0	1 (0.3)	1 (0.1)
関節腫脹	0	1 (0.3)	1 (0.1)
四肢不快感	1 (0.3)	0	1 (0.1)
筋痙縮	1 (0.3)	4 (1.1)	5 (0.7)
筋攣縮	0	1 (0.3)	1 (0.1)
筋骨格系胸痛	1 (0.3)	0	1 (0.1)
筋骨格痛	1 (0.3)	2 (0.5)	3 (0.4)
筋骨格硬直	0	1 (0.3)	1 (0.1)
筋肉痛	5 (1.3)	4 (1.1)	9 (1.2)
頚部腫瘤	0	1 (0.3)	1 (0.1)
頚部痛	2 (0.5)	1 (0.3)	3 (0.4)
骨減少症	0	1 (0.3)	1 (0.1)
四肢痛	2 (0.5)	5 (1.3)	7 (0.9)
足底筋膜炎	1 (0.3)	0	1 (0.1)
滑液嚢腫	0	1 (0.3)	1 (0.1)
顎関節症候群	0	1 (0.3)	1 (0.1)
腱炎	1 (0.3)	1 (0.3)	2 (0.3)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
筋骨格系および結合組織障害 (Cont.)			
腱鞘炎	0	1 (0.3)	1 (0.1)
斜頚	1 (0.3)	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）	8 (2.1)	8 (2.1)	16 (2.1)
結腸腺癌	0	1 (0.3)	1 (0.1)
肛門性器疣贅	0	1 (0.3)	1 (0.1)
良性新生物	0	1 (0.3)	1 (0.1)
精巣の良性新生物	0	1 (0.3)	1 (0.1)
血管腫	1 (0.3)	1 (0.3)	2 (0.3)
ケラトアカントーマ	0	1 (0.3)	1 (0.1)
表皮内悪性黒色腫	0	1 (0.3)	1 (0.1)
結節性筋膜炎	1 (0.3)	0	1 (0.1)
脂漏性角化症	1 (0.3)	0	1 (0.1)
皮膚乳頭腫	5 (1.3)	1 (0.3)	6 (0.8)
子宮平滑筋腫	0	1 (0.3)	1 (0.1)
神経系障害	31 (8.1)	33 (8.7)	64 (8.4)
脳血管発作	0	1 (0.3)	1 (0.1)
注意力障害	1 (0.3)	0	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
神経系障害 (Cont.)			
浮動性めまい	7 (1.8)	4 (1.1)	11 (1.4)
味覚不全	0	2 (0.5)	2 (0.3)
てんかん	0	1 (0.3)	1 (0.1)
頭部不快感	0	1 (0.3)	1 (0.1)
頭痛	17 (4.4)	17 (4.5)	34 (4.5)
過眠症	0	1 (0.3)	1 (0.1)
筋緊張亢進	0	1 (0.3)	1 (0.1)
感覚鈍麻	1 (0.3)	1 (0.3)	2 (0.3)
片頭痛	4 (1.0)	1 (0.3)	5 (0.7)
多発性硬化症再発	0	1 (0.3)	1 (0.1)
神経圧迫	0	1 (0.3)	1 (0.1)
錯感覚	1 (0.3)	1 (0.3)	2 (0.3)
嗅覚錯誤	0	1 (0.3)	1 (0.1)
ヘルペス後神経痛	1 (0.3)	1 (0.3)	2 (0.3)
失神寸前の状態	1 (0.3)	0	1 (0.1)
坐骨神経痛	1 (0.3)	1 (0.3)	2 (0.3)
傾眠	0	1 (0.3)	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
神経系障害 (Cont.)			
失神	0	1 (0.3)	1 (0.1)
三叉神経痛	0	1 (0.3)	1 (0.1)
トンネル状視野	0	1 (0.3)	1 (0.1)
製品の問題	1 (0.3)	0	1 (0.1)
医療機器位置異常	1 (0.3)	0	1 (0.1)
精神障害	10 (2.6)	22 (5.8)	32 (4.2)
感情不安定	1 (0.3)	0	1 (0.1)
不安	3 (0.8)	3 (0.8)	6 (0.8)
双極性障害	0	1 (0.3)	1 (0.1)
抑うつ気分	1 (0.3)	2 (0.5)	3 (0.4)
うつ病	0	1 (0.3)	1 (0.1)
不眠症	2 (0.5)	5 (1.3)	7 (0.9)
故意の自傷行為	0	1 (0.3)	1 (0.1)
易刺激性	1 (0.3)	0	1 (0.1)
リビドー減退	0	1 (0.3)	1 (0.1)
リビドー亢進	1 (0.3)	0	1 (0.1)
精神障害	0	1 (0.3)	1 (0.1)

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精神障害 (Cont.)			
混合性不安抑うつ障害	0	1 (0.3)	1 (0.1)
パニック発作	1 (0.3)	1 (0.3)	2 (0.3)
心的外傷後ストレス障害	0	1 (0.3)	1 (0.1)
睡眠障害	0	2 (0.5)	2 (0.3)
ストレス	0	2 (0.5)	2 (0.3)
自殺念慮	0	1 (0.3)	1 (0.1)
腎および尿路障害	7 (1.8)	6 (1.6)	13 (1.7)
急性腎障害	1 (0.3)	0	1 (0.1)
アルブミン尿	0	1 (0.3)	1 (0.1)
排尿困難	3 (0.8)	0	3 (0.4)
血尿	1 (0.3)	3 (0.8)	4 (0.5)
水腎症	1 (0.3)	0	1 (0.1)
腎結石症	1 (0.3)	0	1 (0.1)
夜間頻尿	1 (0.3)	0	1 (0.1)
多尿	1 (0.3)	0	1 (0.1)
蛋白尿	0	1 (0.3)	1 (0.1)
腎仙痛	0	1 (0.3)	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
生殖系および乳房障害	8 (2.1)	16 (4.2)	24 (3.1)
無月経	0	1 (0.3)	1 (0.1)
萎縮性外陰腟炎	0	1 (0.3)	1 (0.1)
乳房嚢胞	1 (0.3)	0	1 (0.1)
勃起不全	1 (0.3)	3 (0.8)	4 (0.5)
女性化乳房	0	1 (0.3)	1 (0.1)
過少月経	1 (0.3)	0	1 (0.1)
月経過多	1 (0.3)	0	1 (0.1)
月経障害	1 (0.3)	0	1 (0.1)
不規則月経	1 (0.3)	2 (0.5)	3 (0.4)
不正子宮出血	0	1 (0.3)	1 (0.1)
多嚢胞性卵巣	0	1 (0.3)	1 (0.1)
精巣腫瘤	0	2 (0.5)	2 (0.3)
精巣痛	1 (0.3)	3 (0.8)	4 (0.5)
腟分泌物	1 (0.3)	0	1 (0.1)
腟出血	0	1 (0.3)	1 (0.1)
女性外陰部潰瘍	0	1 (0.3)	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
生殖系および乳房障害 (Cont.)			
外陰腟乾燥	1 (0.3)	0	1 (0.1)
呼吸器、胸郭および縦隔障害	43 (11.2)	45 (11.8)	88 (11.5)
失声症	1 (0.3)	0	1 (0.1)
喘息	6 (1.6)	4 (1.1)	10 (1.3)
カタル	2 (0.5)	0	2 (0.3)
慢性閉塞性肺疾患	0	1 (0.3)	1 (0.1)
咳嗽	18 (4.7)	18 (4.7)	36 (4.7)
呼吸困難	2 (0.5)	5 (1.3)	7 (0.9)
鼻出血	4 (1.0)	4 (1.1)	8 (1.0)
喀血	2 (0.5)	0	2 (0.3)
鼻閉	0	1 (0.3)	1 (0.1)
口腔咽頭痛	7 (1.8)	10 (2.6)	17 (2.2)
咽頭腫脹	0	1 (0.3)	1 (0.1)
胸水	1 (0.3)	0	1 (0.1)
湿性咳嗽	1 (0.3)	0	1 (0.1)
肺肉芽腫	0	1 (0.3)	1 (0.1)
肺腫瘤	0	1 (0.3)	1 (0.1)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
気道うっ血	0	2 (0.5)	2 (0.3)
アレルギー性鼻炎	0	2 (0.5)	2 (0.3)
鼻漏	3 (0.8)	3 (0.8)	6 (0.8)
副鼻腔うっ血	0	2 (0.5)	2 (0.3)
くしゃみ	0	1 (0.3)	1 (0.1)
喘息発作重積	1 (0.3)	0	1 (0.1)
咽喉刺激感	0	1 (0.3)	1 (0.1)
上気道うっ血	1 (0.3)	0	1 (0.1)
喘鳴	1 (0.3)	0	1 (0.1)
皮膚および皮下組織障害	108 (28.1)	104 (27.4)	212 (27.7)
ざ瘡	48 (12.5)	54 (14.2)	102 (13.4)
脱毛症	1 (0.3)	0	1 (0.1)
血管浮腫	0	1 (0.3)	1 (0.1)
水疱	2 (0.5)	2 (0.5)	4 (0.5)
冷汗	0	1 (0.3)	1 (0.1)
皮膚嚢腫	2 (0.5)	1 (0.3)	3 (0.4)
皮膚炎	3 (0.8)	1 (0.3)	4 (0.5)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
皮膚および皮下組織障害 (Cont.)			
ざ瘡様皮膚炎	3 (0.8)	2 (0.5)	5 (0.7)
アレルギー性皮膚炎	1 (0.3)	1 (0.3)	2 (0.3)
アトピー性皮膚炎	23 (6.0)	13 (3.4)	36 (4.7)
接触皮膚炎	3 (0.8)	3 (0.8)	6 (0.8)
疱疹状皮膚炎	0	1 (0.3)	1 (0.1)
斑状出血	0	1 (0.3)	1 (0.1)
湿疹	7 (1.8)	5 (1.3)	12 (1.6)
小水疱性湿疹	0	1 (0.3)	1 (0.1)
紅斑	2 (0.5)	1 (0.3)	3 (0.4)
過剰肉芽組織	1 (0.3)	0	1 (0.1)
毛髪成長異常	1 (0.3)	1 (0.3)	2 (0.3)
汗腺炎	0	1 (0.3)	1 (0.1)
多汗症	3 (0.8)	1 (0.3)	4 (0.5)
過角化	1 (0.3)	1 (0.3)	2 (0.3)
多毛症	1 (0.3)	1 (0.3)	2 (0.3)
嵌入爪	0	2 (0.5)	2 (0.3)
苔癬化	0	1 (0.3)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
皮膚および皮下組織障害 (Cont.)			
網状皮斑	0	1 (0.3)	1 (0.1)
稗粒腫	0	1 (0.3)	1 (0.1)
汗疹	1 (0.3)	1 (0.3)	2 (0.3)
寝汗	1 (0.3)	0	1 (0.1)
口囲皮膚炎	1 (0.3)	3 (0.8)	4 (0.5)
光線過敏性反応	0	1 (0.3)	1 (0.1)
そう痒症	2 (0.5)	0	2 (0.3)
偽毛包炎	1 (0.3)	0	1 (0.1)
紫斑	2 (0.5)	0	2 (0.3)
発疹	2 (0.5)	1 (0.3)	3 (0.4)
斑状丘疹状皮疹	0	2 (0.5)	2 (0.3)
丘疹性皮疹	1 (0.3)	3 (0.8)	4 (0.5)
そう痒性皮疹	1 (0.3)	0	1 (0.1)
小水疱性皮疹	1 (0.3)	0	1 (0.1)
酒さ	2 (0.5)	3 (0.8)	5 (0.7)
痂皮	0	2 (0.5)	2 (0.3)
脂漏	1 (0.3)	1 (0.3)	2 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
皮膚および皮下組織障害 (Cont.)			
脂漏性皮膚炎	0	1 (0.3)	1 (0.1)
敏感肌	1 (0.3)	0	1 (0.1)
皮膚障害	0	1 (0.3)	1 (0.1)
皮膚亀裂	1 (0.3)	3 (0.8)	4 (0.5)
皮膚刺激	2 (0.5)	1 (0.3)	3 (0.4)
皮膚腫瘤	0	2 (0.5)	2 (0.3)
皮膚線条	2 (0.5)	0	2 (0.3)
皮膚腫脹	0	1 (0.3)	1 (0.1)
皮膚潰瘍	0	1 (0.3)	1 (0.1)
皮膚熱感	1 (0.3)	0	1 (0.1)
日光黒子	1 (0.3)	0	1 (0.1)
蕁麻疹	8 (2.1)	9 (2.4)	17 (2.2)
圧迫性蕁麻疹	0	1 (0.3)	1 (0.1)
社会環境	1 (0.3)	0	1 (0.1)
歯科補てつ物使用者	1 (0.3)	0	1 (0.1)
外科および内科処置	0	1 (0.3)	1 (0.1)
人工流産	0	1 (0.3)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) n (%)	UPA 30 mg QD + TCS (N=380) n (%)	Total (N=764) n (%)
血管障害	7 (1.8)	7 (1.8)	14 (1.8)
大動脈瘤	0	1 (0.3)	1 (0.1)
深部静脈血栓症	0	1 (0.3)	1 (0.1)
血腫	1 (0.3)	0	1 (0.1)
ほてり	0	1 (0.3)	1 (0.1)
高血圧	5 (1.3)	4 (1.1)	9 (1.2)
起立性低血圧	1 (0.3)	0	1 (0.1)
レイノー現象	0	1 (0.3)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.6.2.3

表 7. ウパダシチニブ投与期間中の有害事象の 100 人年あたりの発現率：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
Any adverse event	1168 (457.7)	1236 (475.5)	2404 (466.7)
血液およびリンパ系障害	8 (3.1)	18 (6.9)	26 (5.0)
貧血	2 (0.8)	4 (1.5)	6 (1.2)
内出血発生の増加傾向	0	2 (0.8)	2 (0.4)
鉄欠乏性貧血	0	1 (0.4)	1 (0.2)
白血球増加症	1 (0.4)	0	1 (0.2)
白血球減少症	1 (0.4)	1 (0.4)	2 (0.4)
リンパ節症	3 (1.2)	2 (0.8)	5 (1.0)
リンパ球増加症	0	1 (0.4)	1 (0.2)
単球減少症	0	1 (0.4)	1 (0.2)
好中球減少症	1 (0.4)	4 (1.5)	5 (1.0)
汎血球減少症	0	1 (0.4)	1 (0.2)
血小板増加症	0	1 (0.4)	1 (0.2)
心臓障害	3 (1.2)	7 (2.7)	10 (1.9)
徐脈	0	1 (0.4)	1 (0.2)
うっ血性心不全	0	1 (0.4)	1 (0.2)
動悸	1 (0.4)	4 (1.5)	5 (1.0)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
心臓障害 (Cont.)			
洞性徐脈	1 (0.4)	1 (0.4)	2 (0.4)
頻脈	1 (0.4)	0	1 (0.2)
先天性、家族性および遺伝性障害	1 (0.4)	1 (0.4)	2 (0.4)
ジルベール症候群	0	1 (0.4)	1 (0.2)
色素性網膜炎	1 (0.4)	0	1 (0.2)
耳および迷路障害	10 (3.9)	6 (2.3)	16 (3.1)
難聴	1 (0.4)	1 (0.4)	2 (0.4)
耳の障害	1 (0.4)	0	1 (0.2)
耳痛	4 (1.6)	2 (0.8)	6 (1.2)
耳垢分泌過多	1 (0.4)	0	1 (0.2)
聴力低下	0	1 (0.4)	1 (0.2)
耳鳴	0	1 (0.4)	1 (0.2)
回転性めまい	2 (0.8)	1 (0.4)	3 (0.6)
頭位性回転性めまい	1 (0.4)	0	1 (0.2)
内分泌障害	2 (0.8)	2 (0.8)	4 (0.8)
甲状腺機能正常症候群	0	1 (0.4)	1 (0.2)
甲状腺機能低下症	1 (0.4)	0	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
内分泌障害 (Cont.)			
甲状腺腫瘤	1 (0.4)	1 (0.4)	2 (0.4)
眼障害	20 (7.8)	32 (12.3)	52 (10.1)
眼瞼炎	1 (0.4)	2 (0.8)	3 (0.6)
白内障	0	2 (0.8)	2 (0.4)
霰粒腫	1 (0.4)	2 (0.8)	3 (0.6)
結膜沈着物	0	1 (0.4)	1 (0.2)
結膜充血	0	1 (0.4)	1 (0.2)
結膜刺激	0	1 (0.4)	1 (0.2)
アレルギー性結膜炎	2 (0.8)	3 (1.2)	5 (1.0)
ドライアイ	3 (1.2)	1 (0.4)	4 (0.8)
眼瞼紅斑	1 (0.4)	0	1 (0.2)
眼のアレルギー	0	1 (0.4)	1 (0.2)
眼の炎症	0	1 (0.4)	1 (0.2)
眼痛	1 (0.4)	1 (0.4)	2 (0.4)
眼の異常感覚	0	1 (0.4)	1 (0.2)
眼そう痒症	0	1 (0.4)	1 (0.2)
眼部腫脹	0	4 (1.5)	4 (0.8)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
眼障害 (Cont.)			
眼瞼障害	0	1 (0.4)	1 (0.2)
緑内障	1 (0.4)	0	1 (0.2)
流涙増加	2 (0.8)	0	2 (0.4)
視神経乳頭浮腫	0	1 (0.4)	1 (0.2)
眼窩周囲浮腫	1 (0.4)	0	1 (0.2)
羞明	0	1 (0.4)	1 (0.2)
網膜剥離	1 (0.4)	1 (0.4)	2 (0.4)
裂孔原性網膜剥離	0	2 (0.8)	2 (0.4)
眼瞼腫脹	1 (0.4)	0	1 (0.2)
潰瘍性角膜炎	1 (0.4)	1 (0.4)	2 (0.4)
春季カタル	0	1 (0.4)	1 (0.2)
霧視	3 (1.2)	1 (0.4)	4 (0.8)
硝子体剥離	0	1 (0.4)	1 (0.2)
眼球乾燥症	1 (0.4)	0	1 (0.2)
胃腸障害	105 (41.1)	107 (41.2)	212 (41.2)
腹部不快感	2 (0.8)	1 (0.4)	3 (0.6)
腹部膨満	2 (0.8)	2 (0.8)	4 (0.8)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
胃腸障害 (Cont.)			
腹痛	10 (3.9)	11 (4.2)	21 (4.1)
上腹部痛	16 (6.3)	4 (1.5)	20 (3.9)
口角口唇炎	0	2 (0.8)	2 (0.4)
肛門直腸不快感	0	1 (0.4)	1 (0.2)
アフタ性潰瘍	2 (0.8)	2 (0.8)	4 (0.8)
便習慣変化	0	1 (0.4)	1 (0.2)
口唇のひび割れ	1 (0.4)	0	1 (0.2)
慢性胃炎	2 (0.8)	0	2 (0.4)
便秘	6 (2.4)	6 (2.3)	12 (2.3)
齲歯	4 (1.6)	5 (1.9)	9 (1.7)
下痢	13 (5.1)	21 (8.1)	34 (6.6)
口内乾燥	0	1 (0.4)	1 (0.2)
消化不良	9 (3.5)	4 (1.5)	13 (2.5)
嚥下障害	0	2 (0.8)	2 (0.4)
変色便	1 (0.4)	0	1 (0.2)
白色便	1 (0.4)	0	1 (0.2)
鼓腸	1 (0.4)	1 (0.4)	2 (0.4)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
胃腸障害 (Cont.)			
排便回数増加	0	1 (0.4)	1 (0.2)
胃炎	1 (0.4)	1 (0.4)	2 (0.4)
胃腸障害	1 (0.4)	0	1 (0.2)
胃腸粘膜障害	1 (0.4)	0	1 (0.2)
胃食道逆流性疾患	1 (0.4)	6 (2.3)	7 (1.4)
舌炎	1 (0.4)	0	1 (0.2)
舌痛	0	1 (0.4)	1 (0.2)
痔核	0	1 (0.4)	1 (0.2)
裂孔ヘルニア	0	1 (0.4)	1 (0.2)
腸閉塞	1 (0.4)	0	1 (0.2)
過敏性腸症候群	0	2 (0.8)	2 (0.4)
口唇水疱	1 (0.4)	0	1 (0.2)
口腔内出血	0	1 (0.4)	1 (0.2)
口腔内潰瘍形成	2 (0.8)	0	2 (0.4)
悪心	13 (5.1)	13 (5.0)	26 (5.0)
嚥下痛	1 (0.4)	0	1 (0.2)
口腔瘻	1 (0.4)	0	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
胃腸障害 (Cont.)			
口腔そう痒症	0	1 (0.4)	1 (0.2)
膵炎	1 (0.4)	0	1 (0.2)
歯周病	1 (0.4)	0	1 (0.2)
無髄歯	0	1 (0.4)	1 (0.2)
レッチング	0	1 (0.4)	1 (0.2)
歯の障害	1 (0.4)	1 (0.4)	2 (0.4)
埋伏歯	1 (0.4)	3 (1.2)	4 (0.8)
歯痛	3 (1.2)	5 (1.9)	8 (1.6)
嘔吐	4 (1.6)	4 (1.5)	8 (1.6)
一般・全身障害および投与部位の状態	61 (23.9)	56 (21.5)	117 (22.7)
胸部不快感	1 (0.4)	1 (0.4)	2 (0.4)
胸痛	4 (1.6)	2 (0.8)	6 (1.2)
悪寒	2 (0.8)	0	2 (0.4)
嚢胞	1 (0.4)	1 (0.4)	2 (0.4)
顔面浮腫	1 (0.4)	0	1 (0.2)
顔面痛	3 (1.2)	0	3 (0.6)
疲労	9 (3.5)	6 (2.3)	15 (2.9)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
一般・全身障害および投与部位の状態 (Cont.)			
熱感	1 (0.4)	0	1 (0.2)
治癒不良	0	1 (0.4)	1 (0.2)
インフルエンザ様疾患	14 (5.5)	17 (6.5)	31 (6.0)
倦怠感	2 (0.8)	0	2 (0.4)
非心臓性胸痛	0	2 (0.8)	2 (0.4)
末梢性浮腫	2 (0.8)	0	2 (0.4)
疼痛	4 (1.6)	2 (0.8)	6 (1.2)
発熱	14 (5.5)	18 (6.9)	32 (6.2)
腫脹	1 (0.4)	1 (0.4)	2 (0.4)
顔面腫脹	2 (0.8)	1 (0.4)	3 (0.6)
血管穿刺部位内出血	0	4 (1.5)	4 (0.8)
肝胆道系障害	4 (1.6)	4 (1.5)	8 (1.6)
肝機能異常	3 (1.2)	1 (0.4)	4 (0.8)
脂肪肝	1 (0.4)	0	1 (0.2)
肝細胞損傷	0	1 (0.4)	1 (0.2)
肝腫大	0	1 (0.4)	1 (0.2)
非アルコール性脂肪性肝炎	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
免疫系障害	5 (2.0)	6 (2.3)	11 (2.1)
アレルギー性浮腫	1 (0.4)	0	1 (0.2)
動物アレルギー	0	1 (0.4)	1 (0.2)
アナフィラキシー反応	0	1 (0.4)	1 (0.2)
薬物過敏症	1 (0.4)	0	1 (0.2)
食物アレルギー	1 (0.4)	2 (0.8)	3 (0.6)
過敏症	2 (0.8)	2 (0.8)	4 (0.8)
感染症および寄生虫症	434 (170.1)	455 (175.0)	889 (172.6)
四肢膿瘍	0	1 (0.4)	1 (0.2)
口腔膿瘍	0	1 (0.4)	1 (0.2)
ダニ皮膚炎	0	1 (0.4)	1 (0.2)
膿疱性ざ瘡	1 (0.4)	2 (0.8)	3 (0.6)
急性副鼻腔炎	1 (0.4)	0	1 (0.2)
肛門膿瘍	1 (0.4)	0	1 (0.2)
虫垂炎	1 (0.4)	0	1 (0.2)
細菌性疾患キャリアー	1 (0.4)	1 (0.4)	2 (0.4)
細菌感染	2 (0.8)	1 (0.4)	3 (0.6)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
細菌性膣症	1 (0.4)	0	1 (0.2)
細菌尿	0	1 (0.4)	1 (0.2)
体部白癬	0	4 (1.5)	4 (0.8)
気管支炎	7 (2.7)	12 (4.6)	19 (3.7)
ウイルス性気管支炎	0	1 (0.4)	1 (0.2)
感染性滑液包炎	0	1 (0.4)	1 (0.2)
カンジダ感染	0	1 (0.4)	1 (0.2)
蜂巣炎	1 (0.4)	3 (1.2)	4 (0.8)
条虫感染	1 (0.4)	0	1 (0.2)
結膜炎	7 (2.7)	4 (1.5)	11 (2.1)
細菌性結膜炎	1 (0.4)	1 (0.4)	2 (0.4)
ウイルス性結膜炎	1 (0.4)	1 (0.4)	2 (0.4)
コロナウイルス感染	1 (0.4)	0	1 (0.2)
膀胱炎	1 (0.4)	1 (0.4)	2 (0.4)
感染性下痢	0	1 (0.4)	1 (0.2)
耳感染	3 (1.2)	1 (0.4)	4 (0.8)
ヘルペス性状湿疹	3 (1.2)	3 (1.2)	6 (1.2)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
膿痂疹性湿疹	0	1 (0.4)	1 (0.2)
感染性湿疹	0	1 (0.4)	1 (0.2)
エンテロバクター感染	1 (0.4)	0	1 (0.2)
蟯虫症	1 (0.4)	0	1 (0.2)
丹毒	1 (0.4)	0	1 (0.2)
眼瞼感染	1 (0.4)	0	1 (0.2)
糸状虫症	0	1 (0.4)	1 (0.2)
毛包炎	14 (5.5)	15 (5.8)	29 (5.6)
真菌感染	1 (0.4)	0	1 (0.2)
皮膚真菌感染	2 (0.8)	2 (0.8)	4 (0.8)
せつ	4 (1.6)	2 (0.8)	6 (1.2)
ウイルス性胃炎	1 (0.4)	0	1 (0.2)
胃腸炎	11 (4.3)	13 (5.0)	24 (4.7)
ウイルス性胃腸炎	0	6 (2.3)	6 (1.2)
消化管感染	1 (0.4)	0	1 (0.2)
陰部ヘルペス	0	2 (0.8)	2 (0.4)
陰部単純ヘルペス	0	3 (1.2)	3 (0.6)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
ジアルジア症	1 (0.4)	0	1 (0.2)
歯肉炎	1 (0.4)	1 (0.4)	2 (0.4)
ヘルペス眼感染	1 (0.4)	2 (0.8)	3 (0.6)
単純ヘルペス	31 (12.1)	20 (7.7)	51 (9.9)
帯状疱疹	6 (2.4)	11 (4.2)	17 (3.3)
皮膚播種性帯状疱疹	1 (0.4)	0	1 (0.2)
耳帯状疱疹	0	1 (0.4)	1 (0.2)
麦粒腫	5 (2.0)	3 (1.2)	8 (1.6)
膿痂疹	4 (1.6)	7 (2.7)	11 (2.1)
感染性皮膚嚢腫	0	1 (0.4)	1 (0.2)
感染	0	1 (0.4)	1 (0.2)
寄生虫感染	1 (0.4)	0	1 (0.2)
インフルエンザ	16 (6.3)	12 (4.6)	28 (5.4)
関節膿瘍	0	1 (0.4)	1 (0.2)
カポジ水痘様発疹	1 (0.4)	3 (1.2)	4 (0.8)
腎感染	1 (0.4)	0	1 (0.2)
喉頭炎	1 (0.4)	0	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
潜伏結核	0	1 (0.4)	1 (0.2)
シラミ寄生	0	1 (0.4)	1 (0.2)
マラセチア感染	1 (0.4)	1 (0.4)	2 (0.4)
細菌性乳腺炎	1 (0.4)	0	1 (0.2)
伝染性軟属腫	0	1 (0.4)	1 (0.2)
鼻ヘルペス	0	4 (1.5)	4 (0.8)
上咽頭炎	102 (40.0)	82 (31.5)	184 (35.7)
爪真菌症	2 (0.8)	3 (1.2)	5 (1.0)
眼部単純ヘルペス	1 (0.4)	8 (3.1)	9 (1.7)
口腔カンジダ症	1 (0.4)	1 (0.4)	2 (0.4)
口腔ヘルペス	34 (13.3)	46 (17.7)	80 (15.5)
外耳炎	3 (1.2)	1 (0.4)	4 (0.8)
中耳炎	1 (0.4)	1 (0.4)	2 (0.4)
急性中耳炎	1 (0.4)	1 (0.4)	2 (0.4)
爪囲炎	1 (0.4)	1 (0.4)	2 (0.4)
歯周炎	1 (0.4)	0	1 (0.2)
眼窩周囲蜂巣炎	1 (0.4)	0	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
扁桃周囲膿瘍	1 (0.4)	0	1 (0.2)
咽頭炎	11 (4.3)	11 (4.2)	22 (4.3)
レンサ球菌性咽頭炎	2 (0.8)	1 (0.4)	3 (0.6)
肺炎	3 (1.2)	3 (1.2)	6 (1.2)
マイコプラズマ性肺炎	0	1 (0.4)	1 (0.2)
ウイルス感染後疲労症候群	0	1 (0.4)	1 (0.2)
術後創感染	0	1 (0.4)	1 (0.2)
歯髄炎	0	1 (0.4)	1 (0.2)
化膿性分泌物	1 (0.4)	0	1 (0.2)
膿疱	0	3 (1.2)	3 (0.6)
腎盂腎炎	1 (0.4)	0	1 (0.2)
膿疱性皮疹	0	1 (0.4)	1 (0.2)
気道感染	3 (1.2)	1 (0.4)	4 (0.8)
ウイルス性気道感染	1 (0.4)	1 (0.4)	2 (0.4)
鼻炎	5 (2.0)	0	5 (1.0)
鼻咽頭炎	0	1 (0.4)	1 (0.2)
ライノウイルス感染	0	1 (0.4)	1 (0.2)

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感染症および寄生虫症 (Cont.)			
副鼻腔炎	3 (1.2)	6 (2.3)	9 (1.7)
皮膚細菌感染	1 (0.4)	1 (0.4)	2 (0.4)
皮膚感染	3 (1.2)	4 (1.5)	7 (1.4)
膿性痰	1 (0.4)	0	1 (0.2)
ブドウ球菌性膿瘍	1 (0.4)	0	1 (0.2)
ブドウ球菌性膿痂疹	1 (0.4)	0	1 (0.2)
ブドウ球菌感染	4 (1.6)	4 (1.5)	8 (1.6)
ブドウ球菌皮膚感染	2 (0.8)	3 (1.2)	5 (1.0)
股部白癬	0	4 (1.5)	4 (0.8)
白癬感染	0	1 (0.4)	1 (0.2)
足部白癬	4 (1.6)	6 (2.3)	10 (1.9)
癜風	0	1 (0.4)	1 (0.2)
扁桃炎	4 (1.6)	4 (1.5)	8 (1.6)
歯感染	3 (1.2)	3 (1.2)	6 (1.2)
気管炎	2 (0.8)	2 (0.8)	4 (0.8)
気管気管支炎	1 (0.4)	0	1 (0.2)
トリコモナス症	0	1 (0.4)	1 (0.2)

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感染症および寄生虫症 (Cont.)			
トリコフィトン感染症	1 (0.4)	0	1 (0.2)
上気道感染	50 (19.6)	49 (18.8)	99 (19.2)
尿道炎	1 (0.4)	0	1 (0.2)
尿路感染	15 (5.9)	16 (6.2)	31 (6.0)
細菌性尿路感染	0	1 (0.4)	1 (0.2)
腟感染	2 (0.8)	1 (0.4)	3 (0.6)
ウイルス感染	1 (0.4)	3 (1.2)	4 (0.8)
ウイルス性咽頭炎	2 (0.8)	2 (0.8)	4 (0.8)
ウイルス性上気道感染	8 (3.1)	11 (4.2)	19 (3.7)
外陰部腟カンジダ症	2 (0.8)	1 (0.4)	3 (0.6)
外陰腟真菌感染	1 (0.4)	1 (0.4)	2 (0.4)
トリコモナス外陰腟炎	1 (0.4)	0	1 (0.2)
傷害、中毒および処置合併症	35 (13.7)	36 (13.8)	71 (13.8)
事故	1 (0.4)	2 (0.8)	3 (0.6)
動物咬傷	1 (0.4)	0	1 (0.2)
節足動物咬傷	0	2 (0.8)	2 (0.4)
骨挫傷	0	1 (0.4)	1 (0.2)

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傷害、中毒および処置合併症 (Cont.)			
軟骨損傷	0	1 (0.4)	1 (0.2)
胸部損傷	0	1 (0.4)	1 (0.2)
鎖骨骨折	0	1 (0.4)	1 (0.2)
挫傷	1 (0.4)	3 (1.2)	4 (0.8)
角膜擦過傷	0	1 (0.4)	1 (0.2)
頭蓋脳損傷	0	1 (0.4)	1 (0.2)
転倒	1 (0.4)	2 (0.8)	3 (0.6)
大腿骨骨折	0	1 (0.4)	1 (0.2)
足骨折	2 (0.8)	1 (0.4)	3 (0.6)
尾骨骨折	1 (0.4)	0	1 (0.2)
熱疲労	0	1 (0.4)	1 (0.2)
損傷	3 (1.2)	1 (0.4)	4 (0.8)
関節損傷	0	1 (0.4)	1 (0.2)
靭帯捻挫	1 (0.4)	0	1 (0.2)
四肢損傷	3 (1.2)	0	3 (0.6)
半月板損傷	1 (0.4)	0	1 (0.2)
肉離れ	3 (1.2)	5 (1.9)	8 (1.6)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
傷害、中毒および処置合併症 (Cont.)			
過量投与	1 (0.4)	0	1 (0.2)
処置による疼痛	1 (0.4)	1 (0.4)	2 (0.4)
橈骨骨折	0	1 (0.4)	1 (0.2)
肋骨骨折	2 (0.8)	1 (0.4)	3 (0.6)
交通事故	0	2 (0.8)	2 (0.4)
皮膚擦過傷	2 (0.8)	1 (0.4)	3 (0.6)
皮膚裂傷	3 (1.2)	1 (0.4)	4 (0.8)
脊椎骨折	1 (0.4)	0	1 (0.2)
スポーツ損傷	1 (0.4)	0	1 (0.2)
胸骨骨折	1 (0.4)	0	1 (0.2)
腱損傷	0	1 (0.4)	1 (0.2)
熱傷	1 (0.4)	0	1 (0.2)
歯牙破折	3 (1.2)	1 (0.4)	4 (0.8)
外傷性血腫	1 (0.4)	0	1 (0.2)
創傷	0	1 (0.4)	1 (0.2)
創部分泌	0	1 (0.4)	1 (0.2)

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臨床検査	88 (34.5)	71 (27.3)	159 (30.9)
アラニンアミノトランスフェラーゼ増加	11 (4.3)	4 (1.5)	15 (2.9)
アスパラギン酸アミノトランスフェラーゼ異常	1 (0.4)	0	1 (0.2)
アスパラギン酸アミノトランスフェラーゼ増加	6 (2.4)	3 (1.2)	9 (1.7)
血中アルカリホスファターゼ増加	1 (0.4)	0	1 (0.2)
血中重炭酸塩減少	0	1 (0.4)	1 (0.2)
血中ビリルビン増加	2 (0.8)	0	2 (0.4)
血中コレステロール増加	3 (1.2)	2 (0.8)	5 (1.0)
血中クレアチンホスホキナーゼ増加	30 (11.8)	31 (11.9)	61 (11.8)
血中クレアチニン増加	1 (0.4)	0	1 (0.2)
血中免疫グロブリン E 増加	1 (0.4)	0	1 (0.2)
血圧上昇	1 (0.4)	1 (0.4)	2 (0.4)
血中トリグリセリド増加	1 (0.4)	4 (1.5)	5 (1.0)
血中尿酸増加	2 (0.8)	0	2 (0.4)
尿中血陽性	0	1 (0.4)	1 (0.2)
体温上昇	0	1 (0.4)	1 (0.2)
好酸球数増加	3 (1.2)	0	3 (0.6)
好酸球百分率増加	1 (0.4)	0	1 (0.2)

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臨床検査 (Cont.)			
真菌検査陽性	1 (0.4)	0	1 (0.2)
ヘモグロビン減少	0	2 (0.8)	2 (0.4)
肝酵素上昇	1 (0.4)	0	1 (0.2)
低比重リポ蛋白増加	0	1 (0.4)	1 (0.2)
単球数増加	0	1 (0.4)	1 (0.2)
結核菌群検査陽性	2 (0.8)	0	2 (0.4)
好中球数減少	4 (1.6)	2 (0.8)	6 (1.2)
好中球百分率減少	1 (0.4)	0	1 (0.2)
尿中蛋白陽性	3 (1.2)	1 (0.4)	4 (0.8)
子宮頚部スミア異常	1 (0.4)	0	1 (0.2)
ブドウ球菌検査陽性	3 (1.2)	0	3 (0.6)
トランスアミナーゼ上昇	0	1 (0.4)	1 (0.2)
トロポニン増加	0	1 (0.4)	1 (0.2)
ビタミン D 減少	0	1 (0.4)	1 (0.2)
体重増加	7 (2.7)	9 (3.5)	16 (3.1)
白血球数減少	1 (0.4)	1 (0.4)	2 (0.4)
白血球数増加	0	1 (0.4)	1 (0.2)

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臨床検査 (Cont.)			
尿中白血球陽性	0	2 (0.8)	2 (0.4)
代謝および栄養障害	18 (7.1)	14 (5.4)	32 (6.2)
食欲減退	2 (0.8)	0	2 (0.4)
脱水	0	1 (0.4)	1 (0.2)
糖尿病	0	2 (0.8)	2 (0.4)
脂質異常症	0	2 (0.8)	2 (0.4)
食物不耐性	1 (0.4)	0	1 (0.2)
痛風	1 (0.4)	1 (0.4)	2 (0.4)
高コレステロール血症	1 (0.4)	2 (0.8)	3 (0.6)
高血糖	1 (0.4)	0	1 (0.2)
高ホモシステイン血症	1 (0.4)	0	1 (0.2)
高脂血症	6 (2.4)	3 (1.2)	9 (1.7)
高ナトリウム血症	1 (0.4)	0	1 (0.2)
高尿酸血症	2 (0.8)	1 (0.4)	3 (0.6)
低マグネシウム血症	1 (0.4)	0	1 (0.2)
食欲亢進	0	2 (0.8)	2 (0.4)
ビタミン B12 欠乏	1 (0.4)	0	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
筋骨格系および結合組織障害	37 (14.5)	50 (19.2)	87 (16.9)
関節痛	7 (2.7)	8 (3.1)	15 (2.9)
関節炎	2 (0.8)	2 (0.8)	4 (0.8)
背部痛	7 (2.7)	5 (1.9)	12 (2.3)
骨痛	0	1 (0.4)	1 (0.2)
滑液包炎	1 (0.4)	3 (1.2)	4 (0.8)
椎間板突出	0	2 (0.8)	2 (0.4)
関節ロック	0	1 (0.4)	1 (0.2)
関節腫脹	0	1 (0.4)	1 (0.2)
四肢不快感	1 (0.4)	0	1 (0.2)
筋痙縮	1 (0.4)	5 (1.9)	6 (1.2)
筋攣縮	0	1 (0.4)	1 (0.2)
筋骨格系胸痛	1 (0.4)	0	1 (0.2)
筋骨格痛	1 (0.4)	2 (0.8)	3 (0.6)
筋骨格硬直	0	1 (0.4)	1 (0.2)
筋肉痛	7 (2.7)	4 (1.5)	11 (2.1)
頚部腫瘤	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
筋骨格系および結合組織障害 (Cont.)			
頚部痛	2 (0.8)	1 (0.4)	3 (0.6)
骨減少症	0	1 (0.4)	1 (0.2)
四肢痛	3 (1.2)	6 (2.3)	9 (1.7)
足底筋膜炎	1 (0.4)	0	1 (0.2)
滑液嚢腫	0	1 (0.4)	1 (0.2)
顎関節症候群	1 (0.4)	2 (0.8)	3 (0.6)
腱炎	1 (0.4)	1 (0.4)	2 (0.4)
腱鞘炎	0	1 (0.4)	1 (0.2)
斜頚	1 (0.4)	0	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	8 (3.1)	9 (3.5)	17 (3.3)
結腸腺癌	0	1 (0.4)	1 (0.2)
肛門性器疣贅	0	1 (0.4)	1 (0.2)
良性新生物	0	1 (0.4)	1 (0.2)
精巣の良性新生物	0	1 (0.4)	1 (0.2)
血管腫	1 (0.4)	1 (0.4)	2 (0.4)
ケラトアカントーマ	0	1 (0.4)	1 (0.2)
表皮内悪性黒色腫	0	1 (0.4)	1 (0.2)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
結節性筋膜炎	1 (0.4)	0	1 (0.2)
脂漏性角化症	1 (0.4)	0	1 (0.2)
皮膚乳頭腫	5 (2.0)	1 (0.4)	6 (1.2)
子宮平滑筋腫	0	1 (0.4)	1 (0.2)
神経系障害	44 (17.2)	56 (21.5)	100 (19.4)
脳血管発作	0	1 (0.4)	1 (0.2)
注意力障害	1 (0.4)	0	1 (0.2)
浮動性めまい	7 (2.7)	7 (2.7)	14 (2.7)
味覚不全	0	2 (0.8)	2 (0.4)
てんかん	0	1 (0.4)	1 (0.2)
頭部不快感	0	1 (0.4)	1 (0.2)
頭痛	27 (10.6)	27 (10.4)	54 (10.5)
過眠症	0	1 (0.4)	1 (0.2)
筋緊張亢進	0	1 (0.4)	1 (0.2)
感覚鈍麻	1 (0.4)	1 (0.4)	2 (0.4)
片頭痛	4 (1.6)	3 (1.2)	7 (1.4)
多発性硬化症再発	0	1 (0.4)	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
神経系障害 (Cont.)			
神経圧迫	0	1 (0.4)	1 (0.2)
錯感覚	1 (0.4)	1 (0.4)	2 (0.4)
嗅覚錯誤	0	1 (0.4)	1 (0.2)
ヘルペス後神経痛	1 (0.4)	1 (0.4)	2 (0.4)
失神寸前の状態	1 (0.4)	1 (0.4)	2 (0.4)
坐骨神経痛	1 (0.4)	1 (0.4)	2 (0.4)
傾眠	0	1 (0.4)	1 (0.2)
失神	0	1 (0.4)	1 (0.2)
三叉神経痛	0	1 (0.4)	1 (0.2)
トンネル状視野	0	1 (0.4)	1 (0.2)
製品の問題	1 (0.4)	0	1 (0.2)
医療機器位置異常	1 (0.4)	0	1 (0.2)
精神障害	13 (5.1)	28 (10.8)	41 (8.0)
感情不安定	1 (0.4)	0	1 (0.2)
不安	4 (1.6)	3 (1.2)	7 (1.4)
注意欠陥多動性障害	0	1 (0.4)	1 (0.2)
双極性障害	0	1 (0.4)	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
精神障害 (Cont.)			
抑うつ気分	1 (0.4)	3 (1.2)	4 (0.8)
うつ病	1 (0.4)	2 (0.8)	3 (0.6)
不眠症	2 (0.8)	5 (1.9)	7 (1.4)
故意の自傷行為	0	1 (0.4)	1 (0.2)
易刺激性	1 (0.4)	0	1 (0.2)
リビドー減退	0	1 (0.4)	1 (0.2)
リビドー亢進	1 (0.4)	0	1 (0.2)
精神障害	0	3 (1.2)	3 (0.6)
混合性不安抑うつ障害	0	1 (0.4)	1 (0.2)
悪夢	1 (0.4)	0	1 (0.2)
パニック発作	1 (0.4)	1 (0.4)	2 (0.4)
心的外傷後ストレス障害	0	1 (0.4)	1 (0.2)
睡眠障害	0	2 (0.8)	2 (0.4)
ストレス	0	2 (0.8)	2 (0.4)
自殺念慮	0	1 (0.4)	1 (0.2)
腎および尿路障害	9 (3.5)	8 (3.1)	17 (3.3)
急性腎障害	1 (0.4)	0	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
腎および尿路障害 (Cont.)			
アルブミン尿	0	1 (0.4)	1 (0.2)
排尿困難	3 (1.2)	0	3 (0.6)
血尿	1 (0.4)	3 (1.2)	4 (0.8)
水腎症	1 (0.4)	0	1 (0.2)
腎結石症	1 (0.4)	0	1 (0.2)
夜間頻尿	1 (0.4)	0	1 (0.2)
多尿	1 (0.4)	0	1 (0.2)
蛋白尿	0	1 (0.4)	1 (0.2)
腎仙痛	0	3 (1.2)	3 (0.6)
生殖系および乳房障害	9 (3.5)	17 (6.5)	26 (5.0)
無月経	0	1 (0.4)	1 (0.2)
萎縮性外陰膣炎	0	1 (0.4)	1 (0.2)
乳房嚢胞	1 (0.4)	0	1 (0.2)
勃起不全	1 (0.4)	3 (1.2)	4 (0.8)
女性化乳房	0	1 (0.4)	1 (0.2)
過少月経	1 (0.4)	0	1 (0.2)
月経過多	1 (0.4)	0	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
生殖系および乳房障害 (Cont.)			
月経障害	1 (0.4)	0	1 (0.2)
不規則月経	1 (0.4)	2 (0.8)	3 (0.6)
不正子宮出血	0	1 (0.4)	1 (0.2)
多嚢胞性卵巣	0	1 (0.4)	1 (0.2)
精巣腫瘤	0	2 (0.8)	2 (0.4)
精巣痛	1 (0.4)	3 (1.2)	4 (0.8)
腟分泌物	1 (0.4)	0	1 (0.2)
腟出血	0	1 (0.4)	1 (0.2)
女性外陰部潰瘍	0	1 (0.4)	1 (0.2)
外陰腟乾燥	1 (0.4)	0	1 (0.2)
呼吸器、胸郭および縦隔障害	73 (28.6)	71 (27.3)	144 (28.0)
アレルギー性気管支炎	1 (0.4)	0	1 (0.2)
失声症	2 (0.8)	0	2 (0.4)
喘息	7 (2.7)	6 (2.3)	13 (2.5)
カタル	5 (2.0)	4 (1.5)	9 (1.7)
慢性閉塞性肺疾患	0	1 (0.4)	1 (0.2)
咳嗽	24 (9.4)	21 (8.1)	45 (8.7)

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呼吸器、胸郭および縦隔障害 (Cont.)			
呼吸困難	2 (0.8)	5 (1.9)	7 (1.4)
鼻出血	6 (2.4)	4 (1.5)	10 (1.9)
喀血	2 (0.8)	0	2 (0.4)
鼻閉	0	1 (0.4)	1 (0.2)
口腔咽頭痛	11 (4.3)	14 (5.4)	25 (4.9)
咽頭腫脹	0	1 (0.4)	1 (0.2)
胸水	1 (0.4)	0	1 (0.2)
湿性咳嗽	2 (0.8)	0	2 (0.4)
肺肉芽腫	0	1 (0.4)	1 (0.2)
肺腫瘤	0	1 (0.4)	1 (0.2)
気道うっ血	0	2 (0.8)	2 (0.4)
アレルギー性鼻炎	0	2 (0.8)	2 (0.4)
鼻漏	6 (2.4)	4 (1.5)	10 (1.9)
副鼻腔うっ血	1 (0.4)	2 (0.8)	3 (0.6)
くしゃみ	0	1 (0.4)	1 (0.2)
喘息発作重積	1 (0.4)	0	1 (0.2)
咽喉刺激感	0	1 (0.4)	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
呼吸器、胸郭および縦隔障害 (Cont.)			
上気道うっ血	1 (0.4)	0	1 (0.2)
喘鳴	1 (0.4)	0	1 (0.2)
皮膚および皮下組織障害	172 (67.4)	171 (65.8)	343 (66.6)
ざ瘡	61 (23.9)	72 (27.7)	133 (25.8)
脱毛症	1 (0.4)	0	1 (0.2)
血管浮腫	0	1 (0.4)	1 (0.2)
水疱	2 (0.8)	2 (0.8)	4 (0.8)
冷汗	0	1 (0.4)	1 (0.2)
皮膚嚢腫	3 (1.2)	1 (0.4)	4 (0.8)
皮膚炎	5 (2.0)	2 (0.8)	7 (1.4)
ざ瘡様皮膚炎	3 (1.2)	3 (1.2)	6 (1.2)
アレルギー性皮膚炎	2 (0.8)	1 (0.4)	3 (0.6)
アトピー性皮膚炎	30 (11.8)	16 (6.2)	46 (8.9)
接触皮膚炎	4 (1.6)	4 (1.5)	8 (1.6)
疱疹状皮膚炎	0	1 (0.4)	1 (0.2)
乾癬様皮膚炎	1 (0.4)	0	1 (0.2)
異汗性湿疹	3 (1.2)	0	3 (0.6)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
斑状出血	0	2 (0.8)	2 (0.4)
湿疹	8 (3.1)	5 (1.9)	13 (2.5)
小水疱性湿疹	0	1 (0.4)	1 (0.2)
紅斑	3 (1.2)	2 (0.8)	5 (1.0)
過剰肉芽組織	1 (0.4)	0	1 (0.2)
毛髪成長異常	1 (0.4)	1 (0.4)	2 (0.4)
汗腺炎	0	1 (0.4)	1 (0.2)
多汗症	3 (1.2)	1 (0.4)	4 (0.8)
過角化	2 (0.8)	1 (0.4)	3 (0.6)
多毛症	1 (0.4)	1 (0.4)	2 (0.4)
嵌入爪	0	2 (0.8)	2 (0.4)
苔癬化	0	1 (0.4)	1 (0.2)
網状皮斑	0	1 (0.4)	1 (0.2)
稗粒腫	0	1 (0.4)	1 (0.2)
汗疹	1 (0.4)	1 (0.4)	2 (0.4)
寝汗	1 (0.4)	0	1 (0.2)
口囲皮膚炎	1 (0.4)	3 (1.2)	4 (0.8)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
光線過敏性反応	0	1 (0.4)	1 (0.2)
そう痒症	4 (1.6)	0	4 (0.8)
偽毛包炎	1 (0.4)	0	1 (0.2)
紫斑	2 (0.8)	0	2 (0.4)
発疹	3 (1.2)	2 (0.8)	5 (1.0)
斑状丘疹状皮疹	0	2 (0.8)	2 (0.4)
丘疹性皮疹	2 (0.8)	3 (1.2)	5 (1.0)
そう痒性皮疹	1 (0.4)	0	1 (0.2)
小水疱性皮疹	1 (0.4)	0	1 (0.2)
酒さ	2 (0.8)	5 (1.9)	7 (1.4)
痂皮	0	2 (0.8)	2 (0.4)
脂漏	1 (0.4)	1 (0.4)	2 (0.4)
脂漏性皮膚炎	0	1 (0.4)	1 (0.2)
敏感肌	1 (0.4)	0	1 (0.2)
皮膚変色	0	1 (0.4)	1 (0.2)
皮膚障害	0	1 (0.4)	1 (0.2)
皮膚亀裂	1 (0.4)	5 (1.9)	6 (1.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
皮膚刺激	2 (0.8)	1 (0.4)	3 (0.6)
皮膚腫瘤	0	2 (0.8)	2 (0.4)
皮膚線条	2 (0.8)	0	2 (0.4)
皮膚腫脹	0	1 (0.4)	1 (0.2)
皮膚潰瘍	0	1 (0.4)	1 (0.2)
皮膚熱感	1 (0.4)	0	1 (0.2)
日光黒子	1 (0.4)	0	1 (0.2)
蕁麻疹	10 (3.9)	13 (5.0)	23 (4.5)
圧迫性蕁麻疹	0	1 (0.4)	1 (0.2)
社会環境	1 (0.4)	0	1 (0.2)
歯科補てつ物使用者	1 (0.4)	0	1 (0.2)
外科および内科処置	0	1 (0.4)	1 (0.2)
人工流産	0	1 (0.4)	1 (0.2)
血管障害	7 (2.7)	10 (3.8)	17 (3.3)
大動脈瘤	0	1 (0.4)	1 (0.2)
深部静脈血栓症	0	1 (0.4)	1 (0.2)
血腫	1 (0.4)	0	1 (0.2)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
血管障害 (Cont.)			
ほてり	0	1 (0.4)	1 (0.2)
高血圧	5 (2.0)	6 (2.3)	11 (2.1)
起立性低血圧	1 (0.4)	0	1 (0.2)
レイノー現象	0	1 (0.4)	1 (0.2)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.7.2.1

表 8. ウパダシチニブ投与期間中の有害事象の 100 人年あたりの発現率：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団，青少年）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
Any adverse event	147 (415.9)	146 (411.3)	293 (413.6)
血液およびリンパ系障害	2 (5.7)	2 (5.6)	4 (5.6)
リンパ節症	2 (5.7)	1 (2.8)	3 (4.2)
単球減少症	0	1 (2.8)	1 (1.4)
耳および迷路障害	2 (5.7)	2 (5.6)	4 (5.6)
難聴	0	1 (2.8)	1 (1.4)
耳痛	2 (5.7)	0	2 (2.8)
耳鳴	0	1 (2.8)	1 (1.4)
内分泌障害	0	1 (2.8)	1 (1.4)
甲状腺機能正常症候群	0	1 (2.8)	1 (1.4)
眼障害	1 (2.8)	3 (8.5)	4 (5.6)
眼瞼炎	0	1 (2.8)	1 (1.4)
霰粒腫	1 (2.8)	0	1 (1.4)
眼痛	0	1 (2.8)	1 (1.4)
春季カタル	0	1 (2.8)	1 (1.4)
胃腸障害	15 (42.4)	17 (47.9)	32 (45.2)
腹痛	1 (2.8)	4 (11.3)	5 (7.1)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
胃腸障害 (Cont.)			
上腹部痛	2 (5.7)	1 (2.8)	3 (4.2)
便秘	0	1 (2.8)	1 (1.4)
下痢	2 (5.7)	4 (11.3)	6 (8.5)
消化不良	2 (5.7)	1 (2.8)	3 (4.2)
変色便	1 (2.8)	0	1 (1.4)
胃食道逆流性疾患	0	1 (2.8)	1 (1.4)
腸閉塞	1 (2.8)	0	1 (1.4)
悪心	3 (8.5)	2 (5.6)	5 (7.1)
歯の障害	1 (2.8)	0	1 (1.4)
嘔吐	2 (5.7)	3 (8.5)	5 (7.1)
一般・全身障害および投与部位の状態	4 (11.3)	11 (31.0)	15 (21.2)
顔面痛	1 (2.8)	0	1 (1.4)
疲労	1 (2.8)	1 (2.8)	2 (2.8)
インフルエンザ様疾患	1 (2.8)	5 (14.1)	6 (8.5)
発熱	1 (2.8)	4 (11.3)	5 (7.1)
顔面腫脹	0	1 (2.8)	1 (1.4)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
肝胆道系障害	1 (2.8)	0	1 (1.4)
肝機能異常	1 (2.8)	0	1 (1.4)
免疫系障害	2 (5.7)	1 (2.8)	3 (4.2)
アレルギー性浮腫	1 (2.8)	0	1 (1.4)
食物アレルギー	1 (2.8)	0	1 (1.4)
過敏症	0	1 (2.8)	1 (1.4)
感染症および寄生虫症	45 (127.3)	51 (143.7)	96 (135.5)
膿疱性ざ瘡	1 (2.8)	2 (5.6)	3 (4.2)
細菌性疾患キャリアー	1 (2.8)	1 (2.8)	2 (2.8)
気管支炎	1 (2.8)	0	1 (1.4)
結膜炎	1 (2.8)	0	1 (1.4)
耳感染	2 (5.7)	0	2 (2.8)
感染性湿疹	0	1 (2.8)	1 (1.4)
エンテロバクター感染	1 (2.8)	0	1 (1.4)
毛包炎	2 (5.7)	2 (5.6)	4 (5.6)
せつ	2 (5.7)	0	2 (2.8)
胃腸炎	1 (2.8)	1 (2.8)	2 (2.8)
ウイルス性胃腸炎	0	1 (2.8)	1 (1.4)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
単純ヘルペス	4 (11.3)	2 (5.6)	6 (8.5)
帯状疱疹	0	2 (5.6)	2 (2.8)
膿痂疹	1 (2.8)	2 (5.6)	3 (4.2)
インフルエンザ	1 (2.8)	2 (5.6)	3 (4.2)
シラミ寄生	0	1 (2.8)	1 (1.4)
伝染性軟属腫	0	1 (2.8)	1 (1.4)
上咽頭炎	13 (36.8)	6 (16.9)	19 (26.8)
爪真菌症	1 (2.8)	0	1 (1.4)
口腔ヘルペス	1 (2.8)	1 (2.8)	2 (2.8)
咽頭炎	3 (8.5)	3 (8.5)	6 (8.5)
レンサ球菌性咽頭炎	0	1 (2.8)	1 (1.4)
肺炎	0	1 (2.8)	1 (1.4)
皮膚感染	0	1 (2.8)	1 (1.4)
ブドウ球菌性膿瘍	1 (2.8)	0	1 (1.4)
ブドウ球菌性膿痂疹	1 (2.8)	0	1 (1.4)
ブドウ球菌感染	1 (2.8)	0	1 (1.4)
ブドウ球菌皮膚感染	1 (2.8)	1 (2.8)	2 (2.8)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
白癬感染	0	1 (2.8)	1 (1.4)
扁桃炎	0	1 (2.8)	1 (1.4)
上気道感染	3 (8.5)	11 (31.0)	14 (19.8)
尿路感染	0	2 (5.6)	2 (2.8)
ウイルス性咽頭炎	1 (2.8)	0	1 (1.4)
ウイルス性上気道感染	0	4 (11.3)	4 (5.6)
外陰部腟カンジダ症	1 (2.8)	0	1 (1.4)
傷害、中毒および処置合併症	3 (8.5)	6 (16.9)	9 (12.7)
事故	0	2 (5.6)	2 (2.8)
挫傷	1 (2.8)	0	1 (1.4)
足骨折	0	1 (2.8)	1 (1.4)
損傷	0	1 (2.8)	1 (1.4)
橈骨骨折	0	1 (2.8)	1 (1.4)
交通事故	0	1 (2.8)	1 (1.4)
スポーツ損傷	1 (2.8)	0	1 (1.4)
熱傷	1 (2.8)	0	1 (1.4)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
臨床検査	16 (45.3)	11 (31.0)	27 (38.1)
アスパラギン酸アミノトランスフェラーゼ増加	1 (2.8)	0	1 (1.4)
血中アルカリホスファターゼ増加	1 (2.8)	0	1 (1.4)
血中コレステロール増加	2 (5.7)	0	2 (2.8)
血中クレアチンホスホキナーゼ増加	3 (8.5)	4 (11.3)	7 (9.9)
血中トリグリセリド増加	1 (2.8)	1 (2.8)	2 (2.8)
血中尿酸増加	1 (2.8)	0	1 (1.4)
好酸球数増加	1 (2.8)	0	1 (1.4)
好酸球百分率増加	1 (2.8)	0	1 (1.4)
結核菌群検査陽性	1 (2.8)	0	1 (1.4)
好中球数減少	1 (2.8)	2 (5.6)	3 (4.2)
好中球百分率減少	1 (2.8)	0	1 (1.4)
尿中蛋白陽性	1 (2.8)	0	1 (1.4)
ブドウ球菌検査陽性	1 (2.8)	0	1 (1.4)
体重増加	0	3 (8.5)	3 (4.2)
白血球数減少	0	1 (2.8)	1 (1.4)
代謝および栄養障害	5 (14.1)	0	5 (7.1)
食欲減退	2 (5.7)	0	2 (2.8)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
代謝および栄養障害 (Cont.)			
食物不耐性	1 (2.8)	0	1 (1.4)
高脂血症	2 (5.7)	0	2 (2.8)
筋骨格系および結合組織障害	1 (2.8)	1 (2.8)	2 (2.8)
四肢痛	0	1 (2.8)	1 (1.4)
顎関節症候群	1 (2.8)	0	1 (1.4)
神経系障害	7 (19.8)	8 (22.5)	15 (21.2)
浮動性めまい	0	1 (2.8)	1 (1.4)
頭痛	7 (19.8)	4 (11.3)	11 (15.5)
片頭痛	0	2 (5.6)	2 (2.8)
失神寸前の状態	0	1 (2.8)	1 (1.4)
精神障害	2 (5.7)	3 (8.5)	5 (7.1)
注意欠陥多動性障害	0	1 (2.8)	1 (1.4)
抑うつ気分	0	1 (2.8)	1 (1.4)
うつ病	1 (2.8)	1 (2.8)	2 (2.8)
悪夢	1 (2.8)	0	1 (1.4)
呼吸器、胸郭および縦隔障害	16 (45.3)	9 (25.4)	25 (35.3)
アレルギー性気管支炎	1 (2.8)	0	1 (1.4)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
呼吸器、胸郭および縦隔障害 (Cont.)			
喘息	1 (2.8)	1 (2.8)	2 (2.8)
カタル	3 (8.5)	4 (11.3)	7 (9.9)
咳嗽	5 (14.1)	2 (5.6)	7 (9.9)
鼻出血	1 (2.8)	0	1 (1.4)
口腔咽頭痛	2 (5.7)	1 (2.8)	3 (4.2)
鼻漏	2 (5.7)	1 (2.8)	3 (4.2)
副鼻腔うっ血	1 (2.8)	0	1 (1.4)
皮膚および皮下組織障害	25 (70.7)	19 (53.5)	44 (62.1)
ざ瘡	9 (25.5)	10 (28.2)	19 (26.8)
皮膚炎	0	1 (2.8)	1 (1.4)
ざ瘡様皮膚炎	0	1 (2.8)	1 (1.4)
アレルギー性皮膚炎	1 (2.8)	0	1 (1.4)
アトピー性皮膚炎	5 (14.1)	2 (5.6)	7 (9.9)
接触皮膚炎	1 (2.8)	0	1 (1.4)
乾癬様皮膚炎	1 (2.8)	0	1 (1.4)
異汗性湿疹	3 (8.5)	0	3 (4.2)
紅斑	1 (2.8)	1 (2.8)	2 (2.8)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=58) (PYS=35.3) Events (E/100PY)	UPA 30 mg QD + TCS (N=54) (PYS=35.5) Events (E/100PY)	Total (N=112) (PYS=70.8) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
過角化	1 (2.8)	0	1 (1.4)
そう痒症	2 (5.7)	0	2 (2.8)
発疹	1 (2.8)	1 (2.8)	2 (2.8)
皮膚変色	0	1 (2.8)	1 (1.4)
蕁麻疹	0	2 (5.6)	2 (2.8)
血管障害	0	1 (2.8)	1 (1.4)
高血圧	0	1 (2.8)	1 (1.4)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of
upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.7.2.2

表 9. ウパダシチニブ投与期間中の有害事象の 100 人年あたりの発現率：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団, 成人）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
Any adverse event	1021 (464.4)	1090 (485.6)	2111 (475.1)
血液およびリンパ系障害	6 (2.7)	16 (7.1)	22 (5.0)
貧血	2 (0.9)	4 (1.8)	6 (1.4)
内出血発生の増加傾向	0	2 (0.9)	2 (0.5)
鉄欠乏性貧血	0	1 (0.4)	1 (0.2)
白血球増加症	1 (0.5)	0	1 (0.2)
白血球減少症	1 (0.5)	1 (0.4)	2 (0.5)
リンパ節症	1 (0.5)	1 (0.4)	2 (0.5)
リンパ球増加症	0	1 (0.4)	1 (0.2)
好中球減少症	1 (0.5)	4 (1.8)	5 (1.1)
汎血球減少症	0	1 (0.4)	1 (0.2)
血小板増加症	0	1 (0.4)	1 (0.2)
心臓障害	3 (1.4)	7 (3.1)	10 (2.3)
徐脈	0	1 (0.4)	1 (0.2)
うっ血性心不全	0	1 (0.4)	1 (0.2)
動悸	1 (0.5)	4 (1.8)	5 (1.1)
洞性徐脈	1 (0.5)	1 (0.4)	2 (0.5)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
心臓障害 (Cont.)			
頻脈	1 (0.5)	0	1 (0.2)
先天性、家族性および遺伝性障害	1 (0.5)	1 (0.4)	2 (0.5)
ジルベール症候群	0	1 (0.4)	1 (0.2)
色素性網膜炎	1 (0.5)	0	1 (0.2)
耳および迷路障害	8 (3.6)	4 (1.8)	12 (2.7)
難聴	1 (0.5)	0	1 (0.2)
耳の障害	1 (0.5)	0	1 (0.2)
耳痛	2 (0.9)	2 (0.9)	4 (0.9)
耳垢分泌過多	1 (0.5)	0	1 (0.2)
聴力低下	0	1 (0.4)	1 (0.2)
回転性めまい	2 (0.9)	1 (0.4)	3 (0.7)
頭位性回転性めまい	1 (0.5)	0	1 (0.2)
内分泌障害	2 (0.9)	1 (0.4)	3 (0.7)
甲状腺機能低下症	1 (0.5)	0	1 (0.2)
甲状腺腫瘤	1 (0.5)	1 (0.4)	2 (0.5)
眼障害	19 (8.6)	29 (12.9)	48 (10.8)
眼瞼炎	1 (0.5)	1 (0.4)	2 (0.5)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
眼障害 (Cont.)			
白内障	0	2 (0.9)	2 (0.5)
霰粒腫	0	2 (0.9)	2 (0.5)
結膜沈着物	0	1 (0.4)	1 (0.2)
結膜充血	0	1 (0.4)	1 (0.2)
結膜刺激	0	1 (0.4)	1 (0.2)
アレルギー性結膜炎	2 (0.9)	3 (1.3)	5 (1.1)
ドライアイ	3 (1.4)	1 (0.4)	4 (0.9)
眼瞼紅斑	1 (0.5)	0	1 (0.2)
眼のアレルギー	0	1 (0.4)	1 (0.2)
眼の炎症	0	1 (0.4)	1 (0.2)
眼痛	1 (0.5)	0	1 (0.2)
眼の異常感覚	0	1 (0.4)	1 (0.2)
眼そう痒症	0	1 (0.4)	1 (0.2)
眼部腫脹	0	4 (1.8)	4 (0.9)
眼瞼障害	0	1 (0.4)	1 (0.2)
緑内障	1 (0.5)	0	1 (0.2)
流涙増加	2 (0.9)	0	2 (0.5)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
眼障害 (Cont.)			
視神経乳頭浮腫	0	1 (0.4)	1 (0.2)
眼窩周囲浮腫	1 (0.5)	0	1 (0.2)
羞明	0	1 (0.4)	1 (0.2)
網膜剥離	1 (0.5)	1 (0.4)	2 (0.5)
裂孔原性網膜剥離	0	2 (0.9)	2 (0.5)
眼瞼腫脹	1 (0.5)	0	1 (0.2)
潰瘍性角膜炎	1 (0.5)	1 (0.4)	2 (0.5)
霧視	3 (1.4)	1 (0.4)	4 (0.9)
硝子体剥離	0	1 (0.4)	1 (0.2)
眼球乾燥症	1 (0.5)	0	1 (0.2)
胃腸障害	90 (40.9)	90 (40.1)	180 (40.5)
腹部不快感	2 (0.9)	1 (0.4)	3 (0.7)
腹部膨満	2 (0.9)	2 (0.9)	4 (0.9)
腹痛	9 (4.1)	7 (3.1)	16 (3.6)
上腹部痛	14 (6.4)	3 (1.3)	17 (3.8)
口角口唇炎	0	2 (0.9)	2 (0.5)
肛門直腸不快感	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
胃腸障害 (Cont.)			
アフタ性潰瘍	2 (0.9)	2 (0.9)	4 (0.9)
便習慣変化	0	1 (0.4)	1 (0.2)
口唇のひび割れ	1 (0.5)	0	1 (0.2)
慢性胃炎	2 (0.9)	0	2 (0.5)
便秘	6 (2.7)	5 (2.2)	11 (2.5)
齲歯	4 (1.8)	5 (2.2)	9 (2.0)
下痢	11 (5.0)	17 (7.6)	28 (6.3)
口内乾燥	0	1 (0.4)	1 (0.2)
消化不良	7 (3.2)	3 (1.3)	10 (2.3)
嚥下障害	0	2 (0.9)	2 (0.5)
白色便	1 (0.5)	0	1 (0.2)
鼓腸	1 (0.5)	1 (0.4)	2 (0.5)
排便回数増加	0	1 (0.4)	1 (0.2)
胃炎	1 (0.5)	1 (0.4)	2 (0.5)
胃腸障害	1 (0.5)	0	1 (0.2)
胃腸粘膜障害	1 (0.5)	0	1 (0.2)
胃食道逆流性疾患	1 (0.5)	5 (2.2)	6 (1.4)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
胃腸障害 (Cont.)			
舌炎	1 (0.5)	0	1 (0.2)
舌痛	0	1 (0.4)	1 (0.2)
痔核	0	1 (0.4)	1 (0.2)
裂孔ヘルニア	0	1 (0.4)	1 (0.2)
過敏性腸症候群	0	2 (0.9)	2 (0.5)
口唇水疱	1 (0.5)	0	1 (0.2)
口腔内出血	0	1 (0.4)	1 (0.2)
口腔内潰瘍形成	2 (0.9)	0	2 (0.5)
悪心	10 (4.5)	11 (4.9)	21 (4.7)
嚥下痛	1 (0.5)	0	1 (0.2)
口腔瘻	1 (0.5)	0	1 (0.2)
口腔そう痒症	0	1 (0.4)	1 (0.2)
膵炎	1 (0.5)	0	1 (0.2)
歯周病	1 (0.5)	0	1 (0.2)
無髄歯	0	1 (0.4)	1 (0.2)
レッチング	0	1 (0.4)	1 (0.2)
歯の障害	0	1 (0.4)	1 (0.2)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
胃腸障害 (Cont.)			
埋伏歯	1 (0.5)	3 (1.3)	4 (0.9)
歯痛	3 (1.4)	5 (2.2)	8 (1.8)
嘔吐	2 (0.9)	1 (0.4)	3 (0.7)
一般・全身障害および投与部位の状態	57 (25.9)	45 (20.0)	102 (23.0)
胸部不快感	1 (0.5)	1 (0.4)	2 (0.5)
胸痛	4 (1.8)	2 (0.9)	6 (1.4)
悪寒	2 (0.9)	0	2 (0.5)
嚢胞	1 (0.5)	1 (0.4)	2 (0.5)
顔面浮腫	1 (0.5)	0	1 (0.2)
顔面痛	2 (0.9)	0	2 (0.5)
疲労	8 (3.6)	5 (2.2)	13 (2.9)
熱感	1 (0.5)	0	1 (0.2)
治癒不良	0	1 (0.4)	1 (0.2)
インフルエンザ様疾患	13 (5.9)	12 (5.3)	25 (5.6)
倦怠感	2 (0.9)	0	2 (0.5)
非心臓性胸痛	0	2 (0.9)	2 (0.5)
末梢性浮腫	2 (0.9)	0	2 (0.5)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
一般・全身障害および投与部位の状態 (Cont.)			
疼痛	4 (1.8)	2 (0.9)	6 (1.4)
発熱	13 (5.9)	14 (6.2)	27 (6.1)
腫脹	1 (0.5)	1 (0.4)	2 (0.5)
顔面腫脹	2 (0.9)	0	2 (0.5)
血管穿刺部位内出血	0	4 (1.8)	4 (0.9)
肝胆道系障害	3 (1.4)	4 (1.8)	7 (1.6)
肝機能異常	2 (0.9)	1 (0.4)	3 (0.7)
脂肪肝	1 (0.5)	0	1 (0.2)
肝細胞損傷	0	1 (0.4)	1 (0.2)
肝腫大	0	1 (0.4)	1 (0.2)
非アルコール性脂肪性肝炎	0	1 (0.4)	1 (0.2)
免疫系障害	3 (1.4)	5 (2.2)	8 (1.8)
動物アレルギー	0	1 (0.4)	1 (0.2)
アナフィラキシー反応	0	1 (0.4)	1 (0.2)
薬物過敏症	1 (0.5)	0	1 (0.2)
食物アレルギー	0	2 (0.9)	2 (0.5)
過敏症	2 (0.9)	1 (0.4)	3 (0.7)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
感染症および寄生虫症	389 (176.9)	404 (180.0)	793 (178.5)
四肢膿瘍	0	1 (0.4)	1 (0.2)
口腔膿瘍	0	1 (0.4)	1 (0.2)
ダニ皮膚炎	0	1 (0.4)	1 (0.2)
急性副鼻腔炎	1 (0.5)	0	1 (0.2)
肛門膿瘍	1 (0.5)	0	1 (0.2)
虫垂炎	1 (0.5)	0	1 (0.2)
細菌感染	2 (0.9)	1 (0.4)	3 (0.7)
細菌性膣症	1 (0.5)	0	1 (0.2)
細菌尿	0	1 (0.4)	1 (0.2)
体部白癬	0	4 (1.8)	4 (0.9)
気管支炎	6 (2.7)	12 (5.3)	18 (4.1)
ウイルス性気管支炎	0	1 (0.4)	1 (0.2)
感染性滑液包炎	0	1 (0.4)	1 (0.2)
カンジダ感染	0	1 (0.4)	1 (0.2)
蜂巣炎	1 (0.5)	3 (1.3)	4 (0.9)
条虫感染	1 (0.5)	0	1 (0.2)

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感染症および寄生虫症 (Cont.)			
結膜炎	6 (2.7)	4 (1.8)	10 (2.3)
細菌性結膜炎	1 (0.5)	1 (0.4)	2 (0.5)
ウイルス性結膜炎	1 (0.5)	1 (0.4)	2 (0.5)
コロナウイルス感染	1 (0.5)	0	1 (0.2)
膀胱炎	1 (0.5)	1 (0.4)	2 (0.5)
感染性下痢	0	1 (0.4)	1 (0.2)
耳感染	1 (0.5)	1 (0.4)	2 (0.5)
ヘルペス性状湿疹	3 (1.4)	3 (1.3)	6 (1.4)
膿痂疹性湿疹	0	1 (0.4)	1 (0.2)
蟯虫症	1 (0.5)	0	1 (0.2)
丹毒	1 (0.5)	0	1 (0.2)
眼瞼感染	1 (0.5)	0	1 (0.2)
糸状虫症	0	1 (0.4)	1 (0.2)
毛包炎	12 (5.5)	13 (5.8)	25 (5.6)
真菌感染	1 (0.5)	0	1 (0.2)
皮膚真菌感染	2 (0.9)	2 (0.9)	4 (0.9)
せつ	2 (0.9)	2 (0.9)	4 (0.9)

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E/100PY = Events per 100 patient-years.

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
ウイルス性胃炎	1 (0.5)	0	1 (0.2)
胃腸炎	10 (4.5)	12 (5.3)	22 (5.0)
ウイルス性胃腸炎	0	5 (2.2)	5 (1.1)
消化管感染	1 (0.5)	0	1 (0.2)
陰部ヘルペス	0	2 (0.9)	2 (0.5)
陰部単純ヘルペス	0	3 (1.3)	3 (0.7)
ジアルジア症	1 (0.5)	0	1 (0.2)
歯肉炎	1 (0.5)	1 (0.4)	2 (0.5)
ヘルペス眼感染	1 (0.5)	2 (0.9)	3 (0.7)
単純ヘルペス	27 (12.3)	18 (8.0)	45 (10.1)
帯状疱疹	6 (2.7)	9 (4.0)	15 (3.4)
皮膚播種性帯状疱疹	1 (0.5)	0	1 (0.2)
耳帯状疱疹	0	1 (0.4)	1 (0.2)
麦粒腫	5 (2.3)	3 (1.3)	8 (1.8)
膿痂疹	3 (1.4)	5 (2.2)	8 (1.8)
感染性皮膚嚢腫	0	1 (0.4)	1 (0.2)
感染	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
寄生虫感染	1 (0.5)	0	1 (0.2)
インフルエンザ	15 (6.8)	10 (4.5)	25 (5.6)
関節膿瘍	0	1 (0.4)	1 (0.2)
カポジ水痘様発疹	1 (0.5)	3 (1.3)	4 (0.9)
腎感染	1 (0.5)	0	1 (0.2)
喉頭炎	1 (0.5)	0	1 (0.2)
潜伏結核	0	1 (0.4)	1 (0.2)
マラセチア感染	1 (0.5)	1 (0.4)	2 (0.5)
細菌性乳腺炎	1 (0.5)	0	1 (0.2)
鼻ヘルペス	0	4 (1.8)	4 (0.9)
上咽頭炎	89 (40.5)	76 (33.9)	165 (37.1)
爪真菌症	1 (0.5)	3 (1.3)	4 (0.9)
眼部単純ヘルペス	1 (0.5)	8 (3.6)	9 (2.0)
口腔カンジダ症	1 (0.5)	1 (0.4)	2 (0.5)
口腔ヘルペス	33 (15.0)	45 (20.0)	78 (17.6)
外耳炎	3 (1.4)	1 (0.4)	4 (0.9)
中耳炎	1 (0.5)	1 (0.4)	2 (0.5)

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E/100PY = Events per 100 patient-years.

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
急性中耳炎	1 (0.5)	1 (0.4)	2 (0.5)
爪囲炎	1 (0.5)	1 (0.4)	2 (0.5)
歯周炎	1 (0.5)	0	1 (0.2)
眼窩周囲蜂巣炎	1 (0.5)	0	1 (0.2)
扁桃周囲膿瘍	1 (0.5)	0	1 (0.2)
咽頭炎	8 (3.6)	8 (3.6)	16 (3.6)
レンサ球菌性咽頭炎	2 (0.9)	0	2 (0.5)
肺炎	3 (1.4)	2 (0.9)	5 (1.1)
マイコプラズマ性肺炎	0	1 (0.4)	1 (0.2)
ウイルス感染後疲労症候群	0	1 (0.4)	1 (0.2)
術後創感染	0	1 (0.4)	1 (0.2)
歯髄炎	0	1 (0.4)	1 (0.2)
化膿性分泌物	1 (0.5)	0	1 (0.2)
膿疱	0	3 (1.3)	3 (0.7)
腎盂腎炎	1 (0.5)	0	1 (0.2)
膿疱性皮疹	0	1 (0.4)	1 (0.2)
気道感染	3 (1.4)	1 (0.4)	4 (0.9)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
ウイルス性気道感染	1 (0.5)	1 (0.4)	2 (0.5)
鼻炎	5 (2.3)	0	5 (1.1)
鼻咽頭炎	0	1 (0.4)	1 (0.2)
ライノウイルス感染	0	1 (0.4)	1 (0.2)
副鼻腔炎	3 (1.4)	6 (2.7)	9 (2.0)
皮膚細菌感染	1 (0.5)	1 (0.4)	2 (0.5)
皮膚感染	3 (1.4)	3 (1.3)	6 (1.4)
膿性痰	1 (0.5)	0	1 (0.2)
ブドウ球菌感染	3 (1.4)	4 (1.8)	7 (1.6)
ブドウ球菌皮膚感染	1 (0.5)	2 (0.9)	3 (0.7)
股部白癬	0	4 (1.8)	4 (0.9)
足部白癬	4 (1.8)	6 (2.7)	10 (2.3)
癜風	0	1 (0.4)	1 (0.2)
扁桃炎	4 (1.8)	3 (1.3)	7 (1.6)
歯感染	3 (1.4)	3 (1.3)	6 (1.4)
気管炎	2 (0.9)	2 (0.9)	4 (0.9)
気管気管支炎	1 (0.5)	0	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
トリコモナス症	0	1 (0.4)	1 (0.2)
トリコフィトン感染症	1 (0.5)	0	1 (0.2)
上気道感染	47 (21.4)	38 (16.9)	85 (19.1)
尿道炎	1 (0.5)	0	1 (0.2)
尿路感染	15 (6.8)	14 (6.2)	29 (6.5)
細菌性尿路感染	0	1 (0.4)	1 (0.2)
腟感染	2 (0.9)	1 (0.4)	3 (0.7)
ウイルス感染	1 (0.5)	3 (1.3)	4 (0.9)
ウイルス性咽頭炎	1 (0.5)	2 (0.9)	3 (0.7)
ウイルス性上気道感染	8 (3.6)	7 (3.1)	15 (3.4)
外陰部腟カンジダ症	1 (0.5)	1 (0.4)	2 (0.5)
外陰腟真菌感染	1 (0.5)	1 (0.4)	2 (0.5)
トリコモナス外陰腟炎	1 (0.5)	0	1 (0.2)
傷害、中毒および処置合併症	32 (14.6)	30 (13.4)	62 (14.0)
事故	1 (0.5)	0	1 (0.2)
動物咬傷	1 (0.5)	0	1 (0.2)
節足動物咬傷	0	2 (0.9)	2 (0.5)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
傷害、中毒および処置合併症 (Cont.)			
骨挫傷	0	1 (0.4)	1 (0.2)
軟骨損傷	0	1 (0.4)	1 (0.2)
胸部損傷	0	1 (0.4)	1 (0.2)
鎖骨骨折	0	1 (0.4)	1 (0.2)
挫傷	0	3 (1.3)	3 (0.7)
角膜擦過傷	0	1 (0.4)	1 (0.2)
頭蓋脳損傷	0	1 (0.4)	1 (0.2)
転倒	1 (0.5)	2 (0.9)	3 (0.7)
大腿骨骨折	0	1 (0.4)	1 (0.2)
足骨折	2 (0.9)	0	2 (0.5)
尾骨骨折	1 (0.5)	0	1 (0.2)
熱疲労	0	1 (0.4)	1 (0.2)
損傷	3 (1.4)	0	3 (0.7)
関節損傷	0	1 (0.4)	1 (0.2)
靭帯捻挫	1 (0.5)	0	1 (0.2)
四肢損傷	3 (1.4)	0	3 (0.7)
半月板損傷	1 (0.5)	0	1 (0.2)

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E/100PY = Events per 100 patient-years.

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
傷害、中毒および処置合併症 (Cont.)			
肉離れ	3 (1.4)	5 (2.2)	8 (1.8)
過量投与	1 (0.5)	0	1 (0.2)
処置による疼痛	1 (0.5)	1 (0.4)	2 (0.5)
肋骨骨折	2 (0.9)	1 (0.4)	3 (0.7)
交通事故	0	1 (0.4)	1 (0.2)
皮膚擦過傷	2 (0.9)	1 (0.4)	3 (0.7)
皮膚裂傷	3 (1.4)	1 (0.4)	4 (0.9)
脊椎骨折	1 (0.5)	0	1 (0.2)
胸骨骨折	1 (0.5)	0	1 (0.2)
腱損傷	0	1 (0.4)	1 (0.2)
歯牙破折	3 (1.4)	1 (0.4)	4 (0.9)
外傷性血腫	1 (0.5)	0	1 (0.2)
創傷	0	1 (0.4)	1 (0.2)
創部分泌	0	1 (0.4)	1 (0.2)
臨床検査	72 (32.8)	60 (26.7)	132 (29.7)
アラニンアミノトランスフェラーゼ増加	11 (5.0)	4 (1.8)	15 (3.4)
アスパラギン酸アミノトランスフェラーゼ異常	1 (0.5)	0	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
臨床検査 (Cont.)			
アスパラギン酸アミノトランスフェラーゼ増加	5 (2.3)	3 (1.3)	8 (1.8)
血中重炭酸塩減少	0	1 (0.4)	1 (0.2)
血中ビリルビン増加	2 (0.9)	0	2 (0.5)
血中コレステロール増加	1 (0.5)	2 (0.9)	3 (0.7)
血中クレアチンホスホキナーゼ増加	27 (12.3)	27 (12.0)	54 (12.2)
血中クレアチニン増加	1 (0.5)	0	1 (0.2)
血中免疫グロブリン E 増加	1 (0.5)	0	1 (0.2)
血圧上昇	1 (0.5)	1 (0.4)	2 (0.5)
血中トリグリセリド増加	0	3 (1.3)	3 (0.7)
血中尿酸増加	1 (0.5)	0	1 (0.2)
尿中血陽性	0	1 (0.4)	1 (0.2)
体温上昇	0	1 (0.4)	1 (0.2)
好酸球数増加	2 (0.9)	0	2 (0.5)
真菌検査陽性	1 (0.5)	0	1 (0.2)
ヘモグロビン減少	0	2 (0.9)	2 (0.5)
肝酵素上昇	1 (0.5)	0	1 (0.2)
低比重リポ蛋白増加	0	1 (0.4)	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
臨床検査 (Cont.)			
単球数増加	0	1 (0.4)	1 (0.2)
結核菌群検査陽性	1 (0.5)	0	1 (0.2)
好中球数減少	3 (1.4)	0	3 (0.7)
尿中蛋白陽性	2 (0.9)	1 (0.4)	3 (0.7)
子宮頚部スミア異常	1 (0.5)	0	1 (0.2)
ブドウ球菌検査陽性	2 (0.9)	0	2 (0.5)
トランスアミナーゼ上昇	0	1 (0.4)	1 (0.2)
トロポニン増加	0	1 (0.4)	1 (0.2)
ビタミン D 減少	0	1 (0.4)	1 (0.2)
体重増加	7 (3.2)	6 (2.7)	13 (2.9)
白血球数減少	1 (0.5)	0	1 (0.2)
白血球数増加	0	1 (0.4)	1 (0.2)
尿中白血球陽性	0	2 (0.9)	2 (0.5)
代謝および栄養障害	13 (5.9)	14 (6.2)	27 (6.1)
脱水	0	1 (0.4)	1 (0.2)
糖尿病	0	2 (0.9)	2 (0.5)
脂質異常症	0	2 (0.9)	2 (0.5)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
代謝および栄養障害 (Cont.)			
痛風	1 (0.5)	1 (0.4)	2 (0.5)
高コレステロール血症	1 (0.5)	2 (0.9)	3 (0.7)
高血糖	1 (0.5)	0	1 (0.2)
高ホモシステイン血症	1 (0.5)	0	1 (0.2)
高脂血症	4 (1.8)	3 (1.3)	7 (1.6)
高ナトリウム血症	1 (0.5)	0	1 (0.2)
高尿酸血症	2 (0.9)	1 (0.4)	3 (0.7)
低マグネシウム血症	1 (0.5)	0	1 (0.2)
食欲亢進	0	2 (0.9)	2 (0.5)
ビタミン B12 欠乏	1 (0.5)	0	1 (0.2)
筋骨格系および結合組織障害	36 (16.4)	49 (21.8)	85 (19.1)
関節痛	7 (3.2)	8 (3.6)	15 (3.4)
関節炎	2 (0.9)	2 (0.9)	4 (0.9)
背部痛	7 (3.2)	5 (2.2)	12 (2.7)
骨痛	0	1 (0.4)	1 (0.2)
滑液包炎	1 (0.5)	3 (1.3)	4 (0.9)
椎間板突出	0	2 (0.9)	2 (0.5)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
筋骨格系および結合組織障害 (Cont.)			
関節ロック	0	1 (0.4)	1 (0.2)
関節腫脹	0	1 (0.4)	1 (0.2)
四肢不快感	1 (0.5)	0	1 (0.2)
筋痙縮	1 (0.5)	5 (2.2)	6 (1.4)
筋攣縮	0	1 (0.4)	1 (0.2)
筋骨格系胸痛	1 (0.5)	0	1 (0.2)
筋骨格痛	1 (0.5)	2 (0.9)	3 (0.7)
筋骨格硬直	0	1 (0.4)	1 (0.2)
筋肉痛	7 (3.2)	4 (1.8)	11 (2.5)
頚部腫瘤	0	1 (0.4)	1 (0.2)
頚部痛	2 (0.9)	1 (0.4)	3 (0.7)
骨減少症	0	1 (0.4)	1 (0.2)
四肢痛	3 (1.4)	5 (2.2)	8 (1.8)
足底筋膜炎	1 (0.5)	0	1 (0.2)
滑液嚢腫	0	1 (0.4)	1 (0.2)
顎関節症候群	0	2 (0.9)	2 (0.5)
腱炎	1 (0.5)	1 (0.4)	2 (0.5)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
筋骨格系および結合組織障害 (Cont.)			
腱鞘炎	0	1 (0.4)	1 (0.2)
斜頚	1 (0.5)	0	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	8 (3.6)	9 (4.0)	17 (3.8)
結腸腺癌	0	1 (0.4)	1 (0.2)
肛門性器疣贅	0	1 (0.4)	1 (0.2)
良性新生物	0	1 (0.4)	1 (0.2)
精巣の良性新生物	0	1 (0.4)	1 (0.2)
血管腫	1 (0.5)	1 (0.4)	2 (0.5)
ケラトアカントーマ	0	1 (0.4)	1 (0.2)
表皮内悪性黒色腫	0	1 (0.4)	1 (0.2)
結節性筋膜炎	1 (0.5)	0	1 (0.2)
脂漏性角化症	1 (0.5)	0	1 (0.2)
皮膚乳頭腫	5 (2.3)	1 (0.4)	6 (1.4)
子宮平滑筋腫	0	1 (0.4)	1 (0.2)
神経系障害	37 (16.8)	48 (21.4)	85 (19.1)
脳血管発作	0	1 (0.4)	1 (0.2)
注意力障害	1 (0.5)	0	1 (0.2)

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神経系障害 (Cont.)			
浮動性めまい	7 (3.2)	6 (2.7)	13 (2.9)
味覚不全	0	2 (0.9)	2 (0.5)
てんかん	0	1 (0.4)	1 (0.2)
頭部不快感	0	1 (0.4)	1 (0.2)
頭痛	20 (9.1)	23 (10.2)	43 (9.7)
過眠症	0	1 (0.4)	1 (0.2)
筋緊張亢進	0	1 (0.4)	1 (0.2)
感覚鈍麻	1 (0.5)	1 (0.4)	2 (0.5)
片頭痛	4 (1.8)	1 (0.4)	5 (1.1)
多発性硬化症再発	0	1 (0.4)	1 (0.2)
神経圧迫	0	1 (0.4)	1 (0.2)
錯感覚	1 (0.5)	1 (0.4)	2 (0.5)
嗅覚錯誤	0	1 (0.4)	1 (0.2)
ヘルペス後神経痛	1 (0.5)	1 (0.4)	2 (0.5)
失神寸前の状態	1 (0.5)	0	1 (0.2)
坐骨神経痛	1 (0.5)	1 (0.4)	2 (0.5)
傾眠	0	1 (0.4)	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
神経系障害 (Cont.)			
失神	0	1 (0.4)	1 (0.2)
三叉神経痛	0	1 (0.4)	1 (0.2)
トンネル状視野	0	1 (0.4)	1 (0.2)
製品の問題	1 (0.5)	0	1 (0.2)
医療機器位置異常	1 (0.5)	0	1 (0.2)
精神障害	11 (5.0)	25 (11.1)	36 (8.1)
感情不安定	1 (0.5)	0	1 (0.2)
不安	4 (1.8)	3 (1.3)	7 (1.6)
双極性障害	0	1 (0.4)	1 (0.2)
抑うつ気分	1 (0.5)	2 (0.9)	3 (0.7)
うつ病	0	1 (0.4)	1 (0.2)
不眠症	2 (0.9)	5 (2.2)	7 (1.6)
故意の自傷行為	0	1 (0.4)	1 (0.2)
易刺激性	1 (0.5)	0	1 (0.2)
リビドー減退	0	1 (0.4)	1 (0.2)
リビドー亢進	1 (0.5)	0	1 (0.2)
精神障害	0	3 (1.3)	3 (0.7)

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精神障害 (Cont.)			
混合性不安抑うつ障害	0	1 (0.4)	1 (0.2)
パニック発作	1 (0.5)	1 (0.4)	2 (0.5)
心的外傷後ストレス障害	0	1 (0.4)	1 (0.2)
睡眠障害	0	2 (0.9)	2 (0.5)
ストレス	0	2 (0.9)	2 (0.5)
自殺念慮	0	1 (0.4)	1 (0.2)
腎および尿路障害	9 (4.1)	8 (3.6)	17 (3.8)
急性腎障害	1 (0.5)	0	1 (0.2)
アルブミン尿	0	1 (0.4)	1 (0.2)
排尿困難	3 (1.4)	0	3 (0.7)
血尿	1 (0.5)	3 (1.3)	4 (0.9)
水腎症	1 (0.5)	0	1 (0.2)
腎結石症	1 (0.5)	0	1 (0.2)
夜間頻尿	1 (0.5)	0	1 (0.2)
多尿	1 (0.5)	0	1 (0.2)
蛋白尿	0	1 (0.4)	1 (0.2)
腎仙痛	0	3 (1.3)	3 (0.7)

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生殖系および乳房障害	9 (4.1)	17 (7.6)	26 (5.9)
無月経	0	1 (0.4)	1 (0.2)
萎縮性外陰腟炎	0	1 (0.4)	1 (0.2)
乳房嚢胞	1 (0.5)	0	1 (0.2)
勃起不全	1 (0.5)	3 (1.3)	4 (0.9)
女性化乳房	0	1 (0.4)	1 (0.2)
過少月経	1 (0.5)	0	1 (0.2)
月経過多	1 (0.5)	0	1 (0.2)
月経障害	1 (0.5)	0	1 (0.2)
不規則月経	1 (0.5)	2 (0.9)	3 (0.7)
不正子宮出血	0	1 (0.4)	1 (0.2)
多嚢胞性卵巣	0	1 (0.4)	1 (0.2)
精巣腫瘤	0	2 (0.9)	2 (0.5)
精巣痛	1 (0.5)	3 (1.3)	4 (0.9)
腟分泌物	1 (0.5)	0	1 (0.2)
腟出血	0	1 (0.4)	1 (0.2)
女性外陰部潰瘍	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
生殖系および乳房障害 (Cont.)			
外陰腟乾燥	1 (0.5)	0	1 (0.2)
呼吸器、胸郭および縦隔障害	57 (25.9)	62 (27.6)	119 (26.8)
失声症	2 (0.9)	0	2 (0.5)
喘息	6 (2.7)	5 (2.2)	11 (2.5)
カタル	2 (0.9)	0	2 (0.5)
慢性閉塞性肺疾患	0	1 (0.4)	1 (0.2)
咳嗽	19 (8.6)	19 (8.5)	38 (8.6)
呼吸困難	2 (0.9)	5 (2.2)	7 (1.6)
鼻出血	5 (2.3)	4 (1.8)	9 (2.0)
喀血	2 (0.9)	0	2 (0.5)
鼻閉	0	1 (0.4)	1 (0.2)
口腔咽頭痛	9 (4.1)	13 (5.8)	22 (5.0)
咽頭腫脹	0	1 (0.4)	1 (0.2)
胸水	1 (0.5)	0	1 (0.2)
湿性咳嗽	2 (0.9)	0	2 (0.5)
肺肉芽腫	0	1 (0.4)	1 (0.2)
肺腫瘤	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
呼吸器、胸郭および縦隔障害 (Cont.)			
気道うっ血	0	2 (0.9)	2 (0.5)
アレルギー性鼻炎	0	2 (0.9)	2 (0.5)
鼻漏	4 (1.8)	3 (1.3)	7 (1.6)
副鼻腔うっ血	0	2 (0.9)	2 (0.5)
くしゃみ	0	1 (0.4)	1 (0.2)
喘息発作重積	1 (0.5)	0	1 (0.2)
咽喉刺激感	0	1 (0.4)	1 (0.2)
上気道うっ血	1 (0.5)	0	1 (0.2)
喘鳴	1 (0.5)	0	1 (0.2)
皮膚および皮下組織障害	147 (66.9)	152 (67.7)	299 (67.3)
ざ瘡	52 (23.7)	62 (27.6)	114 (25.7)
脱毛症	1 (0.5)	0	1 (0.2)
血管浮腫	0	1 (0.4)	1 (0.2)
水疱	2 (0.9)	2 (0.9)	4 (0.9)
冷汗	0	1 (0.4)	1 (0.2)
皮膚嚢腫	3 (1.4)	1 (0.4)	4 (0.9)
皮膚炎	5 (2.3)	1 (0.4)	6 (1.4)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
ざ瘡様皮膚炎	3 (1.4)	2 (0.9)	5 (1.1)
アレルギー性皮膚炎	1 (0.5)	1 (0.4)	2 (0.5)
アトピー性皮膚炎	25 (11.4)	14 (6.2)	39 (8.8)
接触皮膚炎	3 (1.4)	4 (1.8)	7 (1.6)
疱疹状皮膚炎	0	1 (0.4)	1 (0.2)
斑状出血	0	2 (0.9)	2 (0.5)
湿疹	8 (3.6)	5 (2.2)	13 (2.9)
小水疱性湿疹	0	1 (0.4)	1 (0.2)
紅斑	2 (0.9)	1 (0.4)	3 (0.7)
過剰肉芽組織	1 (0.5)	0	1 (0.2)
毛髪成長異常	1 (0.5)	1 (0.4)	2 (0.5)
汗腺炎	0	1 (0.4)	1 (0.2)
多汗症	3 (1.4)	1 (0.4)	4 (0.9)
過角化	1 (0.5)	1 (0.4)	2 (0.5)
多毛症	1 (0.5)	1 (0.4)	2 (0.5)
嵌入爪	0	2 (0.9)	2 (0.5)
苔癬化	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
網状皮斑	0	1 (0.4)	1 (0.2)
稗粒腫	0	1 (0.4)	1 (0.2)
汗疹	1 (0.5)	1 (0.4)	2 (0.5)
寝汗	1 (0.5)	0	1 (0.2)
口囲皮膚炎	1 (0.5)	3 (1.3)	4 (0.9)
光線過敏性反応	0	1 (0.4)	1 (0.2)
そう痒症	2 (0.9)	0	2 (0.5)
偽毛包炎	1 (0.5)	0	1 (0.2)
紫斑	2 (0.9)	0	2 (0.5)
発疹	2 (0.9)	1 (0.4)	3 (0.7)
斑状丘疹状皮疹	0	2 (0.9)	2 (0.5)
丘疹性皮疹	2 (0.9)	3 (1.3)	5 (1.1)
そう痒性皮疹	1 (0.5)	0	1 (0.2)
小水疱性皮疹	1 (0.5)	0	1 (0.2)
酒さ	2 (0.9)	5 (2.2)	7 (1.6)
痂皮	0	2 (0.9)	2 (0.5)
脂漏	1 (0.5)	1 (0.4)	2 (0.5)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
脂漏性皮膚炎	0	1 (0.4)	1 (0.2)
敏感肌	1 (0.5)	0	1 (0.2)
皮膚障害	0	1 (0.4)	1 (0.2)
皮膚亀裂	1 (0.5)	5 (2.2)	6 (1.4)
皮膚刺激	2 (0.9)	1 (0.4)	3 (0.7)
皮膚腫瘤	0	2 (0.9)	2 (0.5)
皮膚線条	2 (0.9)	0	2 (0.5)
皮膚腫脹	0	1 (0.4)	1 (0.2)
皮膚潰瘍	0	1 (0.4)	1 (0.2)
皮膚熱感	1 (0.5)	0	1 (0.2)
日光黒子	1 (0.5)	0	1 (0.2)
蕁麻疹	10 (4.5)	11 (4.9)	21 (4.7)
圧迫性蕁麻疹	0	1 (0.4)	1 (0.2)
社会環境	1 (0.5)	0	1 (0.2)
歯科補てつ物使用者	1 (0.5)	0	1 (0.2)
外科および内科処置	0	1 (0.4)	1 (0.2)
人工流産	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=384) (PYS=219.8) Events (E/100PY)	UPA 30 mg QD + TCS (N=380) (PYS=224.5) Events (E/100PY)	Total (N=764) (PYS=444.3) Events (E/100PY)
血管障害	7 (3.2)	9 (4.0)	16 (3.6)
大動脈瘤	0	1 (0.4)	1 (0.2)
深部静脈血栓症	0	1 (0.4)	1 (0.2)
血腫	1 (0.5)	0	1 (0.2)
ほてり	0	1 (0.4)	1 (0.2)
高血圧	5 (2.3)	5 (2.2)	10 (2.3)
起立性低血圧	1 (0.5)	0	1 (0.2)
レイノー現象	0	1 (0.4)	1 (0.2)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.7.2.3

表 10. 二重盲検投与期で治験薬と関連ありの有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（二重盲検投与期の安全性解析対象集団）

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
Any adverse event	66 (21.8)	112 (37.3)	129 (43.4)	241 (40.4)
血液およびリンパ系障害	1 (0.3)	2 (0.7)	5 (1.7)	7 (1.2)
貧血	0	0	1 (0.3)	1 (0.2)
白血球減少症	0	1 (0.3)	1 (0.3)	2 (0.3)
リンパ節症	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
好中球減少症	0	1 (0.3)	2 (0.7)	3 (0.5)
血小板増加症	0	0	1 (0.3)	1 (0.2)
心臓障害	0	0	1 (0.3)	1 (0.2)
動悸	0	0	1 (0.3)	1 (0.2)
耳および迷路障害	1 (0.3)	0	0	0
耳痛	1 (0.3)	0	0	0
眼障害	2 (0.7)	2 (0.7)	5 (1.7)	7 (1.2)
眼痛	0	1 (0.3)	0	1 (0.2)
眼の異常感覚	0	0	1 (0.3)	1 (0.2)
眼瞼障害	0	0	1 (0.3)	1 (0.2)
流涙増加	0	1 (0.3)	0	1 (0.2)
非感染性結膜炎	1 (0.3)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
眼障害 (Cont.)				
視神経乳頭浮腫	0	0	1 (0.3)	1 (0.2)
羞明	1 (0.3)	0	1 (0.3)	1 (0.2)
網膜剥離	0	1 (0.3)	0	1 (0.2)
閃輝暗点	1 (0.3)	0	0	0
硝子体剥離	0	0	1 (0.3)	1 (0.2)
胃腸障害	8 (2.6)	21 (7.0)	24 (8.1)	45 (7.5)
腹部不快感	1 (0.3)	0	0	0
腹部膨満	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
腹痛	0	4 (1.3)	3 (1.0)	7 (1.2)
上腹部痛	0	6 (2.0)	1 (0.3)	7 (1.2)
口角口唇炎	0	0	1 (0.3)	1 (0.2)
肛門直腸不快感	0	0	1 (0.3)	1 (0.2)
アフタ性潰瘍	0	0	1 (0.3)	1 (0.2)
便習慣変化	0	0	1 (0.3)	1 (0.2)
便秘	1 (0.3)	3 (1.0)	2 (0.7)	5 (0.8)
下痢	1 (0.3)	6 (2.0)	8 (2.7)	14 (2.3)
口内乾燥	1 (0.3)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
胃腸障害 (Cont.)				
消化不良	0	2 (0.7)	3 (1.0)	5 (0.8)
嚥下障害	0	0	1 (0.3)	1 (0.2)
白色便	0	1 (0.3)	0	1 (0.2)
鼓腸	2 (0.7)	0	0	0
排便回数増加	0	0	1 (0.3)	1 (0.2)
胃炎	0	1 (0.3)	0	1 (0.2)
胃腸障害	0	1 (0.3)	0	1 (0.2)
胃食道逆流性疾患	0	0	2 (0.7)	2 (0.3)
口唇水疱	1 (0.3)	0	0	0
口腔内潰瘍形成	0	2 (0.7)	0	2 (0.3)
粘液便	1 (0.3)	0	0	0
悪心	0	5 (1.7)	3 (1.0)	8 (1.3)
嘔吐	0	0	2 (0.7)	2 (0.3)
一般・全身障害および投与部位の状態	2 (0.7)	8 (2.7)	7 (2.4)	15 (2.5)
疲労	0	3 (1.0)	4 (1.3)	7 (1.2)
インフルエンザ様疾患	1 (0.3)	3 (1.0)	1 (0.3)	4 (0.7)
末梢性浮腫	1 (0.3)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
一般・全身障害および投与部位の状態 (Cont.)				
疼痛	0	1 (0.3)	0	1 (0.2)
発熱	0	0	2 (0.7)	2 (0.3)
顔面腫脹	0	1 (0.3)	0	1 (0.2)
感染症および寄生虫症	31 (10.2)	58 (19.3)	58 (19.5)	116 (19.4)
四肢膿瘍	0	0	1 (0.3)	1 (0.2)
虫垂炎	0	1 (0.3)	0	1 (0.2)
細菌感染	0	0	1 (0.3)	1 (0.2)
細菌性外陰腟炎	1 (0.3)	0	0	0
細菌尿	1 (0.3)	0	0	0
体部白癬	0	0	1 (0.3)	1 (0.2)
気管支炎	0	0	1 (0.3)	1 (0.2)
蜂巣炎	1 (0.3)	0	0	0
結膜炎	0	1 (0.3)	1 (0.3)	2 (0.3)
ヘルペス性状湿疹	0	2 (0.7)	1 (0.3)	3 (0.5)
毛包炎	1 (0.3)	4 (1.3)	5 (1.7)	9 (1.5)
せつ	0	1 (0.3)	1 (0.3)	2 (0.3)
胃腸炎	1 (0.3)	2 (0.7)	0	2 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
感染症および寄生虫症 (Cont.)				
陰部ヘルペス	0	0	1 (0.3)	1 (0.2)
歯肉炎	0	0	1 (0.3)	1 (0.2)
ヘルペス眼感染	0	0	1 (0.3)	1 (0.2)
単純ヘルペス	1 (0.3)	6 (2.0)	4 (1.3)	10 (1.7)
帯状疱疹	1 (0.3)	3 (1.0)	5 (1.7)	8 (1.3)
麦粒腫	0	0	1 (0.3)	1 (0.2)
膿痂疹	2 (0.7)	0	0	0
インフルエンザ	0	2 (0.7)	4 (1.3)	6 (1.0)
カポジ水痘様発疹	0	1 (0.3)	1 (0.3)	2 (0.3)
喉頭炎	0	1 (0.3)	0	1 (0.2)
上咽頭炎	8 (2.6)	14 (4.7)	12 (4.0)	26 (4.4)
爪真菌症	0	1 (0.3)	0	1 (0.2)
眼部単純ヘルペス	0	0	3 (1.0)	3 (0.5)
口腔カンジダ症	0	1 (0.3)	1 (0.3)	2 (0.3)
口腔ヘルペス	4 (1.3)	6 (2.0)	16 (5.4)	22 (3.7)
外耳炎	1 (0.3)	0	0	0
中耳炎	1 (0.3)	0	0	0

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
感染症および寄生虫症 (Cont.)				
咽頭炎	0	4 (1.3)	1 (0.3)	5 (0.8)
レンサ球菌性咽頭炎	0	0	1 (0.3)	1 (0.2)
肺炎	0	1 (0.3)	0	1 (0.2)
マイコプラズマ性肺炎	0	0	1 (0.3)	1 (0.2)
膿疱	1 (0.3)	0	0	0
気道感染	1 (0.3)	0	0	0
ウイルス性気道感染	0	1 (0.3)	0	1 (0.2)
鼻炎	0	1 (0.3)	0	1 (0.2)
鼻咽頭炎	0	0	1 (0.3)	1 (0.2)
副鼻腔炎	0	1 (0.3)	0	1 (0.2)
皮膚細菌感染	0	1 (0.3)	0	1 (0.2)
皮膚感染	0	1 (0.3)	1 (0.3)	2 (0.3)
膿性痰	0	1 (0.3)	0	1 (0.2)
ブドウ球菌感染	0	0	1 (0.3)	1 (0.2)
ブドウ球菌性敗血症	1 (0.3)	0	0	0
ブドウ球菌皮膚感染	0	0	1 (0.3)	1 (0.2)
足部白癬	0	1 (0.3)	0	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
感染症および寄生虫症 (Cont.)				
癜風	1 (0.3)	0	0	0
歯感染	0	1 (0.3)	0	1 (0.2)
気管気管支炎	0	1 (0.3)	0	1 (0.2)
上気道感染	5 (1.7)	12 (4.0)	7 (2.4)	19 (3.2)
尿路感染	1 (0.3)	0	3 (1.0)	3 (0.5)
細菌性尿路感染	0	0	1 (0.3)	1 (0.2)
ウイルス性上気道感染	0	2 (0.7)	2 (0.7)	4 (0.7)
外陰腟真菌感染	0	0	1 (0.3)	1 (0.2)
傷害、中毒および処置合併症	0	2 (0.7)	2 (0.7)	4 (0.7)
節足動物咬傷	0	0	1 (0.3)	1 (0.2)
挫傷	0	0	1 (0.3)	1 (0.2)
転倒	0	1 (0.3)	0	1 (0.2)
過量投与	0	1 (0.3)	0	1 (0.2)
臨床検査	10 (3.3)	17 (5.7)	20 (6.7)	37 (6.2)
アラニンアミノトランスフェラーゼ増加	1 (0.3)	3 (1.0)	1 (0.3)	4 (0.7)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.7)	2 (0.7)	1 (0.3)	3 (0.5)
血中ビリルビン増加	0	1 (0.3)	0	1 (0.2)

Note: Treatment-emergent adverse events in DB Period are defined as any adverse events with an onset or worsening date on or after the first dose of study drug and prior to the first dose of study drug in BE Period or no more than 30 days after the last dose of study drug in DB Period, whichever occurs firstly.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
臨床検査 (Cont.)				
血中コレステロール増加	0	1 (0.3)	0	1 (0.2)
血中クレアチンホスホキナーゼ増加	5 (1.7)	7 (2.3)	13 (4.4)	20 (3.4)
血中クレアチニン増加	1 (0.3)	0	0	0
血中トリグリセリド増加	0	1 (0.3)	0	1 (0.2)
体温上昇	0	0	1 (0.3)	1 (0.2)
ヘモグロビン減少	0	0	1 (0.3)	1 (0.2)
単球数増加	0	0	1 (0.3)	1 (0.2)
好中球数減少	0	1 (0.3)	1 (0.3)	2 (0.3)
尿中蛋白陽性	0	1 (0.3)	0	1 (0.2)
ブドウ球菌検査陽性	1 (0.3)	0	0	0
体重増加	3 (1.0)	5 (1.7)	3 (1.0)	8 (1.3)
白血球数減少	0	1 (0.3)	0	1 (0.2)
代謝および栄養障害	6 (2.0)	3 (1.0)	4 (1.3)	7 (1.2)
食欲減退	0	1 (0.3)	0	1 (0.2)
高脂血症	1 (0.3)	2 (0.7)	1 (0.3)	3 (0.5)
高尿酸血症	3 (1.0)	0	1 (0.3)	1 (0.2)
食欲亢進	2 (0.7)	0	2 (0.7)	2 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
筋骨格系および結合組織障害	0	4 (1.3)	5 (1.7)	9 (1.5)
背部痛	0	1 (0.3)	0	1 (0.2)
滑液包炎	0	0	1 (0.3)	1 (0.2)
関節ロック	0	0	1 (0.3)	1 (0.2)
筋痙縮	0	0	2 (0.7)	2 (0.3)
筋肉痛	0	3 (1.0)	2 (0.7)	5 (0.8)
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 (0.7)	2 (0.7)	2 (0.7)	4 (0.7)
肛門性器疣贅	1 (0.3)	0	1 (0.3)	1 (0.2)
ケラトアカントーマ	0	0	1 (0.3)	1 (0.2)
脂漏性角化症	0	1 (0.3)	0	1 (0.2)
皮膚乳頭腫	1 (0.3)	1 (0.3)	0	1 (0.2)
神経系障害	5 (1.7)	8 (2.7)	12 (4.0)	20 (3.4)
灼熱感	1 (0.3)	0	0	0
注意力障害	0	1 (0.3)	0	1 (0.2)
浮動性めまい	1 (0.3)	2 (0.7)	3 (1.0)	5 (0.8)
味覚不全	0	0	1 (0.3)	1 (0.2)
頭痛	4 (1.3)	4 (1.3)	7 (2.4)	11 (1.8)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
神経系障害 (Cont.)				
過眠症	0	0	1 (0.3)	1 (0.2)
錯感覚	0	0	1 (0.3)	1 (0.2)
失神寸前の状態	0	1 (0.3)	0	1 (0.2)
傾眠	0	0	1 (0.3)	1 (0.2)
失神	0	0	1 (0.3)	1 (0.2)
精神障害	1 (0.3)	3 (1.0)	8 (2.7)	11 (1.8)
感情不安定	0	1 (0.3)	0	1 (0.2)
注意欠陥多動性障害	0	0	1 (0.3)	1 (0.2)
抑うつ気分	0	0	1 (0.3)	1 (0.2)
うつ病	0	0	1 (0.3)	1 (0.2)
不眠症	1 (0.3)	0	2 (0.7)	2 (0.3)
リビドー減退	0	0	1 (0.3)	1 (0.2)
リビドー亢進	0	1 (0.3)	0	1 (0.2)
精神障害	0	0	1 (0.3)	1 (0.2)
混合性不安抑うつ障害	0	0	1 (0.3)	1 (0.2)
悪夢	0	1 (0.3)	0	1 (0.2)
睡眠障害	0	0	1 (0.3)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
腎および尿路障害	3 (1.0)	3 (1.0)	1 (0.3)	4 (0.7)
排尿困難	0	1 (0.3)	0	1 (0.2)
血尿	0	0	1 (0.3)	1 (0.2)
夜間頻尿	1 (0.3)	1 (0.3)	0	1 (0.2)
多尿	0	1 (0.3)	0	1 (0.2)
蛋白尿	2 (0.7)	0	0	0
生殖系および乳房障害	0	2 (0.7)	3 (1.0)	5 (0.8)
勃起不全	0	0	2 (0.7)	2 (0.3)
月経過多	0	1 (0.3)	0	1 (0.2)
不規則月経	0	1 (0.3)	0	1 (0.2)
精巣痛	0	1 (0.3)	1 (0.3)	2 (0.3)
呼吸器、胸郭および縦隔障害	3 (1.0)	13 (4.3)	11 (3.7)	24 (4.0)
喘息	0	3 (1.0)	0	3 (0.5)
カタル	0	0	1 (0.3)	1 (0.2)
咳嗽	1 (0.3)	4 (1.3)	4 (1.3)	8 (1.3)
呼吸困難	0	1 (0.3)	1 (0.3)	2 (0.3)
鼻出血	0	2 (0.7)	1 (0.3)	3 (0.5)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)				
鼻閉	0	0	1 (0.3)	1 (0.2)
口腔咽頭痛	2 (0.7)	0	4 (1.3)	4 (0.7)
咽頭腫脹	0	0	1 (0.3)	1 (0.2)
胸水	0	1 (0.3)	0	1 (0.2)
湿性咳嗽	0	1 (0.3)	0	1 (0.2)
鼻漏	0	1 (0.3)	0	1 (0.2)
副鼻腔うっ血	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
皮膚および皮下組織障害	11 (3.6)	42 (14.0)	54 (18.2)	96 (16.1)
ざ瘡	3 (1.0)	27 (9.0)	36 (12.1)	63 (10.6)
脱毛症	0	1 (0.3)	0	1 (0.2)
水疱	1 (0.3)	0	1 (0.3)	1 (0.2)
冷汗	1 (0.3)	0	0	0
ざ瘡様皮膚炎	0	2 (0.7)	3 (1.0)	5 (0.8)
アトピー性皮膚炎	3 (1.0)	3 (1.0)	2 (0.7)	5 (0.8)
湿疹	1 (0.3)	0	1 (0.3)	1 (0.2)
過剰肉芽組織	0	1 (0.3)	0	1 (0.2)
毛髪成長異常	2 (0.7)	1 (0.3)	0	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
皮膚および皮下組織障害 (Cont.)				
汗腺炎	0	0	1 (0.3)	1 (0.2)
多汗症	0	2 (0.7)	0	2 (0.3)
多毛症	0	1 (0.3)	1 (0.3)	2 (0.3)
稗粒腫	0	0	1 (0.3)	1 (0.2)
口囲皮膚炎	0	0	2 (0.7)	2 (0.3)
そう痒症	2 (0.7)	0	0	0
紫斑	0	1 (0.3)	0	1 (0.2)
発疹	0	2 (0.7)	0	2 (0.3)
丘疹性皮疹	0	1 (0.3)	1 (0.3)	2 (0.3)
そう痒性皮疹	0	1 (0.3)	0	1 (0.2)
酒さ	0	1 (0.3)	1 (0.3)	2 (0.3)
痂皮	0	0	1 (0.3)	1 (0.2)
脂漏	0	1 (0.3)	1 (0.3)	2 (0.3)
皮膚障害	0	0	1 (0.3)	1 (0.2)
皮膚腫脹	0	0	1 (0.3)	1 (0.2)
日光黒子	0	1 (0.3)	0	1 (0.2)
蕁麻疹	0	0	2 (0.7)	2 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	Placebo + TCS (N=303) n (%)	Active UPA 15 mg QD + TCS (N=300) n (%)	Active UPA 30 mg QD + TCS (N=297) n (%)	Active Total (N=597) n (%)
血管障害	2 (0.7)	0	1 (0.3)	1 (0.2)
ほてり	1 (0.3)	0	0	0
高血圧	1 (0.3)	0	0	0
レイノー現象	0	0	1 (0.3)	1 (0.2)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.10.1

表 11. ウパダシチニブ投与期間中に治験薬と関連ありの有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
Any adverse event	177 (40.0)	193 (44.5)	370 (42.2)
血液およびリンパ系障害	3 (0.7)	8 (1.8)	11 (1.3)
貧血	1 (0.2)	1 (0.2)	2 (0.2)
内出血発生の増加傾向	0	2 (0.5)	2 (0.2)
白血球減少症	1 (0.2)	1 (0.2)	2 (0.2)
リンパ節症	1 (0.2)	1 (0.2)	2 (0.2)
単球減少症	0	1 (0.2)	1 (0.1)
好中球減少症	1 (0.2)	2 (0.5)	3 (0.3)
血小板増加症	0	1 (0.2)	1 (0.1)
心臓障害	1 (0.2)	3 (0.7)	4 (0.5)
徐脈	0	1 (0.2)	1 (0.1)
動悸	0	2 (0.5)	2 (0.2)
洞性徐脈	1 (0.2)	0	1 (0.1)
耳および迷路障害	0	1 (0.2)	1 (0.1)
難聴	0	1 (0.2)	1 (0.1)
耳鳴	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
眼障害	3 (0.7)	10 (2.3)	13 (1.5)
眼瞼炎	0	1 (0.2)	1 (0.1)
白内障	0	1 (0.2)	1 (0.1)
結膜沈着物	0	1 (0.2)	1 (0.1)
結膜充血	0	1 (0.2)	1 (0.1)
アレルギー性結膜炎	0	1 (0.2)	1 (0.1)
眼痛	1 (0.2)	0	1 (0.1)
眼の異常感覚	0	1 (0.2)	1 (0.1)
眼そう痒症	0	1 (0.2)	1 (0.1)
眼瞼障害	0	1 (0.2)	1 (0.1)
流涙増加	1 (0.2)	0	1 (0.1)
視神経乳頭浮腫	0	1 (0.2)	1 (0.1)
羞明	0	1 (0.2)	1 (0.1)
網膜剥離	1 (0.2)	1 (0.2)	2 (0.2)
裂孔原性網膜剥離	0	1 (0.2)	1 (0.1)
潰瘍性角膜炎	0	1 (0.2)	1 (0.1)
硝子体剥離	0	1 (0.2)	1 (0.1)
眼球乾燥症	1 (0.2)	0	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
胃腸障害	27 (6.1)	27 (6.2)	54 (6.2)
腹部不快感	1 (0.2)	0	1 (0.1)
腹部膨満	1 (0.2)	1 (0.2)	2 (0.2)
腹痛	4 (0.9)	3 (0.7)	7 (0.8)
上腹部痛	8 (1.8)	1 (0.2)	9 (1.0)
口角口唇炎	0	1 (0.2)	1 (0.1)
肛門直腸不快感	0	1 (0.2)	1 (0.1)
アフタ性潰瘍	1 (0.2)	1 (0.2)	2 (0.2)
便習慣変化	0	1 (0.2)	1 (0.1)
便秘	3 (0.7)	2 (0.5)	5 (0.6)
下痢	7 (1.6)	9 (2.1)	16 (1.8)
消化不良	2 (0.5)	3 (0.7)	5 (0.6)
嚥下障害	0	1 (0.2)	1 (0.1)
白色便	1 (0.2)	0	1 (0.1)
鼓腸	1 (0.2)	1 (0.2)	2 (0.2)
排便回数増加	0	1 (0.2)	1 (0.1)
胃炎	1 (0.2)	0	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
胃腸障害 (Cont.)			
胃腸障害	1 (0.2)	0	1 (0.1)
胃食道逆流性疾患	0	2 (0.5)	2 (0.2)
舌炎	1 (0.2)	0	1 (0.1)
過敏性腸症候群	0	1 (0.2)	1 (0.1)
口腔内出血	0	1 (0.2)	1 (0.1)
口腔内潰瘍形成	2 (0.5)	0	2 (0.2)
悪心	6 (1.4)	5 (1.2)	11 (1.3)
嘔吐	1 (0.2)	3 (0.7)	4 (0.5)
一般・全身障害および投与部位の状態	14 (3.2)	11 (2.5)	25 (2.9)
顔面浮腫	1 (0.2)	0	1 (0.1)
顔面痛	1 (0.2)	0	1 (0.1)
疲労	6 (1.4)	5 (1.2)	11 (1.3)
インフルエンザ様疾患	5 (1.1)	2 (0.5)	7 (0.8)
倦怠感	1 (0.2)	0	1 (0.1)
疼痛	1 (0.2)	0	1 (0.1)
発熱	3 (0.7)	4 (0.9)	7 (0.8)
腫脹	1 (0.2)	0	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
顔面腫脹	2 (0.5)	0	2 (0.2)
肝胆道系障害	0	2 (0.5)	2 (0.2)
肝細胞損傷	0	1 (0.2)	1 (0.1)
肝腫大	0	1 (0.2)	1 (0.1)
感染症および寄生虫症	111 (25.1)	103 (23.7)	214 (24.4)
四肢膿瘍	0	1 (0.2)	1 (0.1)
虫垂炎	1 (0.2)	0	1 (0.1)
細菌性疾患キャリアー	0	1 (0.2)	1 (0.1)
細菌感染	0	1 (0.2)	1 (0.1)
体部白癬	0	2 (0.5)	2 (0.2)
気管支炎	1 (0.2)	2 (0.5)	3 (0.3)
条虫感染	1 (0.2)	0	1 (0.1)
結膜炎	2 (0.5)	3 (0.7)	5 (0.6)
ウイルス性結膜炎	0	1 (0.2)	1 (0.1)
耳感染	1 (0.2)	0	1 (0.1)
ヘルペス性状湿疹	2 (0.5)	1 (0.2)	3 (0.3)
感染性湿疹	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
エンテロバクター感染	1 (0.2)	0	1 (0.1)
糸状虫症	0	1 (0.2)	1 (0.1)
毛包炎	6 (1.4)	6 (1.4)	12 (1.4)
せつ	3 (0.7)	1 (0.2)	4 (0.5)
ウイルス性胃炎	1 (0.2)	0	1 (0.1)
胃腸炎	2 (0.5)	4 (0.9)	6 (0.7)
陰部ヘルペス	0	1 (0.2)	1 (0.1)
陰部単純ヘルペス	0	1 (0.2)	1 (0.1)
歯肉炎	0	1 (0.2)	1 (0.1)
ヘルペス眼感染	1 (0.2)	2 (0.5)	3 (0.3)
単純ヘルペス	16 (3.6)	10 (2.3)	26 (3.0)
帯状疱疹	5 (1.1)	8 (1.8)	13 (1.5)
皮膚播種性帯状疱疹	1 (0.2)	0	1 (0.1)
耳帯状疱疹	0	1 (0.2)	1 (0.1)
麦粒腫	0	1 (0.2)	1 (0.1)
膿痂疹	2 (0.5)	1 (0.2)	3 (0.3)
インフルエンザ	4 (0.9)	5 (1.2)	9 (1.0)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
カポジ水痘様発疹	1 (0.2)	2 (0.5)	3 (0.3)
腎感染	1 (0.2)	0	1 (0.1)
喉頭炎	1 (0.2)	0	1 (0.1)
潜伏結核	0	1 (0.2)	1 (0.1)
マラセチア感染	1 (0.2)	1 (0.2)	2 (0.2)
鼻ヘルペス	0	2 (0.5)	2 (0.2)
上咽頭炎	28 (6.3)	22 (5.1)	50 (5.7)
爪真菌症	1 (0.2)	0	1 (0.1)
眼部単純ヘルペス	0	5 (1.2)	5 (0.6)
口腔カンジダ症	1 (0.2)	1 (0.2)	2 (0.2)
口腔ヘルペス	14 (3.2)	22 (5.1)	36 (4.1)
外耳炎	1 (0.2)	0	1 (0.1)
眼窩周囲蜂巣炎	1 (0.2)	0	1 (0.1)
咽頭炎	5 (1.1)	4 (0.9)	9 (1.0)
レンサ球菌性咽頭炎	0	1 (0.2)	1 (0.1)
肺炎	3 (0.7)	1 (0.2)	4 (0.5)
マイコプラズマ性肺炎	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
膿疱	0	1 (0.2)	1 (0.1)
膿疱性皮疹	0	1 (0.2)	1 (0.1)
ウイルス性気道感染	1 (0.2)	1 (0.2)	2 (0.2)
鼻炎	1 (0.2)	0	1 (0.1)
鼻咽頭炎	0	1 (0.2)	1 (0.1)
副鼻腔炎	2 (0.5)	1 (0.2)	3 (0.3)
皮膚細菌感染	1 (0.2)	0	1 (0.1)
皮膚感染	3 (0.7)	1 (0.2)	4 (0.5)
膿性痰	1 (0.2)	0	1 (0.1)
ブドウ球菌性膿瘍	1 (0.2)	0	1 (0.1)
ブドウ球菌感染	0	3 (0.7)	3 (0.3)
ブドウ球菌皮膚感染	1 (0.2)	1 (0.2)	2 (0.2)
股部白癬	0	1 (0.2)	1 (0.1)
足部白癬	2 (0.5)	2 (0.5)	4 (0.5)
扁桃炎	1 (0.2)	1 (0.2)	2 (0.2)
歯感染	1 (0.2)	1 (0.2)	2 (0.2)
気管気管支炎	1 (0.2)	0	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
感染症および寄生虫症 (Cont.)			
上気道感染	15 (3.4)	14 (3.2)	29 (3.3)
尿路感染	2 (0.5)	6 (1.4)	8 (0.9)
細菌性尿路感染	0	1 (0.2)	1 (0.1)
ウイルス感染	0	1 (0.2)	1 (0.1)
ウイルス性咽頭炎	2 (0.5)	0	2 (0.2)
ウイルス性上気道感染	3 (0.7)	3 (0.7)	6 (0.7)
外陰部腟カンジダ症	1 (0.2)	0	1 (0.1)
外陰腟真菌感染	0	1 (0.2)	1 (0.1)
傷害、中毒および処置合併症	2 (0.5)	3 (0.7)	5 (0.6)
節足動物咬傷	0	1 (0.2)	1 (0.1)
挫傷	0	1 (0.2)	1 (0.1)
転倒	1 (0.2)	0	1 (0.1)
過量投与	1 (0.2)	0	1 (0.1)
創部分泌	0	1 (0.2)	1 (0.1)
臨床検査	31 (7.0)	32 (7.4)	63 (7.2)
アラニンアミノトランスフェラーゼ増加	5 (1.1)	3 (0.7)	8 (0.9)
アスパラギン酸アミノトランスフェラーゼ増加	3 (0.7)	1 (0.2)	4 (0.5)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
臨床検査 (Cont.)			
血中アルカリホスファターゼ増加	1 (0.2)	0	1 (0.1)
血中ビリルビン増加	1 (0.2)	0	1 (0.1)
血中コレステロール増加	1 (0.2)	1 (0.2)	2 (0.2)
血中クレアチンホスホキナーゼ増加	12 (2.7)	18 (4.1)	30 (3.4)
血中クレアチニン増加	1 (0.2)	0	1 (0.1)
血圧上昇	1 (0.2)	0	1 (0.1)
血中トリグリセリド増加	1 (0.2)	2 (0.5)	3 (0.3)
体温上昇	0	1 (0.2)	1 (0.1)
好酸球数増加	2 (0.5)	0	2 (0.2)
ヘモグロビン減少	0	2 (0.5)	2 (0.2)
肝酵素上昇	1 (0.2)	0	1 (0.1)
低比重リポ蛋白増加	0	1 (0.2)	1 (0.1)
単球数増加	0	1 (0.2)	1 (0.1)
好中球数減少	4 (0.9)	1 (0.2)	5 (0.6)
好中球百分率減少	1 (0.2)	0	1 (0.1)
尿中蛋白陽性	1 (0.2)	0	1 (0.1)
体重増加	6 (1.4)	5 (1.2)	11 (1.3)

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Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
臨床検査 (Cont.)			
白血球数減少	1 (0.2)	1 (0.2)	2 (0.2)
白血球数増加	0	1 (0.2)	1 (0.1)
代謝および栄養障害	6 (1.4)	7 (1.6)	13 (1.5)
食欲減退	1 (0.2)	0	1 (0.1)
高コレステロール血症	1 (0.2)	2 (0.5)	3 (0.3)
高脂血症	3 (0.7)	2 (0.5)	5 (0.6)
高ナトリウム血症	1 (0.2)	0	1 (0.1)
高尿酸血症	0	1 (0.2)	1 (0.1)
食欲亢進	0	2 (0.5)	2 (0.2)
筋骨格系および結合組織障害	5 (1.1)	8 (1.8)	13 (1.5)
関節痛	0	1 (0.2)	1 (0.1)
背部痛	1 (0.2)	0	1 (0.1)
滑液包炎	0	1 (0.2)	1 (0.1)
関節ロック	0	1 (0.2)	1 (0.1)
筋痙縮	0	2 (0.5)	2 (0.2)
筋肉痛	4 (0.9)	3 (0.7)	7 (0.8)
頚部腫瘤	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) 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）	3 (0.7)	2 (0.5)	5 (0.6)
肛門性器疣贅	0	1 (0.2)	1 (0.1)
ケラトアカントーマ	0	1 (0.2)	1 (0.1)
脂漏性角化症	1 (0.2)	0	1 (0.1)
皮膚乳頭腫	2 (0.5)	0	2 (0.2)
神経系障害	13 (2.9)	15 (3.5)	28 (3.2)
注意力障害	1 (0.2)	0	1 (0.1)
浮動性めまい	2 (0.5)	4 (0.9)	6 (0.7)
味覚不全	0	1 (0.2)	1 (0.1)
頭痛	8 (1.8)	8 (1.8)	16 (1.8)
過眠症	0	1 (0.2)	1 (0.1)
多発性硬化症再発	0	1 (0.2)	1 (0.1)
錯感覚	1 (0.2)	1 (0.2)	2 (0.2)
失神寸前の状態	1 (0.2)	0	1 (0.1)
傾眠	0	1 (0.2)	1 (0.1)
失神	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
精神障害	3 (0.7)	10 (2.3)	13 (1.5)
感情不安定	1 (0.2)	0	1 (0.1)
注意欠陥多動性障害	0	1 (0.2)	1 (0.1)
抑うつ気分	0	2 (0.5)	2 (0.2)
うつ病	0	1 (0.2)	1 (0.1)
不眠症	0	2 (0.5)	2 (0.2)
リビドー減退	0	1 (0.2)	1 (0.1)
リビドー亢進	1 (0.2)	0	1 (0.1)
精神障害	0	1 (0.2)	1 (0.1)
混合性不安抑うつ障害	0	1 (0.2)	1 (0.1)
悪夢	1 (0.2)	0	1 (0.1)
パニック発作	0	1 (0.2)	1 (0.1)
睡眠障害	0	1 (0.2)	1 (0.1)
腎および尿路障害	4 (0.9)	4 (0.9)	8 (0.9)
アルブミン尿	0	1 (0.2)	1 (0.1)
排尿困難	1 (0.2)	0	1 (0.1)
血尿	1 (0.2)	2 (0.5)	3 (0.3)
夜間頻尿	1 (0.2)	0	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
腎および尿路障害 (Cont.)			
多尿	1 (0.2)	0	1 (0.1)
蛋白尿	0	1 (0.2)	1 (0.1)
生殖系および乳房障害	2 (0.5)	3 (0.7)	5 (0.6)
勃起不全	0	2 (0.5)	2 (0.2)
月経過多	1 (0.2)	0	1 (0.1)
不規則月経	1 (0.2)	0	1 (0.1)
精巣痛	1 (0.2)	1 (0.2)	2 (0.2)
呼吸器、胸郭および縦隔障害	18 (4.1)	19 (4.4)	37 (4.2)
失声症	1 (0.2)	0	1 (0.1)
喘息	3 (0.7)	1 (0.2)	4 (0.5)
カタル	0	1 (0.2)	1 (0.1)
咳嗽	7 (1.6)	8 (1.8)	15 (1.7)
呼吸困難	2 (0.5)	2 (0.5)	4 (0.5)
鼻出血	3 (0.7)	1 (0.2)	4 (0.5)
鼻閉	0	1 (0.2)	1 (0.1)
口腔咽頭痛	0	5 (1.2)	5 (0.6)
咽頭腫脹	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
胸水	1 (0.2)	0	1 (0.1)
湿性咳嗽	1 (0.2)	0	1 (0.1)
肺肉芽腫	0	1 (0.2)	1 (0.1)
肺腫瘤	0	1 (0.2)	1 (0.1)
鼻漏	2 (0.5)	0	2 (0.2)
副鼻腔うっ血	1 (0.2)	1 (0.2)	2 (0.2)
皮膚および皮下組織障害	68 (15.4)	79 (18.2)	147 (16.8)
ざ瘡	47 (10.6)	56 (12.9)	103 (11.8)
脱毛症	1 (0.2)	0	1 (0.1)
水疱	0	2 (0.5)	2 (0.2)
皮膚嚢腫	1 (0.2)	0	1 (0.1)
ざ瘡様皮膚炎	3 (0.7)	3 (0.7)	6 (0.7)
アトピー性皮膚炎	5 (1.1)	4 (0.9)	9 (1.0)
接触皮膚炎	0	1 (0.2)	1 (0.1)
乾癬様皮膚炎	1 (0.2)	0	1 (0.1)
異汗性湿疹	1 (0.2)	0	1 (0.1)
湿疹	1 (0.2)	2 (0.5)	3 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
皮膚および皮下組織障害 (Cont.)			
紅斑	1 (0.2)	0	1 (0.1)
過剰肉芽組織	1 (0.2)	0	1 (0.1)
毛髪成長異常	1 (0.2)	1 (0.2)	2 (0.2)
汗腺炎	0	1 (0.2)	1 (0.1)
多汗症	2 (0.5)	0	2 (0.2)
多毛症	1 (0.2)	1 (0.2)	2 (0.2)
苔癬化	0	1 (0.2)	1 (0.1)
稗粒腫	0	1 (0.2)	1 (0.1)
寝汗	1 (0.2)	0	1 (0.1)
口囲皮膚炎	0	2 (0.5)	2 (0.2)
偽毛包炎	1 (0.2)	0	1 (0.1)
紫斑	1 (0.2)	0	1 (0.1)
発疹	2 (0.5)	0	2 (0.2)
丘疹性皮疹	1 (0.2)	2 (0.5)	3 (0.3)
そう痒性皮疹	1 (0.2)	0	1 (0.1)
酒さ	1 (0.2)	1 (0.2)	2 (0.2)
痂皮	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) n (%)	UPA 30 mg QD + TCS (N=434) n (%)	Total (N=876) n (%)
皮膚および皮下組織障害 (Cont.)			
脂漏	1 (0.2)	1 (0.2)	2 (0.2)
皮膚障害	0	1 (0.2)	1 (0.1)
皮膚亀裂	0	2 (0.5)	2 (0.2)
皮膚腫瘤	0	1 (0.2)	1 (0.1)
皮膚線条	1 (0.2)	0	1 (0.1)
皮膚腫脹	0	1 (0.2)	1 (0.1)
日光黒子	1 (0.2)	0	1 (0.1)
蕁麻疹	0	3 (0.7)	3 (0.3)
血管障害	1 (0.2)	3 (0.7)	4 (0.5)
大動脈瘤	0	1 (0.2)	1 (0.1)
深部静脈血栓症	0	1 (0.2)	1 (0.1)
高血圧	1 (0.2)	0	1 (0.1)
レイノー現象	0	1 (0.2)	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.10.2

表 12. ウパダシチニブ投与期間中の治験薬と関連ありの有害事象の 100 人年あたりの発現率：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
Any adverse event	459 (179.9)	504 (193.9)	963 (186.9)
血液およびリンパ系障害	5 (2.0)	9 (3.5)	14 (2.7)
貧血	2 (0.8)	1 (0.4)	3 (0.6)
内出血発生の増加傾向	0	2 (0.8)	2 (0.4)
白血球減少症	1 (0.4)	1 (0.4)	2 (0.4)
リンパ節症	1 (0.4)	1 (0.4)	2 (0.4)
単球減少症	0	1 (0.4)	1 (0.2)
好中球減少症	1 (0.4)	2 (0.8)	3 (0.6)
血小板増加症	0	1 (0.4)	1 (0.2)
心臓障害	1 (0.4)	3 (1.2)	4 (0.8)
徐脈	0	1 (0.4)	1 (0.2)
動悸	0	2 (0.8)	2 (0.4)
洞性徐脈	1 (0.4)	0	1 (0.2)
耳および迷路障害	0	2 (0.8)	2 (0.4)
難聴	0	1 (0.4)	1 (0.2)
耳鳴	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
眼障害	4 (1.6)	15 (5.8)	19 (3.7)
眼瞼炎	0	1 (0.4)	1 (0.2)
白内障	0	1 (0.4)	1 (0.2)
結膜沈着物	0	1 (0.4)	1 (0.2)
結膜充血	0	1 (0.4)	1 (0.2)
アレルギー性結膜炎	0	1 (0.4)	1 (0.2)
眼痛	1 (0.4)	0	1 (0.2)
眼の異常感覚	0	1 (0.4)	1 (0.2)
眼そう痒症	0	1 (0.4)	1 (0.2)
眼瞼障害	0	1 (0.4)	1 (0.2)
流涙増加	1 (0.4)	0	1 (0.2)
視神経乳頭浮腫	0	1 (0.4)	1 (0.2)
羞明	0	1 (0.4)	1 (0.2)
網膜剥離	1 (0.4)	1 (0.4)	2 (0.4)
裂孔原性網膜剥離	0	2 (0.8)	2 (0.4)
潰瘍性角膜炎	0	1 (0.4)	1 (0.2)
硝子体剥離	0	1 (0.4)	1 (0.2)
眼球乾燥症	1 (0.4)	0	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
胃腸障害	44 (17.2)	46 (17.7)	90 (17.5)
腹部不快感	1 (0.4)	0	1 (0.2)
腹部膨満	1 (0.4)	1 (0.4)	2 (0.4)
腹痛	4 (1.6)	5 (1.9)	9 (1.7)
上腹部痛	8 (3.1)	1 (0.4)	9 (1.7)
口角口唇炎	0	1 (0.4)	1 (0.2)
肛門直腸不快感	0	1 (0.4)	1 (0.2)
アフタ性潰瘍	2 (0.8)	2 (0.8)	4 (0.8)
便習慣変化	0	1 (0.4)	1 (0.2)
便秘	3 (1.2)	2 (0.8)	5 (1.0)
下痢	8 (3.1)	14 (5.4)	22 (4.3)
消化不良	2 (0.8)	3 (1.2)	5 (1.0)
嚥下障害	0	1 (0.4)	1 (0.2)
白色便	1 (0.4)	0	1 (0.2)
鼓腸	1 (0.4)	1 (0.4)	2 (0.4)
排便回数増加	0	1 (0.4)	1 (0.2)
胃炎	1 (0.4)	0	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
胃腸障害 (Cont.)			
胃腸障害	1 (0.4)	0	1 (0.2)
胃食道逆流性疾患	0	2 (0.8)	2 (0.4)
舌炎	1 (0.4)	0	1 (0.2)
過敏性腸症候群	0	1 (0.4)	1 (0.2)
口腔内出血	0	1 (0.4)	1 (0.2)
口腔内潰瘍形成	2 (0.8)	0	2 (0.4)
悪心	7 (2.7)	5 (1.9)	12 (2.3)
嘔吐	1 (0.4)	3 (1.2)	4 (0.8)
一般・全身障害および投与部位の状態	22 (8.6)	13 (5.0)	35 (6.8)
顔面浮腫	1 (0.4)	0	1 (0.2)
顔面痛	1 (0.4)	0	1 (0.2)
疲労	6 (2.4)	5 (1.9)	11 (2.1)
インフルエンザ様疾患	5 (2.0)	4 (1.5)	9 (1.7)
倦怠感	1 (0.4)	0	1 (0.2)
疼痛	2 (0.8)	0	2 (0.4)
発熱	3 (1.2)	4 (1.5)	7 (1.4)
腫脹	1 (0.4)	0	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
一般・全身障害および投与部位の状態 (Cont.)			
顔面腫脹	2 (0.8)	0	2 (0.4)
肝胆道系障害	0	2 (0.8)	2 (0.4)
肝細胞損傷	0	1 (0.4)	1 (0.2)
肝腫大	0	1 (0.4)	1 (0.2)
感染症および寄生虫症	184 (72.1)	187 (71.9)	371 (72.0)
四肢膿瘍	0	1 (0.4)	1 (0.2)
虫垂炎	1 (0.4)	0	1 (0.2)
細菌性疾患キャリアー	0	1 (0.4)	1 (0.2)
細菌感染	0	1 (0.4)	1 (0.2)
体部白癬	0	2 (0.8)	2 (0.4)
気管支炎	1 (0.4)	2 (0.8)	3 (0.6)
条虫感染	1 (0.4)	0	1 (0.2)
結膜炎	2 (0.8)	3 (1.2)	5 (1.0)
ウイルス性結膜炎	0	1 (0.4)	1 (0.2)
耳感染	1 (0.4)	0	1 (0.2)
ヘルペス性状湿疹	2 (0.8)	1 (0.4)	3 (0.6)
感染性湿疹	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
エンテロバクター感染	1 (0.4)	0	1 (0.2)
糸状虫症	0	1 (0.4)	1 (0.2)
毛包炎	6 (2.4)	6 (2.3)	12 (2.3)
せつ	3 (1.2)	1 (0.4)	4 (0.8)
ウイルス性胃炎	1 (0.4)	0	1 (0.2)
胃腸炎	3 (1.2)	6 (2.3)	9 (1.7)
陰部ヘルペス	0	2 (0.8)	2 (0.4)
陰部単純ヘルペス	0	1 (0.4)	1 (0.2)
歯肉炎	0	1 (0.4)	1 (0.2)
ヘルペス眼感染	1 (0.4)	2 (0.8)	3 (0.6)
単純ヘルペス	28 (11.0)	15 (5.8)	43 (8.3)
帯状疱疹	5 (2.0)	8 (3.1)	13 (2.5)
皮膚播種性帯状疱疹	1 (0.4)	0	1 (0.2)
耳帯状疱疹	0	1 (0.4)	1 (0.2)
麦粒腫	0	1 (0.4)	1 (0.2)
膿痂疹	2 (0.8)	1 (0.4)	3 (0.6)
インフルエンザ	4 (1.6)	5 (1.9)	9 (1.7)

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E/100PY = Events per 100 patient-years.

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
カポジ水痘様発疹	1 (0.4)	3 (1.2)	4 (0.8)
腎感染	1 (0.4)	0	1 (0.2)
喉頭炎	1 (0.4)	0	1 (0.2)
潜伏結核	0	1 (0.4)	1 (0.2)
マラセチア感染	1 (0.4)	1 (0.4)	2 (0.4)
鼻ヘルペス	0	2 (0.8)	2 (0.4)
上咽頭炎	35 (13.7)	24 (9.2)	59 (11.5)
爪真菌症	1 (0.4)	0	1 (0.2)
眼部単純ヘルペス	0	6 (2.3)	6 (1.2)
口腔カンジダ症	1 (0.4)	1 (0.4)	2 (0.4)
口腔ヘルペス	27 (10.6)	32 (12.3)	59 (11.5)
外耳炎	1 (0.4)	0	1 (0.2)
眼窩周囲蜂巣炎	1 (0.4)	0	1 (0.2)
咽頭炎	7 (2.7)	4 (1.5)	11 (2.1)
レンサ球菌性咽頭炎	0	1 (0.4)	1 (0.2)
肺炎	3 (1.2)	1 (0.4)	4 (0.8)
マイコプラズマ性肺炎	0	1 (0.4)	1 (0.2)

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MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
膿疱	0	1 (0.4)	1 (0.2)
膿疱性皮疹	0	1 (0.4)	1 (0.2)
ウイルス性気道感染	1 (0.4)	1 (0.4)	2 (0.4)
鼻炎	1 (0.4)	0	1 (0.2)
鼻喉頭炎	0	1 (0.4)	1 (0.2)
副鼻腔炎	2 (0.8)	1 (0.4)	3 (0.6)
皮膚細菌感染	1 (0.4)	0	1 (0.2)
皮膚感染	3 (1.2)	1 (0.4)	4 (0.8)
膿性痰	1 (0.4)	0	1 (0.2)
ブドウ球菌性膿瘍	1 (0.4)	0	1 (0.2)
ブドウ球菌感染	0	4 (1.5)	4 (0.8)
ブドウ球菌皮膚感染	1 (0.4)	1 (0.4)	2 (0.4)
股部白癬	0	1 (0.4)	1 (0.2)
足部白癬	2 (0.8)	2 (0.8)	4 (0.8)
扁桃炎	1 (0.4)	1 (0.4)	2 (0.4)
歯感染	1 (0.4)	1 (0.4)	2 (0.4)
気管気管支炎	1 (0.4)	0	1 (0.2)

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感染症および寄生虫症 (Cont.)			
上気道感染	17 (6.7)	17 (6.5)	34 (6.6)
尿路感染	2 (0.8)	6 (2.3)	8 (1.6)
細菌性尿路感染	0	1 (0.4)	1 (0.2)
ウイルス感染	0	1 (0.4)	1 (0.2)
ウイルス性咽頭炎	2 (0.8)	0	2 (0.4)
ウイルス性上気道感染	3 (1.2)	4 (1.5)	7 (1.4)
外陰部腟カンジダ症	1 (0.4)	0	1 (0.2)
外陰腟真菌感染	0	1 (0.4)	1 (0.2)
傷害、中毒および処置合併症	2 (0.8)	3 (1.2)	5 (1.0)
節足動物咬傷	0	1 (0.4)	1 (0.2)
挫傷	0	1 (0.4)	1 (0.2)
転倒	1 (0.4)	0	1 (0.2)
過量投与	1 (0.4)	0	1 (0.2)
創部分泌	0	1 (0.4)	1 (0.2)
臨床検査	50 (19.6)	43 (16.5)	93 (18.1)
アラニンアミノトランスフェラーゼ増加	7 (2.7)	3 (1.2)	10 (1.9)
アスパラギン酸アミノトランスフェラーゼ増加	3 (1.2)	1 (0.4)	4 (0.8)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

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臨床検査 (Cont.)			
血中アルカリホスファターゼ増加	1 (0.4)	0	1 (0.2)
血中ビリルビン増加	2 (0.8)	0	2 (0.4)
血中コレステロール増加	2 (0.8)	2 (0.8)	4 (0.8)
血中クレアチンホスホキナーゼ増加	15 (5.9)	20 (7.7)	35 (6.8)
血中クレアチニン増加	1 (0.4)	0	1 (0.2)
血圧上昇	1 (0.4)	0	1 (0.2)
血中トリグリセリド増加	1 (0.4)	3 (1.2)	4 (0.8)
体温上昇	0	1 (0.4)	1 (0.2)
好酸球数増加	2 (0.8)	0	2 (0.4)
ヘモグロビン減少	0	2 (0.8)	2 (0.4)
肝酵素上昇	1 (0.4)	0	1 (0.2)
低比重リポ蛋白増加	0	1 (0.4)	1 (0.2)
単球数増加	0	1 (0.4)	1 (0.2)
好中球数減少	4 (1.6)	1 (0.4)	5 (1.0)
好中球百分率減少	1 (0.4)	0	1 (0.2)
尿中蛋白陽性	2 (0.8)	0	2 (0.4)
体重増加	6 (2.4)	6 (2.3)	12 (2.3)

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E/100PY = Events per 100 patient-years.

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臨床検査 (Cont.)			
白血球数減少	1 (0.4)	1 (0.4)	2 (0.4)
白血球数増加	0	1 (0.4)	1 (0.2)
代謝および栄養障害	9 (3.5)	7 (2.7)	16 (3.1)
食欲減退	1 (0.4)	0	1 (0.2)
高コレステロール血症	1 (0.4)	2 (0.8)	3 (0.6)
高脂血症	6 (2.4)	2 (0.8)	8 (1.6)
高ナトリウム血症	1 (0.4)	0	1 (0.2)
高尿酸血症	0	1 (0.4)	1 (0.2)
食欲亢進	0	2 (0.8)	2 (0.4)
筋骨格系および結合組織障害	5 (2.0)	10 (3.8)	15 (2.9)
関節痛	0	1 (0.4)	1 (0.2)
背部痛	1 (0.4)	0	1 (0.2)
滑液包炎	0	1 (0.4)	1 (0.2)
関節ロック	0	1 (0.4)	1 (0.2)
筋痙縮	0	3 (1.2)	3 (0.6)
筋肉痛	4 (1.6)	3 (1.2)	7 (1.4)
頚部腫瘤	0	1 (0.4)	1 (0.2)

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良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (1.2)	2 (0.8)	5 (1.0)
肛門性器疣贅	0	1 (0.4)	1 (0.2)
ケラトアカントーマ	0	1 (0.4)	1 (0.2)
脂漏性角化症	1 (0.4)	0	1 (0.2)
皮膚乳頭腫	2 (0.8)	0	2 (0.4)
神経系障害	13 (5.1)	20 (7.7)	33 (6.4)
注意力障害	1 (0.4)	0	1 (0.2)
浮動性めまい	2 (0.8)	6 (2.3)	8 (1.6)
味覚不全	0	1 (0.4)	1 (0.2)
頭痛	8 (3.1)	8 (3.1)	16 (3.1)
過眠症	0	1 (0.4)	1 (0.2)
多発性硬化症再発	0	1 (0.4)	1 (0.2)
錯感覚	1 (0.4)	1 (0.4)	2 (0.4)
失神寸前の状態	1 (0.4)	0	1 (0.2)
傾眠	0	1 (0.4)	1 (0.2)
失神	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
精神障害	3 (1.2)	13 (5.0)	16 (3.1)
感情不安定	1 (0.4)	0	1 (0.2)
注意欠陥多動性障害	0	1 (0.4)	1 (0.2)
抑うつ気分	0	2 (0.8)	2 (0.4)
うつ病	0	1 (0.4)	1 (0.2)
不眠症	0	2 (0.8)	2 (0.4)
リビドー減退	0	1 (0.4)	1 (0.2)
リビドー亢進	1 (0.4)	0	1 (0.2)
精神障害	0	3 (1.2)	3 (0.6)
混合性不安抑うつ障害	0	1 (0.4)	1 (0.2)
悪夢	1 (0.4)	0	1 (0.2)
パニック発作	0	1 (0.4)	1 (0.2)
睡眠障害	0	1 (0.4)	1 (0.2)
腎および尿路障害	4 (1.6)	4 (1.5)	8 (1.6)
アルブミン尿	0	1 (0.4)	1 (0.2)
排尿困難	1 (0.4)	0	1 (0.2)
血尿	1 (0.4)	2 (0.8)	3 (0.6)
夜間頻尿	1 (0.4)	0	1 (0.2)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
腎および尿路障害 (Cont.)			
多尿	1 (0.4)	0	1 (0.2)
蛋白尿	0	1 (0.4)	1 (0.2)
生殖系および乳房障害	3 (1.2)	3 (1.2)	6 (1.2)
勃起不全	0	2 (0.8)	2 (0.4)
月経過多	1 (0.4)	0	1 (0.2)
不規則月経	1 (0.4)	0	1 (0.2)
精巣痛	1 (0.4)	1 (0.4)	2 (0.4)
呼吸器、胸郭および縦隔障害	24 (9.4)	24 (9.2)	48 (9.3)
失声症	2 (0.8)	0	2 (0.4)
喘息	3 (1.2)	1 (0.4)	4 (0.8)
カタル	0	1 (0.4)	1 (0.2)
咳嗽	8 (3.1)	8 (3.1)	16 (3.1)
呼吸困難	2 (0.8)	2 (0.8)	4 (0.8)
鼻出血	3 (1.2)	1 (0.4)	4 (0.8)
鼻閉	0	1 (0.4)	1 (0.2)
口腔咽頭痛	0	6 (2.3)	6 (1.2)
咽頭腫脹	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
呼吸器、胸郭および縦隔障害 (Cont.)			
胸水	1 (0.4)	0	1 (0.2)
湿性咳嗽	2 (0.8)	0	2 (0.4)
肺肉芽腫	0	1 (0.4)	1 (0.2)
肺腫瘤	0	1 (0.4)	1 (0.2)
鼻漏	2 (0.8)	0	2 (0.4)
副鼻腔うっ血	1 (0.4)	1 (0.4)	2 (0.4)
皮膚および皮下組織障害	82 (32.1)	95 (36.5)	177 (34.4)
ざ瘡	50 (19.6)	62 (23.9)	112 (21.7)
脱毛症	1 (0.4)	0	1 (0.2)
水疱	0	2 (0.8)	2 (0.4)
皮膚嚢腫	1 (0.4)	0	1 (0.2)
ざ瘡様皮膚炎	3 (1.2)	3 (1.2)	6 (1.2)
アトピー性皮膚炎	6 (2.4)	4 (1.5)	10 (1.9)
接触皮膚炎	0	1 (0.4)	1 (0.2)
乾癬様皮膚炎	1 (0.4)	0	1 (0.2)
異汗性湿疹	1 (0.4)	0	1 (0.2)
湿疹	1 (0.4)	2 (0.8)	3 (0.6)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
紅斑	1 (0.4)	0	1 (0.2)
過剰肉芽組織	1 (0.4)	0	1 (0.2)
毛髪成長異常	1 (0.4)	1 (0.4)	2 (0.4)
汗腺炎	0	1 (0.4)	1 (0.2)
多汗症	2 (0.8)	0	2 (0.4)
多毛症	1 (0.4)	1 (0.4)	2 (0.4)
苔癬化	0	1 (0.4)	1 (0.2)
稗粒腫	0	1 (0.4)	1 (0.2)
寝汗	1 (0.4)	0	1 (0.2)
口囲皮膚炎	0	2 (0.8)	2 (0.4)
偽毛包炎	1 (0.4)	0	1 (0.2)
紫斑	1 (0.4)	0	1 (0.2)
発疹	2 (0.8)	0	2 (0.4)
丘疹性皮疹	2 (0.8)	2 (0.8)	4 (0.8)
そう痒性皮疹	1 (0.4)	0	1 (0.2)
酒さ	1 (0.4)	1 (0.4)	2 (0.4)
痂皮	0	1 (0.4)	1 (0.2)

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E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=442) (PYS=255.2) Events (E/100PY)	UPA 30 mg QD + TCS (N=434) (PYS=259.9) Events (E/100PY)	Total (N=876) (PYS=515.1) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
脂漏	1 (0.4)	1 (0.4)	2 (0.4)
皮膚障害	0	1 (0.4)	1 (0.2)
皮膚亀裂	0	3 (1.2)	3 (0.6)
皮膚腫瘤	0	1 (0.4)	1 (0.2)
皮膚線条	1 (0.4)	0	1 (0.2)
皮膚腫脹	0	1 (0.4)	1 (0.2)
日光黒子	1 (0.4)	0	1 (0.2)
蕁麻疹	0	3 (1.2)	3 (0.6)
血管障害	1 (0.4)	3 (1.2)	4 (0.8)
大動脈瘤	0	1 (0.4)	1 (0.2)
深部静脈血栓症	0	1 (0.4)	1 (0.2)
高血圧	1 (0.4)	0	1 (0.2)
レイノー現象	0	1 (0.4)	1 (0.2)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
E/100PY = Events per 100 patient-years.

Program Source Code: [redacted]

相互参照：M16-047 試験 CSR W16 Table 14.3__1.10.3

重篤な有害事象の叙述

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肺炎	X	X		X
急性呼吸不全	X	X		
ブドウ球菌性敗血症	X	X		X

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

Medical History	Onset Year
ASTHMA	19[redacted]
SEASONAL ALLERGIES	19[redacted]
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20[redacted]
ATOPIC DERMATITIS	20[redacted]
HYPERTENSION	20[redacted]
HYPERCHOLESTEROLEMIA	20[redacted]
HEPATITIS B VACCINATION	20[redacted]
SEBORRHEIC DERMATITIS - GROIN	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	10 CIGARETTE	40	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 12[redacted]0[redacted] / 71		71

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE W/FORMOTEROL FUMARATE	2 OTHER: PUFFS	BID	Y: 20[redacted]
TIOTROPIUM	18 ug	QD	Y: 20[redacted]
AMLODIPINE	10 mg	QD	Y: 20[redacted]
PRAVASTATIN	40 mg	QD	Y: 20[redacted]
PREDNISONE	20 mg	QD	Y: 20[redacted]
PREDNISONE	60 mg	QD	Y: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METHOTREXATE	15 mg	1 TIME PER WEEK	Y-M: 20[redacted]
METHOTREXATE	20 mg	1 TIME PER WEEK	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted]
TRIAMCINOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -76
NIVEA	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -30

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
BUDESONIDE W/FORMOTEROL FUMARATE	2 OTHER: PUFFS	BID	Y: 20[redacted]	ONGOING
TIOTROPIUM	18 ug	QD	Y: 20[redacted]	ONGOING
AMLODIPINE	10 mg	QD	Y: 20[redacted]	ONGOING
PRAVASTATIN	40 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 81
NIVEA	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -30	ONGOING
FLUTICASONE	2 OTHER: PUFFS	QD	Y-M: 20[redacted] / 82	ONGOING
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 82	ONGOING
SALBUTAMOL	2 OTHER: PUFFS	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 82	ONGOING
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 86
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
BUDESONIDE	0.5 mg	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
COMBIVENT	0.5-2.5/3 OTHER: MG/ML	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
FLUTICASONE FUROATE W/VILANTEROL	100-25 ug	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
FORMOTEROL	20 ug	BID	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89

METHYLPREDNISOLONE	40 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
NICOTINE	21 mg	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
ONDANSETRON	4 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
SODIUM CHLORIDE	75 OTHER: ML/HOUR	OTHER: CONTINUOUS	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
UMECLIDINIUM	62.5 ug	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 89
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted] / 82	Y-M: 20[redacted] / 100
INFLUENZA VACCINE	0.5 mL	OTHER: ONCE	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 83
GUAIFENESIN	400 mg	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 89
PARACETAMOL	650 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 89
VANCOMYCIN	1.5 g	QD	Y-M: 20[redacted] / 85	ONGOING
HYDRALAZINE	10 mg	OTHER: EVERY 2 HOURS	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 89
AZITHROMYCIN	250 mg	QD	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 92
PRAVASTATIN	40 mg	QD	Y-M: 20[redacted] / 90	ONGOING
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 90	Y-M: 20[redacted] / 94
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 95	Y-M: 20[redacted] / 99

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 69
Age at AE Onset	6[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 81): Eosinophils/Leukocytes: 1.2 [0.3 - 6.2] %; Leukocytes: 8.9 [4 - 11] 10^9/L; Lymphocytes: 1.2 [1.1 - 3.3] 10^9/L; Lymphocytes/Leukocytes: 13.1 [15.2 - 43.3] %; Monocytes: 0.7 [0.3 - 1.1] 10^9/L; Monocytes/Leukocytes: 8.1 [5.5 - 13.7] %; Neutrophils: 6.9 [2 - 6.7] 10^9/L; Neutrophils/Leukocytes: 77.4 [39.6 - 74.7] %; [redacted]20[redacted] (RX DAY 83): Eosinophils/Leukocytes: 0 [0.3 - 6.2] %; Leukocytes: 12.4 [4 - 11] 10^9/L; Lymphocytes: 0.6 [1.1 - 3.3] 10^9/L; Lymphocytes/Leukocytes: 5.1 [15.2 - 43.3] %; Monocytes: 0.2 [0.3 - 1.1] 10^9/L; Monocytes/Leukocytes: 1.8 [5.5 - 13.7] %; Neutrophils: 11.6 [2 - 6.7] 10^9/L; Neutrophils/Leukocytes: 93 [39.6 - 74.7] %; [redacted]20[redacted] (RX DAY 88): Leukocytes: 16.1 [4 - 11] 10^9/L
Microbiology	[redacted]20[redacted] (RX DAY 82): BLOOD NPTST010-BLOOD CULTURE: Positive-DIPHTHEROID BACILLI; BLOOD NPTST010-BLOOD CULTURE: Positive-METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 81): 2-VIEW CHEST X-RAY: 1. PATCHY PERIHILAR GROUND-GLASS AIR SPACE DISEASE WITH BRONCHIAL WALL THICKENING MAY REFLECT MILD BRONCHITIS/PNEUMONITIS. 2. QUESTION BACKGROUND OF MILD COPD/EMPHYSEMA; [redacted]20[redacted] (RX DAY 84): SINGLE-VIEW CHEST X-RAY: VASCULAR PROMINENCE AND

	INTERSTITIAL THICKENING WHICH IS SLIGHTLY WORSENED.; [redacted]20[redacted] (RX DAY 86): SINGLE-VIEW CHEST X-RAY: RIGHT UPPER EXTREMITY PICC TERMINATES OVER THE CAVOATRIAL JUNCTION. NO PNEUMOTHORAX IS SEEN. NO ACUTE CARDIOPULMONARY ABNORMALITY IS APPRECIATED. THE HEART IS NOT ENLARGED.; [redacted]20[redacted] (RX DAY 88): SINGLE-VIEW CHEST X-RAY: 1. NO ACUTE CARDIOPULMONARY PROCESS IDENTIFIED 2. STABLE RIGHT UPPER EXTREMITY PICC.
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	2
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	COPD AND CIGARETTE USE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	ACUTE RESPIRATORY FAILURE
Preferred term	急性呼吸不全
AE Onset Date / Rx Day	[redacted]20[redacted] / 81 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 81): Eosinophils/Leukocytes: 1.2 [0.3 - 6.2] %; Leukocytes: 8.9 [4 - 11] 10^9/L; Lymphocytes: 1.2 [1.1 - 3.3] 10^9/L; Lymphocytes/Leukocytes: 13.1 [15.2 - 43.3] %; Monocytes: 0.7 [0.3 - 1.1] 10^9/L; Monocytes/Leukocytes: 8.1 [5.5 - 13.7] %; Neutrophils: 6.9 [2 - 6.7] 10^9/L; Neutrophils/Leukocytes: 77.4 [39.6 - 74.7] %; [redacted]20[redacted] (RX DAY 83): Eosinophils/Leukocytes: 0 [0.3 - 6.2] %; Leukocytes: 12.4 [4 - 11] 10^9/L; Lymphocytes: 0.6 [1.1 - 3.3] 10^9/L; Lymphocytes/Leukocytes: 5.1 [15.2 - 43.3] %; Monocytes: 0.2 [0.3 - 1.1] 10^9/L; Monocytes/Leukocytes: 1.8 [5.5 - 13.7] %; Neutrophils: 11.6 [2 - 6.7] 10^9/L; Neutrophils/Leukocytes: 93 [39.6 - 74.7] %; [redacted]20[redacted] (RX DAY 88): Leukocytes: 16.1 [4 - 11] 10^9/L
Microbiology	[redacted]20[redacted] (RX DAY 82): BLOOD NPTST010-BLOOD CULTURE: Positive-DIPHTHEROID BACILLI; BLOOD NPTST010-BLOOD CULTURE: Positive-METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 81): 2-VIEW CHEST X-RAY: 1. PATCHY PERIHILAR GROUND-GLASS AIR SPACE DISEASE WITH BRONCHIAL WALL THICKENING MAY REFLECT MILD BRONCHITIS/PNEUMONITIS. 2. QUESTION BACKGROUND OF MILD COPD/EMPHYSEMA; [redacted]20[redacted] (RX DAY 84): SINGLE-VIEW CHEST X-RAY: VASCULAR PROMINENCE AND INTERSTITIAL THICKENING WHICH IS SLIGHTLY WORSENED.; [redacted]20[redacted] (RX DAY 86): SINGLE-VIEW CHEST X-RAY: RIGHT UPPER EXTREMITY PICC TERMINATES OVER THE CAVOATRIAL JUNCTION. NO PNEUMOTHORAX IS SEEN. NO ACUTE CARDIOPULMONARY ABNORMALITY IS APPRECIATED. THE HEART IS NOT ENLARGED.; [redacted]20[redacted] (RX DAY 88): SINGLE-VIEW CHEST X-RAY: 1. NO ACUTE CARDIOPULMONARY PROCESS IDENTIFIED 2. STABLE RIGHT UPPER EXTREMITY PICC.
AE Stopped Rx Day	89 (18 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Toxicity Grade	2

Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	SECONDARY TO PNEUMONIA
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections

Event Description	SEPSIS WITH MRSA
Preferred term	ブドウ球菌性敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 84 (13 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 81): Eosinophils/Leukocytes: 1.2 [0.3 - 6.2] %; Leukocytes: 8.9 [4 - 11] 10^9/L; Lymphocytes: 1.2 [1.1 - 3.3] 10^9/L; Lymphocytes/Leukocytes: 13.1 [15.2 - 43.3] %; Monocytes: 0.7 [0.3 - 1.1] 10^9/L; Monocytes/Leukocytes: 8.1 [5.5 - 13.7] %; Neutrophils: 6.9 [2 - 6.7] 10^9/L; Neutrophils/Leukocytes: 77.4 [39.6 - 74.7] %; [redacted]20[redacted] (RX DAY 83): Eosinophils/Leukocytes: 0 [0.3 - 6.2] %; Leukocytes: 12.4 [4 - 11] 10^9/L; Lymphocytes: 0.6 [1.1 - 3.3] 10^9/L; Lymphocytes/Leukocytes: 5.1 [15.2 - 43.3] %; Monocytes: 0.2 [0.3 - 1.1] 10^9/L; Monocytes/Leukocytes: 1.8 [5.5 - 13.7] %; Neutrophils: 11.6 [2 - 6.7] 10^9/L; Neutrophils/Leukocytes: 93 [39.6 - 74.7] %; [redacted]20[redacted] (RX DAY 88): Leukocytes: 16.1 [4 - 11] 10^9/L
Microbiology	[redacted]20[redacted] (RX DAY 82): BLOOD NPTST010-BLOOD CULTURE: Positive-DIPHTHEROID BACILLI; BLOOD NPTST010-BLOOD CULTURE: Positive-METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 81): 2-VIEW CHEST X-RAY: 1. PATCHY PERIHILAR GROUND-GLASS AIR SPACE DISEASE WITH BRONCHIAL WALL THICKENING MAY REFLECT MILD BRONCHITIS/PNEUMONITIS. 2. QUESTION BACKGROUND OF MILD COPD/EMPHYSEMA; [redacted]20[redacted] (RX DAY 84): SINGLE-VIEW CHEST X-RAY: VASCULAR PROMINENCE AND INTERSTITIAL THICKENING WHICH IS SLIGHTLY WORSENED.; [redacted]20[redacted] (RX DAY 86): SINGLE-VIEW CHEST X-RAY: RIGHT UPPER EXTREMITY PICC TERMINATES OVER THE CAVOATRIAL JUNCTION. NO PNEUMOTHORAX IS SEEN. NO ACUTE CARDIOPULMONARY ABNORMALITY IS APPRECIATED. THE HEART IS NOT ENLARGED.; [redacted]20[redacted] (RX DAY 88): SINGLE-VIEW CHEST X-RAY: 1. NO ACUTE CARDIOPULMONARY PROCESS IDENTIFIED 2. STABLE RIGHT UPPER EXTREMITY PICC.
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬，トリアムシノロンアセトニド及びヒドロコルチゾンを投与され，メチシリン耐性黄色ブドウ球菌（以下「MRSA」）性敗血症，肺炎及び急性呼吸不全を発現した。被験者は喫煙者（紙巻タバコ 10 本／日，40 年間）かつ非飲酒者であり，関連する病歴は喘息，季節性アレルギー，慢性閉塞性肺疾患，高血圧，高コレステロール血症，アトピー性皮膚炎，アレルギー性鼻炎であった。

20[redacted] 年[redacted] 月[redacted] 日，被験者は肺炎を発現した。20[redacted] 年[redacted] 月[redacted] 日，被験者は急性呼吸不全を発現した。20[redacted] 年[redacted] 月[redacted] 日，被験者は MRSA 性敗血症を発現した。20[redacted] 年[redacted] 月[redacted] 日，急性呼吸不全は消失した。

20[redacted] 年[redacted] 月[redacted] 日，被験者は入院した。入院当初の喀痰は緑色であったが，徐々に無色になった。被験者の訴えでは，喀痰を伴う咳嗽が 1 週間持続しており，胸痛，動悸及び失神する感覚はなかった。胸部 X 線像で肺門周囲の肺胞含気腔の斑状すりガラス病変及び気管支壁肥厚が認められ，軽度の気管支炎／肺臓炎が疑われた。血液培養の結果から敗血症と判断された。被験者は呼吸器科で併診され，内科治療を受けた。末梢挿入型中心静脈カテーテル（以下「PICC」）も留置された。PICC を介した抗生物質投与計画が立てられ，2[redacted]9 年[redacted] 月[redacted] 日，被験者は退院した。

PULMICORT RESPULES，塩化ナトリウム，メチルプレドニゾロン，ZOFRAN，インフルエンザワクチン，グアイフェネシン，vancomycin，アセトアミノフェン，フルチカゾンフランカルボン酸エステル/vilanterol，albuterol，prednisone，INCRUSE ELLIPTA，formoterol，fluticasone，azithromycin，DUONEB 及び ROCEPHIN が投与された。

The patient's past medications include:

PREDNISONE for ATOPIC DERMATITIS (20[redacted] - 20[redacted], 2016 - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

TRIAMCINOLONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Sepsis MRSA (10049253) (Staphylococcal sepsis (10056430)) [v.22.1] [10049253]

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

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

Dechallenge: Not Applicable

2) Pneumonia (10035664) (Pneumonia (10035664)) [v.22.1] [10035664]

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

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

Dechallenge: No

3) Acute respiratory failure (10001053) (Acute respiratory failure (10001053)) [v.22.1] [10001053]

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

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

Dechallenge: Not Applicable

Causality for TRIAMCINOLONE ACETONIDE (Open Label)

---

1) Sepsis MRSA (10049253) (Staphylococcal sepsis (10056430)) [v.22.1] [10049253]

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

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

Dechallenge: Not Applicable

2) Pneumonia (10035664) (Pneumonia (10035664)) [v.22.1] [10035664]

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.22.1] [10001053]

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

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

Dechallenge: Not Applicable

Causality for HYDROCORTISONE (Open Label)

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1) Sepsis MRSA (10049253) (Staphylococcal sepsis (10056430)) [v.22.1] [10049253]

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

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

Dechallenge: Not Applicable

2) Pneumonia (10035664) (Pneumonia (10035664)) [v.22.1] [10035664]

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.22.1] [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 SEPSIS WITH MRSA

- Investigator: NOT APPLICABLE

- AbbVie: EVENT IS MORE LIKELY A COMPLICATION FROM PRECEDING PNEUMONIA.

Event of PNEUMONIA

- Investigator: COPD and cigarette use

- AbbVie: RISK FACTORS INCLUDE CURRENT LONG TERM SMOKING HISTORY, PRE-EXISTING CHRONIC OBSTRUCTIVE PULMONARY DISEASE, AND PRE-EXISTING ASTHMA.

Event of ACUTE RESPIRATORY FAILURE

- Investigator: SECONDARY TO PNEUMONIA

- AbbVie: EVENT IS MORE LIKELY A COMPLICATION FROM PRECEDING PNEUMONIA.

Alternative Etiology for TRIAMCINOLONE ACETONIDE (Open Label)

Event of SEPSIS WITH MRSA

- Investigator: NOT REPORTED

- AbbVie: EVENT IS MORE LIKELY A COMPLICATION FROM PRECEDING PNEUMONIA.

Event of PNEUMONIA

- Investigator: LOCAL FACTORS RAIN AND COLD.

- AbbVie: RISK FACTORS INCLUDE CURRENT LONG TERM SMOKING HISTORY, PRE-EXISTING CHRONIC OBSTRUCTIVE PULMONARY DISEASE, AND PRE-EXISTING ASTHMA.

Event of ACUTE RESPIRATORY FAILURE

- Investigator: SECONDARY TO PNEUMONIA

- AbbVie: EVENT IS MORE LIKELY A COMPLICATION FROM PRECEDINGPNEUMONIA.

Alternative Etiology for HYDROCORTISONE (Open Label)

Event of SEPSIS WITH MRSA

- Investigator: NOT REPORTED

- AbbVie: EVENT IS MORE LIKELY A COMPLICATION FROM PRECEDING PNEUMONIA.

Event of PNEUMONIA

- Investigator: LOCAL FACTORS RAIN AND COLD.

- AbbVie: RISK FACTORS INCLUDE CURRENT LONG TERM SMOKING HISTORY, PRE-EXISTING CHRONIC OBSTRUCTIVE PULMONARY DISEASE, AND PRE-EXISTING ASTHMA.

Event of ACUTE RESPIRATORY FAILURE

- Investigator: SECONDARY TO PNEUMONIA

- AbbVie: EVENT IS MORE LIKELY A COMPLICATION FROM PRECEDING PNEUMONIA.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **2-VIEW CHEST X-RAY:** 1. PATCHY PERIHILAR GROUND-GLASS AIR SPACE DISEASE WITH BRONCHIAL WALL THICKENING MY REFLECT MILD BRONCHITIS/PNEUMONITIS.2. QUESTION BACKGROUND OF MILD COPD/EMPHYSEMA

[redacted] **BLOOD CULTURE:** METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS

[redacted] **CHEST X-RAY:** normal

[redacted] **EOSINOPHILS %:** 1.2 % (normal 0.3 to 6.2)

[redacted] **EOSINOPHILS %:** 0.0 % (normal 0.3 to 6.2)

[redacted] **LYMPHOCYTES %:** 13.1 % (normal 15.2 to 43.3)

[redacted] **LYMPHOCYTES %:** 5.1 % (normal 15.2 to 43.3)

[redacted] **LYMPHOCYTES ABS:** 1.2 10^3/uL (normal 1.1 to 3.3)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.6 10^3/uL (normal 1.1 to 3.3)

[redacted] **20[redacted] MONOCYTES %:** 8.1 % (normal 5.5 to 13.7)

[redacted] **20[redacted] MONOCYTES %:** 1.8 % (normal 5.5 to 13.7)

[redacted] **20[redacted] MONOCYTES ABS:** 0.7 10^3/uL (normal 0.3 to 1.1)

[redacted] **20[redacted] MONOCYTES ABS:** 0.2 10^3/uL (normal 0.3 to 1.1)

[redacted] **20[redacted] NEUTROPHILS %:** 77.4 % (normal 39.6 to 74.7)

[redacted] **20[redacted] NEUTROPHILS %:** 93.0 % (normal 39.6 to 74.7)

[redacted] **20[redacted] NEUTROPHILS ABS:** 6.9 X10**3/MM**3 (normal 2.0 to 6.7)

[redacted] **20[redacted] NEUTROPHILS ABS:** 11.6 X10**3/MM**3 (normal 2.0 to 6.7)

[redacted] **20[redacted] SINGLE-VIEW CHEST X-RAY:** VASCULAR PROMINENCE AND INTERSTITIAL THICKENING, WHICH IS SLIGHTLY WORSENED.

[redacted] **20[redacted] SINGLE-VIEW CHEST X-RAY:** RIGHT UPPER EXTREMITY PICC TERMINATES OVER THE CAVOATRIAL JUNCTION. NO PNEUMOTHORAX IS SEEN. NO ACUTE CARDIOPULMONARY ABNORMALITY IS APPRECIATED. THE HEART IS NOT ENLARGED.

[redacted] **20[redacted] SINGLE-VIEW CHEST X-RAY:** 1. NO ACUTE CARDIOPULMONARY PROCESS IDENTIFIED 2. STABLE RIGHT UPPER EXTREMITY PICC.

[redacted] **20[redacted] BLOOD CULTURE:** Positive DIPHTHEROID BACILLI

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.9 10^3/uL (normal 4.0 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 12.4 10^3/uL (normal 4.0 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 16.1 10^3/uL (normal 4.0 to 11.0)

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
PET DANDER ALLERGY	19[redacted]
POLEN ALLERGY	19[redacted]
CERVICAL SPINAL STENOSIS	20[redacted]
ANXIETY	20[redacted]
DEPRESSION	20[redacted]
INTERMITTENT HYPERTENSION	20[redacted]
HERNIA	20[redacted]
SQUAMOUS CELL CARCINOMA (NMSC)	20[redacted]
LEFT HIP PAIN	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: SURGICAL DECOMPRESSION	20[redacted]
PRIOR PROCEDURES: HERNIOPLASTY	20[redacted]
PRIOR PROCEDURES: EXCISIONAL SURGERY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 CIGARETTE	5	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	More than 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 10	[redacted]0[redacted] / 104	104

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day

VITAMINS NOS	1 OTHER: CAP	QD	Y: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	40 OTHER: SESSIONS	OTHER: 3 TIMES PER WEEK	Y: 20[redacted]
DOXEPIN	25 mg	QD	Y: 20[redacted]
PREDNISONE	10 mg	QD	Y: 20[redacted]
TRIAMCINOLONE	0.1 %	BID	Y: 20[redacted]
AQUAPHOR	1 OTHER: APPLICATION	BID	Y: 20[redacted]
BUPROPION	50 mg	QD	Y: 20[redacted]
IBUPROFEN	200 mg	QD	Y-M: 20[redacted] / -320

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
VITAMINS NOS	1 OTHER: CAP	QD	Y: 20[redacted]	ONGOING
DOXEPIN	25 mg	QD	Y: 20[redacted]	ONGOING
AQUAPHOR	1 OTHER: APPLICATION	BID	Y: 20[redacted]	ONGOING
BUPROPION	50 mg	QD	Y: 20[redacted]	ONGOING
IBUPROFEN	200 mg	QD	Y-M: 20[redacted] / -320	ONGOING
BISMUTH	30 mL	PRN	Y-M: 20[redacted] / 41	ONGOING
IBUPROFEN	600 mg	PRN	Y-M: 20[redacted] / 100	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 100	ONGOING
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 102

Event #1: Serious Adverse Event

Event Description	PLEURAL EFFUSION
Preferred term	胸水
AE Onset Date / Rx Day	[redacted]20[redacted] / 100
Age at AE Onset	6[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 100): CHEST X-RAY: PER SUBJECT REPORT, CXR SHOWED FLUID AROUND LUNGS
AE Stopped Rx Day	102
Duration of AE	3 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬，トリアムシノロンアセトニド及びヒドロコルチゾンを投与され，胸水を発現した。被験者は元喫煙者（紙巻タバコ 20 本／日，5 年間）かつ飲酒者（4 杯超／日）であり，関連する病歴はアトピー性皮膚炎，間欠性高血圧，非黒色腫皮膚癌，扁平上皮癌であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸水を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胸水は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は息切れ及び胸部不快感の症状で入院した。被験者によれば，胸部 X 線検査を受けたところ肺周囲に胸水が認められ，その後胸水のドレナージ及び疼痛に対する治療を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

PREDNISONE for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

TRIAMCINOLONE for ATOPIC DERMATITIS (20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pleural effusion (10035598) (Pleural effusion (10035598)) [v.22.1] [10035598]

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

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

Dechallenge: Not Applicable

Causality for TRIAMCINOLONE ACETONIDE (Open Label)

---

1) Pleural effusion (10035598) (Pleural effusion (10035598)) [v.22.1] [10035598]

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

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

Dechallenge: Not Applicable

Causality for HYDROCORTISONE (Open Label)

---

1) Pleural effusion (10035598) (Pleural effusion (10035598)) [v.22.1] [10035598]

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 PLEURAL EFFUSION

- Investigator: Not applicable.

- AbbVie: Event with multiple underlying etiologies.

Alternative Etiology for TRIAMCINOLONE ACETONIDE (Open Label)

Event of PLEURAL EFFUSION

- Investigator: More likely related to Upadacitinib/placebo.

- AbbVie: Lack of temporal association with last dose of study drug close to 10 weeks prior to onset of event .

Alternative Etiology for HYDROCORTISONE (Open Label)

Event of PLEURAL EFFUSION

- Investigator: More likely related to Upadacitinib/placebo.

- AbbVie: Lack of temporal association with last dose of study drug close to 9 weeks prior to onset of event .

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST XRAY:** Fluid around lungs

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
水腎症	X			
腎結石症	X			
急性腎障害				X
潰瘍性角膜炎	X			X
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	3[redacted]	MALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
NECK PAIN	20[redacted]
CHOLECYSTITIS	20[redacted]
RUL PULMONARY NODULE	20[redacted]
HERPES SIMPLEX VIRUS INFECTION LEFT CORNEA	20[redacted]
LEFT CORNEAL ULCER	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: CERVICAL FUSION	20[redacted]
PRIOR PROCEDURES: CHOLECYSTECTOMY	20[redacted]
PRIOR PROCEDURES: BRONCHOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	FORMER			
CIGARETTES	FORMER	10 CIGARETTE	10	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 115	115
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 116		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	12.5 mg	1 TIME PER WEEK	Y-M: 20[redacted]
PIMECROLIMUS	1 OTHER: APPLICATION	BID	Y: 20[redacted]
TRIAMCINOLONE	1 OTHER: APPLICATION	BID	Y: 20[redacted]
MYCOPHENOLIC ACID	1000 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted] / -158
OTHER EMOLLIENTS AND PROTECTIVES	N/A OTHER: N/A	BID	Y-M: 20[redacted] / -12

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
OTHER EMOLLIENTS AND PROTECTIVES	N/A OTHER: N/A	BID	Y-M: 20[redacted] / -12	NOT REPORTED
KETOROLAC	15 mg	OTHER: ONCE	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 93
METHYLPREDNISOLONE	125 mg	OTHER: ONCE	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 93
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 93
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 93
PREDNISONE	20 mg	BID	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 95
HYDROMORPHONE	1 mg	OTHER: Q3H PRN	Y-M: 20[redacted] / 95	Y-M: 20[redacted] / 97
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 95	Y-M: 20[redacted] / 98
FLEBOBAG RING LACT	1000 mL	OTHER: NOT SPECIFIED	Y-M: 20[redacted] / 95	Y-M: 20[redacted] / 98
ONDANSETRON	4 mg	OTHER: Q4H, PRN	Y-M: 20[redacted] / 95	Y-M: 20[redacted] / 98
OXYCODONE	5 mg	OTHER: Q4H, PRN	Y-M: 20[redacted] / 95	Y-M: 20[redacted] / 98

PARACETAMOL	325 mg	OTHER: Q4H, PRN	Y-M: 20[redacted]-[redacted] / 95	Y-M: 20[redacted]-[redacted] / 98
LIDOCAINE	2 %	OTHER: ONE TIME	Y-M: 20[redacted]-[redacted] / 96	Y-M: 20[redacted]-[redacted] / 96
DOCUSATE	100 mg	QD	Y-M: 20[redacted]-[redacted] / 96	Y-M: 20[redacted]-[redacted] / 98
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted]-[redacted] / 96	Y-M: 20[redacted]-[redacted] / 98
SODIUM CHLORIDE	1000 mL	OTHER: NOT SPECIFIED	Y-M: 20[redacted]-[redacted] / 96	Y-M: 20[redacted]-[redacted] / 98
MORPHINE	2 mg	OTHER: Q4H, PRN	Y-M: 20[redacted]-[redacted] / 97	Y-M: 20[redacted]-[redacted] / 98
OXYCOCET	5-325 mg	TID	Y-M: 20[redacted]-[redacted] / 98	Y-M: 20[redacted]-[redacted] / 105
EYE STREAM	15 mL	OTHER: ONE TIME	Y-M: 20[redacted]-[redacted] / 228	Y-M: 20[redacted]-[redacted] / 228
FLUORESCEIN	1 mg	OTHER: ONE TIME	Y-M: 20[redacted]-[redacted] / 228	Y-M: 20[redacted]-[redacted] / 228
TETRACAINE	0.5 %	OTHER: ONE TIME	Y-M: 20[redacted]-[redacted] / 228	Y-M: 20[redacted]-[redacted] / 228
PARACETAMOL	650 mg	OTHER: EVERY 4 HOURS AS NEEDED	Y-M: 20[redacted]-[redacted] / 229	Y-M: 20[redacted]-[redacted] / 229
TOBRAMYCIN	15 OTHER: MG/ML	OTHER: Q1H	Y-M: 20[redacted]-[redacted] / 229	Y-M: 20[redacted]-[redacted] / 230
VANCOMYCIN	50 OTHER: MG/ML	OTHER: Q1H	Y-M: 20[redacted]-[redacted] / 229	Y-M: 20[redacted]-[redacted] / 230
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted]-[redacted] / 229	Y-M: 20[redacted]-[redacted] / 231
OXYCOCET	5-325 mg	OTHER: EVERY 6 HOURS AS NEEDED	Y-M: 20[redacted]-[redacted] / 229	Y-M: 20[redacted]-[redacted] / 231
ACICLOVIR	400 mg	OTHER: 5 TIMES DAILY	Y-M: 20[redacted]-[redacted] / 229	Y-M: 20[redacted]-[redacted] / 233
ATROPINE	1 %	BID	Y-M: 20[redacted]-[redacted] / 229	Y-M: 20[redacted]-[redacted] / 249
TOBRAMYCIN	15 OTHER: MG/ML	OTHER: Q1H WHILE AWAKE	Y-M: 20[redacted]-[redacted] / 230	Y-M: 20[redacted]-[redacted] / 231

VANCOMYCIN	50 OTHER: MG/ML	OTHER: Q1H WHILE AWAKE	Y-M: 20[redacted] / 230	Y-M: 20[redacted] / 231
PROCHLORPERAZINE	10 mg	OTHER: EVERY 6 HOURS AS NEEDED	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
TOBRAMYCIN	0.3 %	OTHER: EVERY 2 HOURS WHILE AWAKE	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 233
VANCOMYCIN	50 OTHER: MG/ML	OTHER: EVERY 2 HOURS WHILE AWAKE	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 233
OXYCOCET	5-325 mg	OTHER: EVERY 4 HOURS AS NEEDED	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 236
TOBRAMYCIN	0.3 %	OTHER: 6 TIMES PER DAY	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 240
VANCOMYCIN	50 OTHER: MG/ML	OTHER: 6 TIMES PER DAY	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 240
ACICLOVIR	400 mg	BID	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 400
OFLOXACIN	0.3 %	OTHER: 6 TIMES PER DAY	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 249
POLYMYXIN B W/TRIMETHOPRIM	10000 - 0.1 OTHER: UNIT/ML - %	OTHER: 6 TIMES PER DAY	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 249
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 281
OFLOXACIN	0.3 %	QID	Y-M: 20[redacted] / 249	Y-M: 20[redacted] / 263
POLYMYXIN B W/TRIMETHOPRIM	10000 - 0.1 OTHER: UNIT/ML - %	QID	Y-M: 20[redacted] / 249	Y-M: 20[redacted] / 263
OFLOXACIN	0.3 %	BID	Y-M: 20[redacted] / 263	Y-M: 20[redacted] / 400
POLYMYXIN B W/TRIMETHOPRIM	10000 - 0.1 OTHER: UNIT/ML - %	BID	Y-M: 20[redacted] / 263	Y-M: 20[redacted] / 400
CEFTRIAXONE	1000 mg	OTHER: UNK	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 365
IOPAMIDOL	75 mL	OTHER: ONCE	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 365
MAGNESIUM SULFATE	2 g	OTHER: UNK	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 365

COMBIVENT	0.5-2.5/3 OTHER: MG/ML	OTHER: Q4H WHILE AWAKE	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 368
METHYLPREDNISOLONE	125 mg	OTHER: UNK	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 368
ALUMINIUM W/MAGNESIUM HYDROXIDE/SIMETICONE	30 mL	OTHER: Q4H, PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
AZITHROMYCIN	UNKNOWN OTHER: UNK	PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
CEFTRIAXONE	2000/50 OTHER: MG/ML	OTHER: UNKNOWN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
MAGNESIUM HYDROXIDE	30 mL	OTHER: QD, PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
ONDANSETRON	4 mg	OTHER: Q4H, PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
PARACETAMOL	650 mg	OTHER: Q4H, PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
SALBUTAMOL	2.5/3 OTHER: MG/ML	OTHER: Q2H	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
BUDESONIDE	0.5/2 OTHER: MG/ML	BID	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 368
GUAIFENESIN	1200 MG mg	OTHER: Q12H	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 368
KETOROLAC	15/1 OTHER: MG/ML	OTHER: Q6H, PRN	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 368
FLUTICASONE	44 OTHER: MCG/INHALATION	BID	Y-M: 20[redacted] / 368	Y-M: 20[redacted] / 383
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 374
LEVOFLOXACIN	750 mg	QD	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 383
ACICLOVIR	400 mg	OTHER: 4 TIMES PER DAY	Y-M: 20[redacted] / 400	Y-M: 20[redacted] / 442
OFLOXACIN	0.3 %	OTHER: 1 DROP IN LEFT EYE 6 TIMES PER DAY	Y-M: 20[redacted] / 400	Y-M: 20[redacted] / 442

POLYMYXIN B W/TRIMETHOPRIM	10000 - 0.1 OTHER: UNIT/ML - %	OTHER: 1 DROP IN BOTH EYES 6 TIMES PER DAY	Y-M: 20[redacted]-[redacted] / 400	Y-M: 20[redacted]-[redacted] / 442

Event #1: Serious Adverse Event

Event Description	RENAL CALCULI W/ HYDRONEPHROSIS
Preferred term	水腎症
AE Onset Date / Rx Day	[redacted]20[redacted] / 93
Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 93): NPTST079-UA BLOOD: MODERATE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 96): Creatinine: 139 [53 - 115] UMOL/L; [redacted]20[redacted] (RX DAY 97): Creatinine: 78 [53 - 115] UMOL/L; [redacted]20[redacted] (RX DAY 98): Creatinine: 80 [53 - 115] UMOL/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 93): CT ABD/PEL W/ CONTRAST: NO ACUTE INTRA-ABDOMINAL ABNORMALITY; ECG: SINUS BRADYCARDIA WITH SINUS ARRHYTHMIA; [redacted]20[redacted] (RX DAY 95): CT ABD/PEL W/O CONTRAST: MODERATE TO SEVERE LEFT HYDRONEPHROSIS SECONDARY TO 4MM DISTAL LEFT URETERAL CALCULUS, JUST PROXIMAL TO THE LEFT URETEROVESICULAR JUNCTION. NON-OBSTRUCTING 1 MM LEFT INTRARENAL CALCULUS NO RIGHT-SIDED NEPHROLITHIASIS; [redacted]20[redacted] (RX DAY 96): CYSTOSCOPY/URETEROSCOPY WITH STONE REMOVAL AND STENT PLACEMENT: STENT PLACED; FLUOROSCOPY: CANNULATION OF THE LEFT URETER VIA RETROGRADE BLADDER ACCESS WITH INSTILLATION OF WATER SOLUBLE CONTRAST. A WIRE IS EXTENDED PROXIMAL TO THE OBSTRUCTING DISTAL CALCULUS WITH CONTRAST INSTALLATION DEMONSTRATING URETERAL DISTENTION AND HYDRONEPHROSIS WHICH APPEARS STABLE COMPARED TO THE PRIOR CT
AE Stopped Rx Day	98
Duration of AE	6 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	UNKNOWN - PER SUB-I, EVENT COULD POSSIBLY HAVE BEEN CAUSED BY DEHYDRATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	RENAL CALCULI W/ HYDRONEPHROSIS
Preferred term	腎結石症
AE Onset Date / Rx Day	[redacted]20[redacted] / 93
Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 93): NPTST079-UA BLOOD: MODERATE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 96): Creatinine: 139 [53 - 115] UMOL/L; [redacted]20[redacted] (RX DAY 97): Creatinine: 78 [53 - 115] UMOL/L; [redacted]20[redacted] (RX DAY 98): Creatinine: 80 [53 - 115] UMOL/L

Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 93): CT ABD/PEL W/ CONTRAST: NO ACUTE INTRA-ABDOMINAL ABNORMALITY; ECG: SINUS BRADYCARDIA WITH SINUS ARRHYTHMIA; [redacted]20[redacted] (RX DAY 95): CT ABD/PEL W/O CONTRAST: MODERATE TO SEVERE LEFT HYDRONEPHROSIS SECONDARY TO 4MM DISTAL LEFT URETERAL CALCULUS, JUST PROXIMAL TO THE LEFT URETEROVESICULAR JUNCTION. NON-OBSTRUCTING 1 MM LEFT INTRARENAL CALCULUS NO RIGHT-SIDED NEPHROLITHIASIS; [redacted]20[redacted] (RX DAY 96): CYSTOSCOPY/URETEROSCOPY WITH STONE REMOVAL AND STENT PLACEMENT: STENT PLACED; FLUOROSCOPY: CANNULATION OF THE LEFT URETER VIA RETROGRADE BLADDER ACCESS WITH INSTILLATION OF WATER SOLUBLE CONTRAST. A WIRE IS EXTENDED PROXIMAL TO THE OBSTRUCTING DISTAL CALCULUS WITH CONTRAST INSTALLATION DEMONSTRATING URETERAL DISTENTION AND HYDRONEPHROSIS WHICH APPEARS STABLE COMPARED TO THE PRIOR CT
AE Stopped Rx Day	98
Duration of AE	6 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	UNKNOWN - PER SUB-I, EVENT COULD POSSIBLY HAVE BEEN CAUSED BY DEHYDRATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Event of Interest - Renal Dysfunction

Event Description	ACUTE KIDNEY INJURY
Preferred term	急性腎障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 96
Age at AE Onset	3[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	97
Duration of AE	2 DAYS
Toxicity Grade	1
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	CORNEAL ULCER - LEFT
Preferred term	潰瘍性角膜炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 222
Age at AE Onset	3[redacted]

Laboratory Testing	NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 228): OTHER EYE SMEAR NPTST008-BACTERIAL CULTURE: Positive-ONE COLONY CORYNEBACTERIUM STRIATUM; OTHER LEFT CORNEA SWAB NPTST039-HERPES SIMPLEX VIRUS PCR, VARIES: Positive-HSV POSITIVE
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Toxicity Grade	4
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #5: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS, OTHER, PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 362
Age at AE Onset	3[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 365): CHEST CT: HYPEREXPANDED LUNG VOLUME. MILD MEDIAL ANTERIOR RIGHT UPPER LOB PATCHY GROUND-GLASS OPACITIES.; CHEST X-RAY: NO ACUTE PULMONARY PROCESS; [redacted]20[redacted] (RX DAY 366): EKG: NORMAL ECG - OVERALL STABLE FROM PRIOR [redacted] 20[redacted]
AE Stopped Rx Day	383
Duration of AE	22 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者は米国の 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及びトリアムシノロンアセトニドを投与され，水腎症を伴う腎結石を発現した。被験者は元喫煙者（紙巻タバコ 10 本／日，10 年間），元噛みタバコ使用者かつ元飲酒者（2～4 杯／日）であり，関連する病歴はアトピー性皮膚炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は水腎症を伴う腎結石を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，水腎症を伴う腎結石は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急治療室を受診し，左側の腹痛を訴えた。検尿で血尿が認められ，被験者は救急治療室でメチルプレドニゾロン，オンダンセトロン，Toradol 及び生理食塩液のボーラス投与を受けてから prednisone の処方を受けて帰宅した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左側の腹部痛及び潮紅の症状で入院した。静脈内輸液及び鎮痛薬の静脈内投与が行われた。コンピュータ断層撮影が行われ，4 mm 径の尿管結石とその続発症である中等度から重度の左側水腎症が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，X 線透視撮影検査で左側の遠位尿管結石が認められた。同日，膀胱鏡検査，逆行性腎盂造影，尿管鏡検査，ホルミウムレーザー及びバスケットカテーテルによる結石除去操作並びにステント留置が行われた。被験者は急性腎障害（非重篤）も発現し，クレアチニン値は 1.57 mg/dL であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，泌尿器科及びかかり付け医の経過観察を受けた。

TORADOL，DILAUDID，PERCOCET，MORPHINE PRESERVATIVE FREE，オンダンセトロン，アセトアミノフェン，LEVAQUIN，morphine，DOCUSATE，enoxaparin，乳酸リンゲル液，リドカイン，prednisone，メチルプレドニゾロン，PERCOCET 及び oxycodone が投与された。

The patient's past medications include:

METHOTREXATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ELIDEL for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

KENALOG for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

CELLCEPT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IMURAN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

OTEZLA for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Renal calculi (10038385) (Nephrolithiasis (10029148)) [v.22.0] [10038385]

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

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

Dechallenge: Not Applicable

2) Hydronephrosis (10020524) (Hydronephrosis (10020524)) [v.22.0] [10020524]

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

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

Dechallenge: Not Applicable

Causality for TRIAMCINOLONE ACETONIDE (Open Label)

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1) Renal calculi (10038385) (Nephrolithiasis (10029148)) [v.22.0] [10038385]

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

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

Dechallenge: Not Applicable

2) Hydronephrosis (10020524) (Hydronephrosis (10020524)) [v.22.0] [10020524]

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 RENAL CALCULI W/ HYDRONEPHROSIS

- Investigator: UNKNOWN - PER SUB-I, EVENT COULD POSSIBLY HAVE BEEN CAUSED BY DEHYDRATION

- AbbVie: Renal stone disease is a common event in the male population with an estimated 19 percent of men diagnosed with a kidney stone by the age of 70 years. Hydronephrosis is more likely related to left sided renal

calculus.

Alternative Etiology for TRIAMCINOLONE ACETONIDE (Open Label)

Event of RENAL CALCULI W/ HYDRONEPHROSIS

- Investigator: UNKNOWN - PER SUB-I, EVENT COULD POSSIBLY HAVE BEEN CAUSED BY DEHYDRATION

- AbbVie: Renal stone disease is a common event in the male population with an estimated 19 percent of men diagnosed with a kidney stone by the age of 70 years. Hydronephrosis is more likely related to left sided renal calculus.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CBC:** No clinical significant.

[redacted] **20[redacted] CMP:** No clinical significant.

[redacted] **20[redacted] CREATININE:** 1.57 mg/dL (normal 0.60 to 1.30)

[redacted] **20[redacted] CREATININE:** 0.88 mg/dL (normal 0.60 to 1.30)

[redacted] **20[redacted] CREATININE:** 0.90 mg/dL (normal 0.60 to 1.30)

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** Moderate to severe left sided hydronephrosis secondary to a 4mm ureteral calculus, just proximal to the left ureterovesicular junction. Non-obstructing 1 mm left intrarenal calculus No right-sided nephrolithiasis

[redacted] **20[redacted] CT ABDOMEN AND PELVIS WITH CONTRAST:** No acute intra-abdominal abnormality

[redacted] **20[redacted] ECG:** Sinus bradycardia with sinus arrhythmia.

[redacted] **20[redacted] FLUOROSCOPY:** Cannulation of the left ureter via retrograde bladder access with instillation of water soluble contrast. A wire is extended proximal to the obstructing distal calculus with contrast installation demonstrating ureteral distention and hydronephrosis which appears stable compared to the prior CT

[redacted] **20[redacted] UA BLOOD:** Negative

[redacted] **20[redacted] URINALYSIS:** Hematuria.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者は米国の 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及びトリアムシノロンアセトニドを投与され，角膜潰瘍（左眼）を発現した。被験者は元喫煙者（紙巻タバコ 0.5 箱／日，10 年間），元噛みタバコ使用者かつ元飲酒者（2～4 杯／日）であり，関連する病歴はアトピー性皮膚炎及び左眼の角膜潰瘍であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は盲検継続投与期に移行し，盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は角膜潰瘍（左眼）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左眼の眼痛，発赤，羞明及び霧視を発現した。詳しい診察のため，被験者は救急治療室に案内された。同日，被験者は帰宅した。治験責任医師の報告によれば，被験者は処方薬を何も使用せず，2[redacted]9 年 [redacted] 月 [redacted] 日に救急治療室を再受診して同じ症状を訴えた。フルオレセイン及び tetracaine が投与され，眼洗浄が行われた。被験者は臨床検査を受け，角膜潰瘍と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，抗生物質及び抗ウイルス治療を投与された。20[redacted] 年 [redacted] 月 [redacted] 日，視力検査が行われ，左眼視力は 20/200（0.1 相当）と判定された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者の申告では，20[redacted] 年に眼外傷を受傷した。また，20[redacted] 年に角膜潰瘍と診断され，単純ヘルペスウイルス（以下「HSV」）感染が疑われたが，その際は HSV 検査が行われなかった。20[redacted] 年 [redacted] 月，被験者は黄色ブドウ球菌感染を発現しており，治療を受けた。

tetracaine，フルオレセイン，oxycodone 及びアセトアミノフェン，ATROPINE OPHTHALMIC，アシクロビル，アセトアミノフェン，プロクロルペラジン，VANCOMYCIN TOPICAL OPHTHALMIC SOLUTION，トブラマイシン，polymyxin B - トリメトプリム，オフロキサシン並びに doxycycline が投与された。

The patient's past medications include:

METHOTREXATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ELIDEL for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

KENALOG for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

CELLCEPT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IMURAN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

OTEZLA for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Corneal ulcer (10048492) (Ulcerative keratitis (10064996)) [v.23.0] [10048492]

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

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

Dechallenge: Not Applicable

Causality for TRIAMCINOLONE ACETONIDE (Open Label)

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1) Corneal ulcer (10048492) (Ulcerative keratitis (10064996)) [v.23.0] [10048492]

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 CORNEAL ULCER - LEFT

- Investigator: Not reported.

- AbbVie: Event is more likely related to pre-existing left corneal ulcer.

Alternative Etiology for TRIAMCINOLONE ACETONIDE (Open Label)

Event of CORNEAL ULCER - LEFT

- Investigator: Not reported

- AbbVie: Event is more likely related to pre-existing left corneal ulcer.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] EYE SMEAR BACTERIAL CULTURE: POSITIVE: ONE COLONY CORYNEBACTERIUM STRIATUM

[redacted] 20[redacted] LEFT CORNEAL SWAB HERPES SIMPLEX VIRUS PCR, VARIES: HSV POSITIVE

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者は米国の 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，トリアムシノロンアセトニド及びベタメタゾンジプロピオン酸エステルを投与され，肺炎（呼吸器，胸郭，縦隔のその他疾患）を発現した。被験者は元喫煙者（紙巻タバコ 10 本／日，10 年間）かつ元飲酒者（2～4 杯／日）であり，関連する病歴はアトピー性皮膚炎，右肺上葉の肺結節（影）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎（呼吸器，胸郭，縦隔のその他疾患）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎（呼吸器，胸郭，縦隔のその他疾患）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日（第 52 週の規定来院日），被験者は上気道感染の症状（喘鳴，咳嗽及び息切れ）を訴え，これらは 3 日間持続した。被験者によれば，これらの症状は 20[redacted] 年 [redacted] 月 [redacted] 日の朝に始まったばかりであった。20[redacted] 年 [redacted] 月 [redacted] 日の夜に症状が悪化したため，20[redacted] 年 [redacted] 月 [redacted] 日の早朝に被験者は救急治療室を受診した。被験者は肺炎の診断で入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者のコメント：被験者の記憶によれば，過去 2～3 年間に肺炎の診断を 2，3 回受けているが，詳細や具体的な診断時期（年月日）は思い出せなかった。

IPRATROPIUM/albuterol，メチルプレドニゾロン，magnesium sulfate，ceftriaxone，アセトアミノフェン，aluminum hydroxide/水酸化マグネシウム/simethicone，albuterol，ROCEPHIN，azithromycin，ketorolac，MUCINEX，PULMICORT，fluticasone，levofloxacin，prednisone 及び酸素が投与された。

The patient's past medications include:

METHOTREXATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ELIDEL for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

KENALOG for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

CELLCEPT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IMURAN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

OTEZLA for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Pneumonia (10035664) (Pneumonia (10035664)) [v.23.0] [10035664]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Causality for TRIAMCINOLONE ACETONIDE (Open Label)

---

1) Pneumonia (10035664) (Pneumonia (10035664)) [v.23.0] [10035664]

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

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

Dechallenge: Not Applicable

Causality for BETAMETHASONE DIPROPIONATE (Open Label)

---

1) Pneumonia (10035664) (Pneumonia (10035664)) [v.23.0] [10035664]

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 RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS, OTHER, PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Alternative Etiology for TRIAMCINOLONE ACETONIDE (Open Label)

Event of RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS, OTHER, PNEUMONIA

- Investigator: Not reported

- AbbVie: Risk factors include history of smoking and pre-existing atopic dermatitis, as ex-smokers have an increased risk of developing pneumonia and patients with atopic dermatitis have an increased risk of developing systemic infections, including pneumonia.

Alternative Etiology for BETAMETHASONE DIPROPIONATE (Open Label)

Event of RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS, OTHER, PNEUMONIA

- Investigator: Not reported

- AbbVie: Risk factors include history of smoking and pre-existing atopic dermatitis, as ex-smokers have an increased risk of developing pneumonia and patients with atopic dermatitis have an increased risk of developing systemic infections, including pneumonia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST CT:** HYPEREXPANDED LUNG VOLUME. MILD MEDIAL ANTERIOR RIGHT UPPER LOB PATCHY GROUND-GLASS OPACITIES.

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

[redacted] **20[redacted] CHEST X-RAY:** NO ACUTE PULMONARY PROCESS.

[redacted] **20[redacted] EKG:** NORMAL ECG - OVERALL STABLE FROM PRIOR [redacted] 20[redacted]

非重篤な有害事象

被験者は急性腎障害を発現し，水腎症及び腎結石症を併発していた。治験薬の投与に変更はなかった。急性腎障害は消失した。

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
感染性湿疹	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD/UPA 30 MG QD	1[redacted]	FEMALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	20[redacted]
RECURRENT TONSILLITIS	20[redacted]
BUG BITE ALLERGY	20[redacted]
POOR VISION	20[redacted]
ACNE	20[redacted]
ANXIETY	20[redacted]
ASTHMA	20[redacted]
ACNE	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: ADENOIDECTOMY	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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 114	114
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 115		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 20[redacted]

CILEST	1 OTHER: TABLET	QD	Y: 20[redacted]
MOMETASONE	0.1 %	QD	Y-M: 20[redacted] / -252
FLUTICASONE	125 mg	QD	Y-M: 20[redacted] / -84
FLUOCINONIDE	0.05 %	BID	Y-M: 20[redacted] / -48
CETAPHIL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -21

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
CILEST	1 OTHER: TABLET	QD	Y: 20[redacted]	NOT REPORTED
FLUTICASONE	125 mg	QD	Y-M: 20[redacted] / -84	NOT REPORTED
CETAPHIL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -21	NOT REPORTED
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 215	Y-M: 20[redacted] / 217
CEFALEXIN	500 mg	QID	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 219

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

Event Description	SUPERINFECTED ECZEMA OF THE HANDS
Preferred term	感染性湿疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 215
Age at AE Onset	1[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 215): Leukocytes: 22.1 [4 - 10] 10^9/L; Neutrophils: 19.8 [2 - 7.5] 10^9/L; [redacted]20[redacted] (RX DAY 216): NPTST012-C REACTIVE PROTEIN: 112.0 [NOT REPORTED - 3] mg/L; [redacted]20[redacted] (RX DAY 217): Leukocytes: 7.8 [4 - 10] 10^9/L; NPTST012-C REACTIVE PROTEIN: 62.2 [NOT REPORTED - 3] mg/L; Neutrophils: 5.4 [2 - 7.5] 10^9/L; [redacted]20[redacted] (RX DAY 218): Leukocytes: 11.9 [4 - 10] 10^9/L; Neutrophils: 9 [2 - 7.5] 10^9/L
Microbiology	[redacted]20[redacted] (RX DAY 215): BLOOD NPTST010-BLOOD CULTURE: Negative; [redacted]20[redacted] (RX DAY 216): WOUND NPTST038-HERPES SIMPLEX VIRUS DETECTION: Negative; URINE NPTST083-URINE CULTURE: Negative; WOUND NPTST089-WOUND CULTURE: Positive-GROUP A STREPTOCOCCUS; STAPHYLOCOCCUS AUREUS
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	218
Duration of AE	4 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者はカナダの 1[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬，トリアムシノロンアセトニド及びヒドロコルチゾン酢酸エステルを投与され，両手の重複感染性湿疹を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両手の重複感染性湿疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，両手の重複感染性湿疹は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両手の重複感染性湿疹のため入院した。被験者は発熱及び軽度の悪心を発現した。被験者は感染症内科に紹介され，抗生物質の経口投与を勧められた。入院中，被験者の状態は次第に改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

cephalexin，KEFLEX 及び ceftriaxone が投与された。

Causality for UPADACITINIB (Blinded)

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1) Eczema infected (10014199) (Eczema infected (10014199)) [v.22.1] [10014199]

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

Causality for TRIAMCINOLONE ACETONIDE (Open Label)

---

1) Eczema infected (10014199) (Eczema infected (10014199)) [v.22.1] [10014199]

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

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

Dechallenge: Not Applicable

Causality for HYDROCORTISONE ACETATE (Open Label)

---

1) Eczema infected (10014199) (Eczema infected (10014199)) [v.22.1] [10014199]

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 SUPERINFECTED ECZEMA ON HER HANDS

- Investigator: Not applicable

- AbbVie: Event is more likely a complication of pre-existing atopic dermatitis.

Alternative Etiology for TRIAMCINOLONE ACETONIDE (Open Label)

Event of SUPERINFECTED ECZEMA ON HER HANDS

- Investigator: Not applicable

- AbbVie: Event is more likely a complication of pre-existing atopic dermatitis.

Alternative Etiology for HYDROCORTISONE ACETATE (Open Label)

Event of SUPERINFECTED ECZEMA ON HER HANDS

- Investigator: Not applicable

- AbbVie: Event is more likely a complication of pre-existing atopic dermatitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABSOLUTE NEUTROPHILS:** 19.8 X10**9/L (normal 2.0 to 7.5)

[redacted] **20[redacted] ABSOLUTE NEUTROPHILS:** 5.4 X10**9/L (normal 2.0 to 7.5)

[redacted] **20[redacted] ABSOLUTE NEUTROPHILS:** 9.0 X10**9/L (normal 2.0 to 7.5)

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

[redacted] **20[redacted] CRP:** 112 MG/L (normal <3.0)

[redacted] **20[redacted] CRP:** 43 MG/L (normal <3.0)

[redacted] **20[redacted] HERPES SIMPLEX VIRUS DETECTION:** Negative

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

[redacted] **20[redacted] WBC:** 22.1 X10**9/L (normal 4.0 to 10)

[redacted] **20[redacted] WBC:** 7.8 X10**9/L (normal 4.0 to 10.0)

[redacted] **20[redacted] WBC:** 11.9 X10**9/L (normal 4.0 to 10.0)

[redacted] **20[redacted] WOUND CULTURE:** Positive for group A strep

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
網膜剥離	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
MYOPIA	19[redacted]
ACUTE APPENDICITIS	20[redacted]
ALLERGIC RHINOCONJUCTIVITIS	20[redacted]
MYOPIA GRADE 2	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.5 CIGARETTE	5	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 105	105
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 106		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CORTICOSTEROIDS, TOPICAL	1 OTHER: APPLICATION	PRN	Y: 19[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: RADIATION	1 TIME PER WEEK	Y-M: 20[redacted]-[redacted]

HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
DESLORATADINE	5 mg	PRN	Y: 20[redacted]
PSORALENS FOR SYSTEMIC USE	1 OTHER: APPLICATION	1 TIME PER WEEK	Y-M: 20[redacted]
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -322
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -21

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
DESLORATADINE	5 mg	PRN	Y: 20[redacted]	NOT REPORTED
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -21	NOT REPORTED
GENTAMICIN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 54
GENTAMICIN	5 mL	OTHER: 4 TIMES DAILY	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 54

Event #1: Serious Adverse Event

Event Description	RETINAL DETACHMENT OF LEFT EYE
Preferred term	網膜剥離
AE Onset Date / Rx Day	[redacted]20[redacted] / 43
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 46): VITRECTOMY + CRYOAPPLICATION + ENDOLASER + SILICONE FILLING LEFT EYE: DISMISSED [redacted] IN RECOVERING STATE; [redacted]20[redacted] (RX DAY 54): CONTROL WITH AUTOREFRACTOMETER, TONOMETRY, FUNDUS: GOOD STATE LEFT EYE; [redacted]20[redacted] (RX DAY 57): CONTROL WITH AUTOREFRACTOMETER, TONOMETRY: GOOD STATE LEFT EYE; [redacted]20[redacted] (RX DAY 149): EXCHANGE OF LEFT EYE LENSE AND REMOVAL OF SILICON OIL: PROCEDURE COMPLETED
AE Stopped Rx Day	47
Duration of AE	5 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	PATIENT WOKE UP AND COULD NOT SEE CLEARLY, SIGHT WAS BLURRED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者はオーストリアの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬，モメタゾンフランカルボン酸エステル，ヒドロコルチゾン酢酸エステル及びピメクロリムスを投与され，左眼の網膜剥離を発現した。被験者は喫煙者（紙巻タバコ 0.5 本／日，5 年間）かつ非飲酒者で，関連する病歴はアトピー性皮膚炎，アレルギー性鼻炎結膜炎及び近視（グレード 2）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左眼の網膜剥離を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左眼の網膜剥離は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は起床してから，視界がぼやけてよく見えない状態であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両眼の霧視（左眼-3，右眼-7）のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，左眼の硝子体切除，凍結療法，眼内レーザー及びシリコン充填術が完了した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，左眼内レンズ交換及びシリコンオイルの除去が行われた。

DORZASTAD，DIAMOX, DEXAGENTA DROPS，DEXAGENTA OINTMENT 及び KETOVISION が投与された。

The patient's past medications include:

UNKNOWN TOPICAL CORTICOSTEROID for ATOPIC DERMATITIS (19[redacted] - [redacted] 20[redacted])

URBASON for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Retinal detachment (10038848) (Retinal detachment (10038848)) [v.23.0] [10038848]

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

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

Dechallenge: Not Applicable

Causality for MOMETASONE FUROATE (Open Label)

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1) Retinal detachment (10038848) (Retinal detachment (10038848)) [v.23.0] [10038848]

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

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

Dechallenge: Not Applicable

Causality for HYDROCORTISONE ACETATE (Open Label)

---

1) Retinal detachment (10038848) (Retinal detachment (10038848)) [v.23.0] [10038848]

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

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

Dechallenge: Not Applicable

Causality for PIMECROLIMUS (Open Label)

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1) Retinal detachment (10038848) (Retinal detachment (10038848)) [v.23.0] [10038848]

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 RETINAL DETACHMENT OF LEFT EYE

- Investigator: Not applicable

- AbbVie: Event not consistent with study drug's mechanism of action and is more likely due to the subjects pre-existing atopic dermatitis (Takahashi,., et.al., Retinal detachment associated with atopic dermatitis. British

Journal of Ophthalmology 1996; 80: 54-57).

Alternative Etiology for MOMETASONE FUROATE (Open Label)

Event of RETINAL DETACHMENT OF LEFT EYE

- Investigator: Not applicable

- AbbVie: Event not consistent with study drug's mechanism of action and is more likely due to the subjects pre-existing atopic dermatitis (Takahashi,., et.al., Retinal detachment associated with atopic dermatitis. British Journal of Ophthalmology 1996; 80: 54-57).

Alternative Etiology for HYDROCORTISONE ACETATE (Open Label)

Event of RETINAL DETACHMENT OF LEFT EYE

- Investigator: Not applicable

- AbbVie: Event not consistent with study drug's mechanism of action and is more likely due to the subjects pre-existing atopic dermatitis (Takahashi,., et.al., Retinal detachment associated with atopic dermatitis. British Journal of Ophthalmology 1996; 80: 54-57).

Alternative Etiology for PIMECROLIMUS (Open Label)

Event of RETINAL DETACHMENT OF LEFT EYE

- Investigator: More likely related to Upadactinib/Placebo(if applicable), Mometasone and Hydrocortisone.

- AbbVie: Event not consistent with study drug's mechanism of action and is more likely due to the subjects pre-existing atopic dermatitis (Takahashi,., et.al., Retinal detachment associated with atopic dermatitis. British Journal of Ophthalmology 1996; 80: 54-57).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CONTROL WITH AUTOREFRACTOMETER, TONOMETRY: GOOD STATE LEFT EYE

[redacted] 20[redacted] CONTROL WITH AUTOREFRACTOMETER, TONOMETRY, FUNDUS: GOOD STATE LEFT EYE

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
口腔咽頭痛	X			
扁桃周囲膿瘍	X			X
過量投与	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ATOPIC DERMATITIS	20[redacted]
ERYTHEMA NODOSUM	20[redacted]
FAINTNESS	20[redacted]
HYPOTENSION	20[redacted]
DEPRESSION	20[redacted]
SLEEP DISORDERS	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	20 CIGARETTE	4	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1[redacted]20[redacted] / 79		79

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HYDROCORTISONE	UNK OTHER: UNK	QD	Y: 20[redacted]
EMOLLIENTS AND PROTECTIVES	UNK OTHER: UNK	BID	Y: 20[redacted]

BETAMETHASONE	UNK OTHER: UNK	QD	Y: 20[redacted]
HEPTAMINOL	UNK OTHER: UNK	PRN	Y: 20[redacted]
INTRAUTERINE CONTRACEPTIVE DEVICE	UNK OTHER: UNK	OTHER: CONTINUOUS	Y: 20[redacted]
FLUTICASONE	UNK OTHER: UNK	QD	Y-M: 20[redacted]-[redacted] / -101

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
EMOLLIENTS AND PROTECTIVES	UNK OTHER: UNK	BID	Y: 20[redacted]	ONGOING
HEPTAMINOL	UNK OTHER: UNK	PRN	Y: 20[redacted]	ONGOING
INTRAUTERINE CONTRACEPTIVE DEVICE	UNK OTHER: UNK	OTHER: CONTINUOUS	Y: 20[redacted]	ONGOING
BETAMETHASONE	0.1 %	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted] / 1	Y-M: 20[redacted]-[redacted] / 22
MOMETASONE	UNKNOWN ug	QD	Y-M: 20[redacted]-[redacted] / 12	Y-M: 20[redacted]-[redacted] / 30
PREDNISOLONE			Y-M: 20[redacted]-[redacted] / 16	Y-M: 20[redacted]-[redacted] / 19
AMOXICILLIN	3 g	QD	Y-M: 20[redacted]-[redacted] / 16	Y-M: 20[redacted]-[redacted] / 23
PARACETAMOL	AS NEEDED mg	PRN	Y-M: 20[redacted]-[redacted] / 16	Y-M: 20[redacted]-[redacted] / 23
AMOXICILLIN	1 g	TID	Y-M: 20[redacted]-[redacted] / 56	ONGOING
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted]-[redacted] / 56	ONGOING
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted]-[redacted] / 56	Y-M: 20[redacted]-[redacted] / 59
DEXCHLORPHENIRAMINE	5MG/1 ML mg	OTHER: 1 INFUSION	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 79
IBUPROFEN	UNKNOWN mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 79
INVESTIGATIONAL DRUG	150 mg/kg	OTHER: 1 HOUR	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 79
INVESTIGATIONAL DRUG	50 mg/kg	OTHER: DURING 4 HOURS	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 79
PARACETAMOL	16 g	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 79
TRAMADOL	700 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 79
INVESTIGATIONAL DRUG	100 mg/kg	OTHER: DURING 16HOURS	Y-M: 20[redacted]-[redacted] / 79	Y-M: 20[redacted]-[redacted] / 80

Event #1: Serious Adverse Event

Event Description	TONSILLAR PHLEGMON INFECTION, THROAT PAIN SINCE ONE DAY
Preferred term	口腔咽頭痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 13
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	16
Duration of AE	4 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	THE CAUSE OF EVENT IS STILL UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Event Description	TONSILLAR PHLEGMON INFECTION, THROAT PAIN SINCE ONE DAY
Preferred term	扁桃周囲膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 13
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	16
Duration of AE	4 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	THE CAUSE OF EVENT IS STILL UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #3: Serious Adverse Event

Event Description	OVERDOSE BY DRUGS (PARACETAMOL, IBUPROFENE, TRAMADOL)
Preferred term	過量投与
AE Onset Date / Rx Day	[redacted]20[redacted] / 79
Age at AE Onset	2[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 79): NPTST054-PARACETOLEMY: 9.9 [10 - 30] MG/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 79): ECG: NORMAL
AE Stopped Rx Day	81 (2 DAYS AFTER LAST TREATMENT)

Duration of AE	3 DAYS
Toxicity Grade	4
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, IS LIFE THREATENING

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者はフランスの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及びベタメタゾン吉草酸エステルを投与され，扁桃蜂窩織炎感染及び咽喉痛を発現した。被験者は喫煙者（紙巻タバコ 20 本／日，4 年間）かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎及び結節性紅斑であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は扁桃蜂窩織炎感染及び咽喉痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，扁桃蜂窩織炎感染及び咽喉痛は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は咽喉痛のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

amoxicilline，プレドニゾロン及び DOLIPRANE が投与された。

The patient's past medications include:

LOCOID for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

DIPROLENE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

FLIXOVATE for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Throat pain (10043523) (Oropharyngeal pain (10068319)) [v.22.1] [10043523]

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) Phlegmonous angina (10074276) (Peritonsillar abscess (10034686)) [v.22.1] [10074276]

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

Causality for BETAMETHASONE VALERATE (Open Label)

---

1) Throat pain (10043523) (Oropharyngeal pain (10068319)) [v.22.1] [10043523]

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

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

Dechallenge: Not Applicable

2) Phlegmonous angina (10074276) (Peritonsillar abscess (10034686)) [v.22.1] [10074276]

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 TONSILLAR PHLEGMON INFECTION, THROAT PAIN SINCE ONE DAY

- Investigator: The cause of event is still unknown

- AbbVie: Risk factors for tonsillar phlegmon infection include current smoking status and subject's age and event of throat pain is more likely related to concurrent tonsillar phlegmon infection.

Alternative Etiology for BETAMETHASONE VALERATE (Open Label)

Event of TONSILLAR PHLEGMON INFECTION, THROAT PAIN SINCE ONE DAY

- Investigator: The cause of event is still unknown.

- AbbVie: Risk factors for tonsillar phlegmon infection include current smoking status and subject's age and event of throat pain is more likely related to concurrent tonsillar phlegmon infection.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者はフランスの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬，ベタメタゾン吉草酸エステル及びフルチカゾンプロピオン酸エステルを投与され，薬剤（paracetamol，IBUPROFENE 及び tramadol）の過量投与を発現した。被験者は喫煙者（紙巻タバコ 20 本／日，4 年間）かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎，浮動性めまい感，低血圧，うつ病及び睡眠障害であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は薬剤（paracetamol，IBUPROFENE 及び tramadol）の過量投与を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，薬剤（paracetamol，IBUPROFENE 及び tramadol）の過量投与は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は過量投与（paracetamol，ibuprofene 及び tramadol）のため入院した。入院時，被験者は眠気を呈していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

NAC が投与された。

The patient's past medications include:

LOCOID for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

DIPROLENE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

FLIXOVATE for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PREDNISOLONE for TONSILLAR PHLEGMON and SORE THROAT ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Drug overdose (10068719) (Overdose (10033295)) [v.22.1] [10068719]

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

Causality for BETAMETHASONE VALERATE (Open Label)

---

1) Drug overdose (10068719) (Overdose (10033295)) [v.22.1] [10068719]

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

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

Dechallenge: Not Applicable

Causality for FLUTICASONE PROPIONATE (Open Label)

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1) Drug overdose (10068719) (Overdose (10033295)) [v.22.1] [10068719]

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 OVERDOSE BY DRUGS (PARACETAMOL, IBUPROFENE, TRAMADOL)

- Investigator: Not applicable.

- AbbVie: Event is more likely related to pre-existing depression and atopic dermatitis. Patients with atopic dermatitis are at significantly increased risk of suicidal ideation and suicide attempts.

Alternative Etiology for BETAMETHASONE VALERATE (Open Label)

Event of OVERDOSE BY DRUGS (PARACETAMOL, IBUPROFENE, TRAMADOL)

- Investigator: Upadacitinib

- AbbVie: Etiology of the event is not consistent with the study drug's mechanism of action. Additionally, lack of temporal association, with last dose of study drug over 7 weeks prior to the event.

Alternative Etiology for FLUTICASONE PROPIONATE (Open Label)

Event of OVERDOSE BY DRUGS (PARACETAMOL, IBUPROFENE, TRAMADOL)

- Investigator: Upadacitinib

- AbbVie: Etiology of the event is not consistent with the study drug's mechanism of action. Additionally, lack of temporal association, with last dose of study drug approximately 6 weeks prior to the event.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ECG:** Normal

[redacted] **20[redacted] PARACETOLEMY:** 9.9 MG/L (normal 10 to 30)

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	2[redacted]	MALE	WHITE

Medical History	Onset Year
ASTHMA	19[redacted]
ATOPIC DERMATITIS	19[redacted]
ALLERGIC RHINITIS	19[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	10 CIGARETTE	8	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 117	117
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 118	[redacted]20[redacted] / 194	77

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BETAMETHASONE	1 OTHER: APPLICATION	PRN	Y: 19[redacted]
PIMECROLIMUS	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]-[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: TREATMENT	OTHER: 3 TIMES A WEEK	Y-M: 20[redacted]-[redacted]

ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: TREATMENT	OTHER: 3 TIMES A WEEK	Y-M: 20[redacted]
CETOMACROGOL	1 OTHER: APPLICATION	BID	Y: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
TACROLIMUS	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -273

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
CETOMACROGOL	1 OTHER: APPLICATION	BID	Y: 20[redacted]	ONGOING

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

Event Description	ACUTE APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 48
Age at AE Onset	2[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 48): Leukocytes: 15.4 [4 - 11] 10^9/L; Neutrophils: 12.2 [2 - 7.7] 10^9/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 48): ABDOMINAL ULTRASOUND: INFLAMMED APPENDIX; LAPAROSCOPIC APPENDECTOMY: NORMAL PROCEDURE WITH NO COMPLICATIONS.
AE Stopped Rx Day	49
Duration of AE	2 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者はイスラエルの 2[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，ベタメタゾン吉草酸エステル及びヒドロコルチゾンを投与され，急性虫垂炎を発現した。被験者は元喫煙者（紙巻タバコ 10 本／日，8 年間）かつ適量飲酒者であり，関連する病歴

はアトピー性皮膚炎，アレルギー性鼻炎及び喘息であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性虫垂炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性虫垂炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右側腹痛及び嘔吐を呈し，救急治療室を受診した。身体的診察で反跳痛を伴う右上腹部痛が認められた。超音波検査で急性虫垂炎と確認された。同日，被験者は入院し，腹腔鏡下虫垂切除術を受け，合併症なく経過した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

BETACORTEN OINTMENT for ATOPIC DERMATITIS (1993 - [redacted] 20[redacted])

ELIDEL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PROTOPIC for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.21.1] [10000677]

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

Causality for BETAMETHASONE VALERATE (Open Label)

---

1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.21.1] [10000677]

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

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

Dechallenge: Not Applicable

Causality for HYDROCORTISONE (Open Label)

---

1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.21.1] [10000677]

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 ACUTE APPENDICITIS

- Investigator: Not Applicable

- AbbVie: EVENT IS COMMON IN THE GENERAL POPULATION; IT COMPRISES 5 TO 10 PERCENT OF EMERGENCY DEPARTMENT (ED) VISIT. (KENDALL, JL. EVALUATION OF THE ADULT WITH ABDOMINAL PAIN IN THE EMERGENCY DEPARTMENT. IN: UPTODATE, POST TW (ED), UPTODATE, WALTHAM, MA. (ACCESSED ON [redacted], 20[redacted].))

Alternative Etiology for BETAMETHASONE VALERATE (Open Label)

Event of ACUTE APPENDICITIS

- Investigator: Not applicable

- AbbVie: EVENT IS COMMON IN THE GENERAL POPULATION; IT COMPRISES 5 TO 10 PERCENT OF EMERGENCY DEPARTMENT (ED) VISIT. (KENDALL, JL. EVALUATION OF THE ADULT WITH ABDOMINAL PAIN IN THE EMERGENCY DEPARTMENT. IN: UPTODATE, POST TW (ED), UPTODATE, WALTHAM, MA. (ACCESSED ON [redacted], 20[redacted].))

Alternative Etiology for HYDROCORTISONE (Open Label)

Event of ACUTE APPENDICITIS

- Investigator: Not applicable

- AbbVie: EVENT IS COMMON IN THE GENERAL POPULATION; IT COMPRISES 5 TO 10 PERCENT OF EMERGENCY DEPARTMENT (ED) VISIT. (KENDALL, JL. EVALUATION OF THE ADULT WITH

ABDOMINAL PAIN IN THE EMERGENCY DEPARTMENT. IN: UPTODATE, POST TW (ED), UPTODATE, WALTHAM, MA. (ACCESSED ON [redacted] 20[redacted].))

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] NEUTROPHILS ABS:** 12.2 10^3/uL

[redacted] **20[redacted] ULTRASOUND:** Inflamed appendix

[redacted] **20[redacted] WHITE BLOOD CELLS:** 15.4 10^3/uL

Subject [redacted] ([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
ヘモグロビン減少	X	X		X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD/UPA 30 MG QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
HYPERTENSION	19[redacted]
HEPATITIS	19[redacted]
ATOPIC DERMATITIS	20[redacted]
INTERVERTEBRAL DISC HERNIATION	20[redacted]
SPINAL PAIN	20[redacted]
BENIGN PROSTATA HYPERTROPHY	20[redacted]
CYST OF KIDNEY	20[redacted]
LEFT LOWER LEG MUSCLE PARESIS	20[redacted]
OSTEOPOROSIS	20[redacted]
SPINAL STENOSIS	20[redacted]
STEATOSIS HEPATIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	19[redacted]
PRIOR PROCEDURES: SURGERY OF INTERVERTEBRAL DISC HERNIATION	20[redacted]
PRIOR PROCEDURES: SURGERY OF KERATHOACANTHOMA	20[redacted]
PRIOR PROCEDURES: SPINE SURGERY	20[redacted]
PRIOR PROCEDURES: SPINE SURGERY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	15 CIGARETTE	53	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 110	110
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 111	[redacted]20[redacted] / 126	16

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: 19[redacted]
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
AMLODIPINE	5 mg	QD	Y: 19[redacted]
METOPROLOL	50 mg	QD	Y: 19[redacted]
VASERETIC	20/12,5 mg	QD	Y: 19[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 IU	QD	Y: 20[redacted]
CICLOSPORIN	200 mg	QD	Y-M: 20[redacted]-[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y: 20[redacted]
FENTANYL	50 ug	OTHER: EVERY 72 HOURS	Y-M: 20[redacted]-[redacted]
FAMOTIDINE	20 mg	QD	Y: 20[redacted]
CLOBETASOL	1 IU	QD	Y-M: 20[redacted]-[redacted] / -65
CLOBETASOL	1 OTHER: FINGERTIP	QD	Y-M: 20[redacted]-[redacted] / -65
ERGOCALCIFEROL	3000 IU	QD	Y-M: 20[redacted]-[redacted] / -65
ATODERM	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted] / -10

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
AMLODIPINE	5 mg	QD	Y: 19[redacted]	ONGOING
METOPROLOL	50 mg	QD	Y: 19[redacted]	ONGOING
VASERETIC	20/12,5 mg	QD	Y: 19[redacted]	ONGOING
FENTANYL	50 ug	OTHER: EVERY 72 HOURS	Y-M: 20[redacted]-[redacted]	ONGOING
ERGOCALCIFEROL	3000 IU	QD	Y-M: 20[redacted]-[redacted] / -65	ONGOING
ATODERM	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted] / -10	ONGOING
SOLUZIONE BORO SALICILICA	1 OTHER: APPLICATION	OTHER: AS NEEDED	Y-M: 20[redacted]-[redacted] / 54	ONGOING

Event #1: Event of Interest - Anemia

Event Description	ANAEMIA
Preferred term	貧血

AE Onset Date / Rx Day	[redacted]20[redacted] / 85
Age at AE Onset	6[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	125
Duration of AE	41 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	UPADACITINIB/PLACEBO|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 of Interest - Anemia

Event Description	FURTHER DECREASE OF HAEMOGLOBIN LEVEL
Preferred term	ヘモグロビン減少
AE Onset Date / Rx Day	[redacted]20[redacted] / 126
Age at AE Onset	6[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 125): Erythrocytes: 1.5 [4.7 - 6.1] 10^12/L; Hematocrit: 0.17 [0.39 - 0.5] UNIT NOT REPORTED; Hemoglobin: 59 [130 - 165] G/L; Leukocytes: 11.5 [4.5 - 10.8] 10^9/L; NPTST033-FERRITIN: 904.7 [30 - 400] UG/L; NPTST034-FOLATE: 16.1 [10.4 - 42.4] NMOL/L; NPTST044-IRON: 10.4 [10.6 - 28.3] UMOL/L; NPTST085-VITAMIN B12: 233.6 [145 - 637] PMOL/L; [redacted]20[redacted] (RX DAY 128): Erythrocytes: 2.3 [4.7 - 6.1] 10^12/L; Hematocrit: 0.22 [0.39 - 0.5] UNIT NOT REPORTED; Hemoglobin: 79 [130 - 165] G/L; Leukocytes: 9.2 [4.5 - 10.8] 10^9/L; [redacted]20[redacted] (RX DAY 129): Erythrocytes: 2.8 [4.7 - 6.1] 10^12/L; Hematocrit: 0.26 [0.39 - 0.5] UNIT NOT REPORTED; Hemoglobin: 94 [130 - 165] G/L; Leukocytes: 10.5 [4.5 - 10.8] 10^9/L; [redacted]20[redacted] (RX DAY 130): Erythrocytes: 2.9 [4.7 - 6.1] 10^12/L; Hematocrit: 0.27 [0.39 - 0.5] UNIT NOT REPORTED; Hemoglobin: 98 [130 - 165] G/L; Leukocytes: 9.1 [4.5 - 10.8] 10^9/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 125): BONE MARROW BIOPSY: NEGATIV; [redacted]20[redacted] (RX DAY 127): ABDOMINAL ULTRASOUND: HEPATOMEGALY, CHOLECYSTOPATHY, KIDNEY CYST,; CHEST XRAY: NEGATIV
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者はハンガリーの 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，モメタゾンフランカルボン酸エステル，ヒドロコルチゾン及びクロベタゾールプロピオン酸エステルを投与され，ヘモグロビン値の更なる低下を発現した。被験者は元喫煙者（紙巻タバコ 15 本／日，53 年間）かつ飲酒者（2 杯未満／日）であり，関連する病歴は高血圧，肝炎，アトピー性皮膚炎，ケラトアカントーマ，良性前立腺肥大，腎嚢胞及び脂肪肝であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はヘモグロビン値の更なる低下を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日から同年 [redacted] 月 [redacted] 日まで，被験者は貧血（非重篤）を発現していた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はヘモグロビン値の更なる低下を発現し，加療を目的に入院した。赤血球濃厚液が輸血された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。被験者は本試験を中止した。

赤血球濃厚液が輸血された。

The patient's past medications include:

CLOBETASOL PROPIONATE for ATOPIC DERMATITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Decreased hemoglobin (10011964) (Haemoglobin decreased (10018884)) [v.22.0] [10011964]

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

Causality for MOMETASONE FUROATE (Open Label)

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1) Decreased hemoglobin (10011964) (Haemoglobin decreased (10018884)) [v.22.0] [10011964]

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

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

Dechallenge: Not Applicable

Causality for HYDROCORTISONE (Open Label)

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1) Decreased hemoglobin (10011964) (Haemoglobin decreased (10018884)) [v.22.0] [10011964]

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

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

Dechallenge: Not Applicable

Causality for CLOBETASOL PROPIONATE (Open Label)

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1) Decreased hemoglobin (10011964) (Haemoglobin decreased (10018884)) [v.22.0] [10011964]

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 FURTHER DECREASE OF HEMOGLOBIN LEVEL

- Investigator: Not applicable.

- AbbVie: Risk factors include pre-existing autoimmune disorder of atopic dermatitis and subject's advanced age.

Alternative Etiology for MOMETASONE FUROATE (Open Label)

Event of FURTHER DECREASE OF HEMOGLOBIN LEVEL

- Investigator: Not reported.

- AbbVie: Lack of temporal association with last dose of mometasone furoate 4 months prior to onset of event.

Alternative Etiology for HYDROCORTISONE (Open Label)

Event of FURTHER DECREASE OF HEMOGLOBIN LEVEL

- Investigator: Not reported.

- AbbVie: Lack of temporal association with last dose of hydrocortisone 4 months prior to onset of event.

Alternative Etiology for CLOBETASOL PROPIONATE (Open Label)

Event of FURTHER DECREASE OF HEMOGLOBIN LEVEL

- Investigator: Not reported.

- AbbVie: Lack of temporal association with last dose of clobetasol propionate 5 months prior to onset of event.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL ULTRASOUND:** Hepatomegaly, cholecystopathy, kidney cyst.

[redacted] **BONE MARROW BIOPSY:** Negative

[redacted] **CXR:** Negative

[redacted] **FERRITIN:** 904.7 MCG/L (normal 30 to 400)

[redacted] **FOLATE:** 16.1 NMOL/L (normal 10.4 to 42.4)

[redacted] **HCT:** 0.17 NO UNITS (normal 0.39 to 0.5)

[redacted] **HCT:** 0.22 NO UNITS (normal 0.39 to 0.5)

[redacted] **20**[redacted] **HCT:** 0.26 NO UNITS (normal 0.39 to 0.5)

[redacted] **20**[redacted] **HCT:** 0.27 NO UNITS (normal 0.39 to 0.5)

Unknown date HEMOGLOBIN: Further decrease

[redacted] **20**[redacted] **HGB:** 59 G/L (normal 130 to 165)

[redacted] **20**[redacted] **HGB:** 79 G/L (normal 130 to 165)

[redacted] **20**[redacted] **HGB:** 94 G/L (normal 130 to 165)

[redacted] **20**[redacted] **HGB:** 98 G/L (normal 130 to 165)

[redacted] **20**[redacted] **IRON:** 10.4 MCMOL/L (normal 10.6 to 28.3)

[redacted] **20**[redacted] **RBC:** 1.53 X10**12/L (normal 4.7 to 6.1)

[redacted] **20**[redacted] **RBC:** 2.29 X10**12/L (normal 4.7 to 6.1)

[redacted] **20**[redacted] **RBC:** 2.89 X10**12/L (normal 4.7 to 6.1)

[redacted] **20**[redacted] **VITAMIN B12:** 233.6 PMOL/L (normal 145 to 637)

[redacted] **20**[redacted] **WBC:** 9.23 X10**9/L (normal 4.5 to 10.8)

[redacted] **20**[redacted] **WBC:** 10.52 GIGA/L (normal 4.5 to 6.1)

[redacted] **20**[redacted] **WBC:** 9.12 X10**9/L (normal 4.5 to 10.8)

[redacted] **20**[redacted] **WHITE BLOOD CELLS:** 11.49 X10**9/L (normal 4.5 to 10.8)

非重篤な有害事象

被験者は貧血を発現した。治験薬の投与に変更はなかった。貧血は消失した。

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
裂孔原性網膜剥離	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 30 MG QD/UPA 30 MG QD	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ALLERGIC ASTHMA	20[redacted]
ALLERGIC RHINITIS	20[redacted]
ATOPIC DERMATITIS	20[redacted]
EYES MYOPIA	20[redacted]
SINUS BRADYCARDIA	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 119	119
UPA	30 MG	ORAL	QD	[redacted]20[redacted] / 120		

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: 19[redacted]
HYDROCORTISONE	A MODERATE AMOUNT OF g	BID	Y: 20[redacted]
CAMPHOR W/MENTHOL	A MODERATE AMOUNT OF g	BID	Y: 20[redacted]
DIPROSPAN	1 ML mL	OTHER: ONCE	Y-M: 20[redacted]
PIMECROLIMUS	A MODERATE AMOUNT OF g	BID	Y-M: 20[redacted]

TACROLIMUS	A MODERATE AMOUNT OF g	BID	Y-M: 20[redacted]
HALOMETASONE	A MODERATE AMOUNT OF mg	BID	Y-M: 20[redacted]
EMOLLIENTS AND PROTECTIVES	A MODERATE AMOUNT OF g	BID	Y-M: 20[redacted] / -18

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
EMOLLIENTS AND PROTECTIVES	A MODERATE AMOUNT OF g	BID	Y-M: 20[redacted] / -18	NOT REPORTED
ATROPINE	0.5 g	OTHER: ST	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 124
BROMFENAC	2 OTHER: DROPS	OTHER: ST	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 124
HYALURONIC ACID	100 OTHER: DROPS	TID	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 124
PREDNISONE	2 OTHER: DROPS	OTHER: ST	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 124
TOBRADEX	0.1 g	OTHER: QN	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 124
TROPICAMIDE	1 OTHER: DROPS	BID	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 124
ATROPINE	0.5 g	TID	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 126
LEVOFLOXACIN	1 OTHER: DROPS	QID	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 126
INDOCYANINE GREEN	1 OTHER: A PIECE OF	QD	Y-M: 20[redacted] / 126	Y-M: 20[redacted] / 126
DEXAMETHASONE	5 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
GENTAMICIN	1 OTHER: A PIECE OF	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
LIDOCAINE	1 OTHER: A PIECE OF	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
OFLOXACIN	1 OTHER: A PIECE OF	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
PROXYMETACAINE	1 OTHER: A PIECE OF	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
SODIUM CHLORIDE	A MODERATE AMOUNT OF %	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
ATROPINE	0.5 g	OTHER: QN	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 144
BROMFENAC	1 OTHER: DROPS	BID	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 144
LEVOFLOXACIN	1 OTHER: DROPS	QID	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 144
PREDNISONE	2 OTHER: DROPS	QID	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 144
TOBRADEX	0.1 g	OTHER: QN	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 144

TROPICAMIDE	1 OTHER: DROPS	BID	Y-M: 20[redacted] Y-M: 20[redacted] / / 128 144
LEVOFLOXACIN	1 OTHER: DROPS	TID	Y-M: 20[redacted] Y-M: 20[redacted] / / 201 205
TROPICAMIDE	2 OTHER: DROPS	TID	Y-M: 20[redacted] Y-M: 20[redacted] / / 201 205
ATROPINE	0.5 g	OTHER: ST	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
DEXAMETHASONE	0.5 g	OTHER: ST	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
DEXAMETHASONE	5 mg	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
GENTAMICIN	1 OTHER: A PIECE OF	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
HYALURONIC ACID	1 OTHER: A PIECE OF	QID	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
LEVOFLOXACIN	1 OTHER: DROPS	OTHER: ST	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
OFLOXACIN	1 OTHER: A PIECE OF	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
PREDNISOLONE	1 OTHER: DROPS	OTHER: ST	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
PROXYMETACAINE	1 OTHER: A PIECE OF	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
SODIUM CHLORIDE	A MODERATE AMOUNT OF OTHER: A MODERATE AMOUNT OF	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
TROPICAMIDE	2 OTHER: DROPS	OTHER: ST	Y-M: 20[redacted] Y-M: 20[redacted] / / 205 205
ATROPINE	0.5 g	QD	Y-M: 20[redacted] Y-M: 20[redacted] / / 206 223
DEXAMETHASONE	0.5 g	OTHER: QN	Y-M: 20[redacted] Y-M: 20[redacted] / / 206 223
LEVOFLOXACIN	1 OTHER: DROPS	QID	Y-M: 20[redacted] Y-M: 20[redacted] / / 206 223
PREDNISOLONE	2 OTHER: DROPS	QID	Y-M: 20[redacted] Y-M: 20[redacted] / / 206 223
TROPICAMIDE	2 OTHER: DROPS	BID	Y-M: 20[redacted] Y-M: 20[redacted] / / 206 223

Event #1: Serious Adverse Event

Event Description	RHEGMATOGENOUS RETINAL DETACHMENT OF THE RIGHT EYE
Preferred term	裂孔原性網膜剥離
AE Onset Date / Rx Day	[redacted]20[redacted] / 124
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 124): ECG: NODAL TACHYCARDIA; EYES ULTRASOUND: VITREOUS OPACITY IN BOTH EYES, RETINAL DETACHMENT.; [redacted]20[redacted] (RX DAY 127): RETINAL REDUCTION WITH SCLERAL RING IN RIGHT EYE: PATIENTS RECOVER
AE Stopped Rx Day	130

Duration of AE	7 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	RHEGMATOGENOUS RETINAL DETACHMENT OF LEFT EYE
Preferred term	裂孔原性網膜剥離
AE Onset Date / Rx Day	[redacted]20[redacted] / 201
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 201): LEFT EYE B ULTRASONIC: VITREOUS OPACITY IN LEFT EYE, DETACHED RETINA.; LEFT EYE OCT: LEFT EYE RETINAL DETACHMENT, NO MACULAR INVOLVEMENT.; [redacted]20[redacted] (RX DAY 205): LEFT EYE SCLERAL BUCKLING RETINAL REPAIRS: THE OPERATION SMOOTHLY,NO COMPLICATIONS.
AE Stopped Rx Day	208
Duration of AE	8 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者は中国の 2[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，モメタゾンフランカルボン酸エステル，desonide 及び tacrolimus を投与され，右眼の裂孔原性網膜剥離を発現した。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮

膚炎及び両眼の近視であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は盲検継続投与期に移行し，盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右眼の裂孔原性網膜剥離を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右眼の裂孔原性網膜剥離は消失した。

本事象に先行し，2[redacted]9 年 [redacted] 月 [redacted] 日から同年 [redacted] 月 [redacted] 日まで，眼底浮腫（非重篤）が発現していた。

右眼の状態が 15 日間悪化し続け，両眼視力低下が 3 ヵ月持続したため，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。同日，被験者は左眼の併発白内障及び左眼の網膜剥離（いずれも非重篤）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右眼の網膜強膜締結術及び術後の局所抗炎症療法を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師の報告によれば，被験者には近視（400 degrees）があったほか，顔面に発疹があり両眼周囲の皮膚を時々こすっていた。右眼の損傷及び外傷は認められなかった。治験責任医師が確認したところ，被験者に糖尿病及び眼科手術歴はなかった。眼疾患や眼症状の家族歴もなかった。

COMPOUND TROPICAMIDE EYE DROPS，TOBRAMYCIN/DEXAMETHASONE EYE CREAM，PREDNISONE ACETATE EYE DROPS，ATROPINE SULFATE EYE GEL，bromfenac sodium，LEVOFLOXACIN EYE DROPS，インドシアニングリーン，デキサメタゾンリン酸エステルナトリウム，ゲンタマイシン硫酸塩，OFLOXACIN EYE CREAM，塩化ナトリウム及びリドカイン塩酸塩が投与された。

The patient's past medications include:

HYDROCORTISONE BUTYRATE CREAM for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

MENTHOLATUM SKIN CREAM MOISTURIZER for ATOPIC DERMATITIS (20[redacted] - [redacted] [redacted] 20[redacted])

DIPROSPAN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PIMECROLIMUS CREAM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HALOMETASONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IODIZED LECITHIN for FUNDUS EDEMA ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

MECOBALAMIN for FUNDUS EDEMA ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Rhegmatogenous retinal detachment (10065569) (Rhegmatogenous retinal detachment (10065569)) [v.22.1] [10065569]

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

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

Dechallenge: Not Applicable

Causality for MOMETASONE FUROATE (Open Label)

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1) Rhegmatogenous retinal detachment (10065569) (Rhegmatogenous retinal detachment (10065569)) [v.22.1] [10065569]

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

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

Dechallenge: Not Applicable

Causality for DESONIDE (Open Label)

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1) Rhegmatogenous retinal detachment (10065569) (Rhegmatogenous retinal detachment (10065569)) [v.22.1] [10065569]

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

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

Dechallenge: Not Applicable

Causality for TACROLIMUS (Open Label)

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1) Rhegmatogenous retinal detachment (10065569) (Rhegmatogenous retinal detachment (10065569)) [v.22.1] [10065569]

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 RHEGMATOGENOUS RETINAL DETACHMENT OF THE RIGHT EYE

- Investigator: Not applicable

- AbbVie: The event is more likely related to pre-existing myopia. Additional risk factor includes facial rash with resulting eye rubbing per the investigator.

Alternative Etiology for MOMETASONE FUROATE (Open Label)

Event of RHEGMATOGENOUS RETINAL DETACHMENT OF THE RIGHT EYE

- Investigator: More likely related to Upadacitinib/placebo

- AbbVie: The event is more likely related to pre-existing myopia. Additional risk factor includes facial rash with resulting eye rubbing per the investigator.

Alternative Etiology for DESONIDE (Open Label)

Event of RHEGMATOGENOUS RETINAL DETACHMENT OF THE RIGHT EYE

- Investigator: More likely related to Upadacitinib/placebo

- AbbVie: The event is more likely related to pre-existing myopia. Additional risk factor includes facial rash with resulting eye rubbing per the investigator.

Alternative Etiology for TACROLIMUS (Open Label)

Event of RHEGMATOGENOUS RETINAL DETACHMENT OF THE RIGHT EYE

- Investigator: More likely related to Upadacitinib/placebo

- AbbVie: The event is more likely related to pre-existing myopia. Additional risk factor includes facial rash with resulting eye rubbing per the investigator.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ULTRASOUND EYES:** Vitreous opacity in both eyes, retinal detachment.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者は中国の 2[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，モメタゾンフランカルボン酸エステル，desonide 及び tacrolimus を投与され，左眼の裂孔原性網膜剥離を発現した。被験者は非喫煙者で禁酒しており，関連する病歴はアトピー性皮膚炎及び両眼の近視であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は盲検継続投与期に移行し，盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左眼の裂孔原性網膜剥離を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左眼の裂孔原性網膜剥離は消失した。

本事象発現に先行し，2[redacted]0 年 [redacted] 月，被験者は左眼の併発白内障及び左眼の網膜剥離（いずれも非重篤）を発現した。

治験責任医師は，関連するリスク因子として被験者が 3 ヵ月前に繰り返し目をこすっていたことを挙げた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左眼の裂孔原性網膜剥離及び霧視のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左眼の網膜再建術（強膜内陥術）を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，合併症なく経過し，被験者は退院した。

デキサメタゾンリン酸エステルナトリウム，ゲンタマイシン硫酸塩，PROMEVACAINE HYDROCHLORIDE EYE DROPS，OFLOXACIN EYE CREAM，SODIUM HYALURONATE EYE DROPS，ATROPINE SULFATE EYE GEL，COMPOUND TOPICAMIDE EYE DROPS，LEVOFLOXACIN EYE DROPS 及び PREDNISOLONE ACETATE EYE DROPS が投与された。

The patient's past medications include:

HYDROCORTISONE BUTEPRATE EYE DROPS for ATOPIC DERMATITIS (20[redacted] - 20[redacted])

MENTHOLATUM AD for ATOPIC DERMATITIS (20[redacted] - [redacted] [redacted] 20[redacted])

DIPROSPAN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PIMECROLIMUS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HALOMETASONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ATROPINE SULFATE EYE GEL for RHEGMATOGENOUS RETINAL DETACHMENTOF THE RIGHT EYE, COMPLICATED CATARACT IN THE LEFT EYE and RETINAL DETACHMENT OF THE LEFT EYE ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

COMPOUND TOPICAMIDE EYE DROPS for RHEGMATOGENOUS RETINAL DETACHMENTOF THE RIGHT EYE, COMPLICATED CATARACT IN THE LEFT EYE and RETINAL DETACHMENT OF THE LEFT EYE ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PREDNISONE ACETATE EYE DROPS for RHEGMATOGENOUS RETINAL DETACHMENTOF THE RIGHT EYE, COMPLICATED CATARACT IN THE LEFT EYE and RETINAL DETACHMENT OF THE LEFT EYE ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

SODIUM BROMOFENAC EYE DROPS for RHEGMATOGENOUS RETINAL DETACHMENTOF THE RIGHT EYE, COMPLICATED CATARACT IN THE LEFT EYE and RETINAL DETACHMENT OF THE LEFT EYE ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

TOBRAMYCIN/DEXAMETHASONE EYE CREAM for RHEGMATOGENOUS RETINAL DETACHMENTOF THE RIGHT EYE, COMPLICATED CATARACT IN THE LEFT EYE and RETINAL DETACHMENT OF THE LEFT EYE ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Rhegmatogenous retinal detachment (10065569) (Rhegmatogenous retinal detachment (10065569)) [v.23.0] [10065569]

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

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

Dechallenge: Not Applicable

Causality for MOMETASONE FUROATE (Open Label)

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1) Rhegmatogenous retinal detachment (10065569) (Rhegmatogenous retinal detachment (10065569)) [v.23.0] [10065569]

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

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

Dechallenge: Not Applicable

Causality for DESONIDE (Open Label)

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1) Rhegmatogenous retinal detachment (10065569) (Rhegmatogenous retinal detachment (10065569)) [v.23.0] [10065569]

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

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

Dechallenge: Not Applicable

Causality for TACROLIMUS (Open Label)

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1) Rhegmatogenous retinal detachment (10065569) (Rhegmatogenous retinal detachment (10065569)) [v.23.0] [10065569]

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 RHEGMATOGENOUS RETINAL DETACHMENT OF LEFT EYE

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing myopia of eyes, recent retinal detachment of both eyes in the last 6 months and repeated rubbing of eye three months prior as reported by PI.

Alternative Etiology for MOMETASONE FUROATE (Open Label)

Event of RHEGMATOGENOUS RETINAL DETACHMENT OF LEFT EYE

- Investigator: More likely related to Upadacitinib/placebo

- AbbVie: Risk factors include pre-existing myopia of eyes, recent retinal detachment of both eyes in the last 6 months and repeated rubbing of eye three months prior as reported by PI.

Alternative Etiology for DESONIDE (Open Label)

Event of RHEGMATOGENOUS RETINAL DETACHMENT OF LEFT EYE

- Investigator: More likely related to Upadacitinib/placebo

- AbbVie: Risk factors include pre-existing myopia of eyes, recent retinal detachment of both eyes in the last 6 months and repeated rubbing of eye three months prior as reported by PI.

Alternative Etiology for TACROLIMUS (Open Label)

Event of RHEGMATOGENOUS RETINAL DETACHMENT OF LEFT EYE

- Investigator: More likely related to Upadacitinib/placebo

- AbbVie: Risk factors include pre-existing myopia of eyes, recent retinal detachment of both eyes in the last 6 months and repeated rubbing of eye three months prior as reported by PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] LEFT EYE B ULTRASOUND:** VITREOUS OPACITY IN LEFT EYE, DETACHED RETINA.

[redacted] **20[redacted] LEFT EYE OPHTHALMOLOGICAL EXAMINATION:** LEFT EYE RETINAL DETACHMENT, NO MACULAR INVOLVEMENT.

[redacted] **20[redacted] ULTRASOUND EYE:** Vitreous opacity in both eyes, retinal detachment.

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
皮膚播種性帯状疱疹	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 MG QD/UPA 15 MG QD	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ASTHMA	19[redacted]
ATOPIC DERMATITIS	19[redacted]
FOOD ALLERGY(EGG WHITE, SALMON)	19[redacted]
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 112	112
UPA	15 MG	ORAL	QD	[redacted]20[redacted] / 113		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
OLOPATADINE	5 mg	BID	Y-M: 20[redacted]
DIFLUPREDNATE	OPTOMUM DPSE OTHER: NA	BID	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]

HYDROPHILIC	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BECLOMETASONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
ZINC	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
BECLOMETASONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
DIFLUPREDNATE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
CELESTAMINE	1 OTHER: T	TID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
FLUOCINONIDE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
DIFLUPREDNATE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	PRN	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
FLUOCINONIDE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BIOTIN	1.5 g	TID	Y-M: 20[redacted]
CLOSTRIDIUM BUTYRICUM	1 g	TID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
DIFLUPREDNATE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
DIFLUPREDNATE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
PRANLUKAST	112.5 mg	BID	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BUTENAFINE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]

CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	PRN	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
LANOCONAZOLE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
DIFLUPREDNATE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
OLOPATADINE	1 OTHER: TAB	BID	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	PRN	Y-M: 20[redacted]
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
TACROLIMUS	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
HYDROCORTISONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
HEPARINOID	OPTIMUM DOSE OTHER: NA	PRN	Y-M: 20[redacted]
DIFLUPREDNATE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted]
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -342
DEPRODONE	1 OTHER: PATCH	QD	Y-M: 20[redacted] / -342
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -244
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -244
HEPARINOID	OPTIMUM DOSE OTHER: NA	PRN	Y-M: 20[redacted] / -202
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -153
SALICYLIC ACID	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -153
BETAMETHASONE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -125
KETOCONAZOLE	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -125
CLOBETASOL	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -49
CLOBETASOL	OPTIMUM DOSE OTHER: NA	TID	Y-M: 20[redacted] / -49
WHITE SOFT PARAFFIN	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -7

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
BIOTIN	1.5 g	TID	Y-M: 20[redacted]	NOT REPORTED
CLOSTRIDIUM BUTYRICUM	1 g	TID	Y-M: 20[redacted]	NOT REPORTED
PRANLUKAST	112.5 mg	BID	Y-M: 20[redacted]	NOT REPORTED
OLOPATADINE	1 OTHER: TAB	BID	Y-M: 20[redacted]	NOT REPORTED
WHITE SOFT PARAFFIN	OPTIMUM DOSE OTHER: NA	BID	Y-M: 20[redacted] / -7	NOT REPORTED
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 245
PARACETAMOL	200 mg	TID	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 259
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 259

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

Event Description	CUTANEOUS GENERALIZED HERPES ZOSTER
Preferred term	皮膚播種性帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 234
Age at AE Onset	2[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 238): Lymphocytes: 0.8 [0.96 - 3.1] 10^9/L; [redacted]20[redacted] (RX DAY 239): Lymphocytes: 1.37 [0.96 - 3.1] 10^9/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	251
Duration of AE	18 DAYS
Toxicity Grade	3
Relation to Study Drug by Investigator	MULTIPLE
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M16-047

本被験者は日本の 2[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，フルオシノロンアセトニド及びプレドニゾロンを投与され，皮膚播種性帯状疱疹を発現し

た。被験者は非喫煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎であった。

被験者は本試験開始時の 16 週間の二重盲検投与期に参加していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は盲検継続投与期に移行し，盲検下でウパダシチニブ投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は皮膚播種性帯状疱疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，皮膚播種性帯状疱疹は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。受診時，被験者の体温は約 38°C であった。被験者は，右胸部から背部にかけて暗赤色の紅斑を伴う小水疱を，体幹及び体肢に小水疱及び丘疹を発現していた。罹患範囲による分類は，右胸部から背部にかけての皮膚病変は単一分節であり，体幹上部及び下腿の皮膚病変は播種性であった。被験者の病歴及び身体的診察の所見から皮膚播種性帯状疱疹と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，薬剤投与を中断したため，アトピー性皮膚炎が増悪した。20[redacted] 年 [redacted] 月 [redacted] 日，播種性帯状疱疹の潰瘍病変は乾燥及び上皮形成した。被験者は回復したと判断され，治験薬投与が再開された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

アシクロビル及び FLUCORT が投与された。

The patient's past medications include:

ALLELOCK for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HIRUDOID for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MYSER for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PROTOPIC for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

NIZORAL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LOCOID for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HYDROPHILIC OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PROPADERM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ZINC OXIDE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CELESTAMINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ANTEBATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TOPSYM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VOLLEY for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DERMOVATE for ATOPIC DERMATITIS ([redacted])

ASTAT for ATOPIC DERMATITIS ([redacted])

DELSPART for ATOPIC DERMATITIS ([redacted])

ECLAR PLASTER for ATOPIC DERMATITIS ([redacted])

SALICYLIC ACID for ATOPIC DERMATITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster cutaneous disseminated (10074297) (Herpes zoster cutaneous disseminated (10074297)) [v.22.1] [10074297]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Causality for FLUOCINOLONE ACETONIDE (Open Label)

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1) Herpes zoster cutaneous disseminated (10074297) (Herpes zoster cutaneous disseminated (10074297)) [v.22.1] [10074297]

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

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

Dechallenge: Not Applicable

Causality for PREDNISOLONE (Open Label)

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1) Herpes zoster cutaneous disseminated (10074297) (Herpes zoster cutaneous disseminated (10074297)) [v.22.1] [10074297]

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 CUTANEOUS GENERALIZED HERPES ZOSTER

- Investigator: Not applicable

- AbbVie: Not applicable

Alternative Etiology for FLUOCINOLONE ACETONIDE (Open Label)

Event of CUTANEOUS GENERALIZED HERPES ZOSTER

- Investigator: More likely related to Upadacitinib/placebo

- AbbVie: Weak temporal association. Last dose of study drug was approximately 7 months prior to event onset.

Alternative Etiology for PREDNISOLONE (Open Label)

Event of CUTANEOUS GENERALIZED HERPES ZOSTER

- Investigator: More likely related to Upadacitinib/placebo

- AbbVie: Weak temporal association. Last dose of study drug was nearly 7 months prior to event onset.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **LYMPHOCYTES ABS:** 0.80 10^3/uL (normal 0.96 to 3.10)

[redacted] **LYMPHOCYTES ABS:** 1.37 10^3/uL (normal 0.96 to 3.10)

M16-047 試験（投与 52 週時）

治験の標題： 中等症から重症の青少年及び成人アトピー性皮膚炎患者を対象としたステロイド外用薬併用下のウパダシチニブの第 III 相，ランダム化，プラセボ対照，二重盲検試験	
治験実施施設： 22 ヵ国（オーストラリア，オーストリア，ベルギー，カナダ，中国［香港］，チェコ共和国，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，オランダ，ニュージーランド，ノルウェー，スロバキア，スペイン，スウェーデン，英国及び米国［プエルトリコ］）の 170 施設	
治験調整医師： [redacted] MD, PhD	
公表文献（参考資料）： なし	
試験期間（年数）： 最初の被験者の初回来院日：2018 年 8 月 9 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日（投与 52 週時）	開発のフェーズ：III
目的： 全身療法の対象である中等症から重症の青少年及び成人アトピー性皮膚炎患者の治療における副腎皮質ステロイド外用薬併用下のウパダシチニブの有効性及び安全性を評価する。 16 週間の二重盲検投与期では，副腎皮質ステロイド外用薬併用下で，ウパダシチニブ 30 mg 及び 15 mg を 1 日 1 回（以下「QD」）投与時の安全性及び有効性をプラセボ投与時と比較する。盲検継続投与期では，二重盲検投与期を完了した中等症から重症の青少年及び成人アトピー性皮膚炎患者を対象として，副腎皮質ステロイド外用薬併用下でウパダシチニブ 30 mg 及び 15 mg QD 投与時の長期的な安全性，忍容性及び有効性を評価する。	
被験者数（計画時と解析時）： 計画時：810 名，解析時：880 名	
診断と主要な組入れ基準： 選択基準は以下のとおりであった。 1）スクリーニング来院時に 12 歳以上 75 歳以下の男性及び女性，2）12 歳以上 18 歳未満の場合，ベースライン来院時の体重が 40 kg 以上である，3）スクリーニング来院時の病歴聴取，臨床検査，身体検査，胸部 X 線検査及び 12 誘導心電図の結果に基づき，治験責任（担当）医師により全般的な健康状態が良好である（アトピー性皮膚炎を除く）と評価された，4）Hanifin & Rajka の診断基準に基づく慢性アトピー性皮膚炎であり，ベースラインの少なくとも 3 年前に発症している，5）以下の疾患活動性基準をすべて満たす：スクリーニング及びベースライン来院時に湿疹面積重症度指数（以下「EASI」）スコア 16 以上，スクリーニング及びベースライン来院時にバリデートされた治験責任医師による包括的評価-アトピー性皮膚炎（以下「vIGA-AD」）スコア 3 以上，スクリーニング及びベースライン来院時にアトピー性皮膚炎病変の体表面積 10%以上，及び毎日の最悪のかゆみの数値評価尺度（以下「NRS」）のベースライン来院時の週平均値 4 以上，6）副腎皮質ステロイド外用薬若しくはカルシニューリン阻害外用薬が効果不十分であったことを示す記録がある（ベースライン来院前 6 ヵ月以内），又はアトピー性皮膚炎に対するベースライン来院前 6 ヵ月以内の全身療法の記録がある，7）ベースライン来院前の少なくとも連続する 7 日間，外用エモリエント（保湿剤）を 1 日 2 回使用している。	
治験方法： 本試験は，主試験（青少年及び成人を対象）及び青少年サブスタディ（青少年を対象）で構成された。主試験及び青少年サブスタディのいずれも，35 日間のスクリーニング期間，16 週間の二重盲検投与期（主要解析は投与 16 週完了時に実施）及び最長で投与 260 週時までの盲検継続投与期から構成され，治験薬の最終投与から約 30 日後に追跡調査来院を行う。主試験の適格性基準を満たした被験者を，3 つの治験薬投与群（ウパダシチニブ	

15 mg 群，ウパダシチニブ 30 mg 群又はプラセボ群）のいずれかに 1:1:1 の割合でランダム化し，副腎皮質ステロイド外用薬併用下で経口投与（QD）した。主試験への目標例数（810 名）の登録が完了後，引き続き追加試験（青少年サブスタディ）への青少年被験者の登録を行い，青少年被験者の登録数が試験全体（主試験 + 青少年サブスタディ）で計 180 名になるまで継続することとした。主要解析（投与 16 週完了時に実施）及びデータカットオフ日までに得られた結果を含む，主試験の中間解析結果を 16 週時総括報告書に示した。主試験の投与 52 週時の解析は，すべての試験実施中の被験者が投与 52 週時来院を完了後に実施した。 主試験では，ベースライン疾患重症度，年齢及び地理的地域による層別ランダム化を行った。二重盲検投与期終了時に，プラセボ群の被験者を 1:1 の割合で盲検継続投与期におけるウパダシチニブ 30 mg 又は 15 mg の経口投与（QD）に再度割り付け（EASI 50 レスポンダー，地理的地域及び年齢による層別ランダム化を行った），260 週時来院まで継続することとした。初めにウパダシチニブ群にランダム化された被験者には，盲検継続投与期も継続して同じ用量のウパダシチニブを投与することとした。投与 4 週時～投与 24 週時の間の直近 2 回の規定来院時に EASI スコアのベースラインからの 50%以上の低下（以下「EASI 50」）を達成していない被験者に対し，医学的に必要な場合，レスキュー治療を行うことができることとした。投与 24 週後は，規定来院又は規定外来院時に EASI 50 を達成していない被験者に対し，医学的に必要な場合，レスキュー治療を行うことができることとした。
被験薬，用量 / 含量 / 濃度，投与法，ロット番号： ウパダシチニブ 15 mg 錠（経口），バルクロット番号：[redacted] ウパダシチニブ 30 mg 徐放錠（経口），バルクロット番号：[redacted] 治療期間：二重盲検投与期：16 週間，盲検継続投与期：最長で投与 260 週時まで
対照薬，用量 / 含量 / 濃度，投与法，ロット番号： ウパダシチニブに対応するプラセボ（経口），バルクロット番号：[redacted]

評価基準：

有効性：

共主要評価項目は，投与 16 週時に EASI スコアのベースラインからの 75%以上の低下（以下「EASI 75」）を達成した被験者の割合，及び投与 16 週時の vIGA-AD スコアが 0（消失）又は 1（ほぼ消失）であり，かつベースラインと比較して 2 グレード以上改善（低下）した被験者の割合であった。

欧州当局 / 欧州医薬品庁（以下「EMA」）及び米国当局 / 米国食品医薬品局（以下「FDA」）の両方の規制に対応する重要な副次評価項目では，他に明記されていない限り，多重性の調整の下，各用量のウパダシチニブのプラセボに対する優越性を証明することとした。

重要な副次評価項目（FDA）	重要な副次評価項目（EMA）
投与 16 週時に最悪のかゆみの NRS がベースラインから 4 以上改善（低下）した被験者の割合	投与 16 週時に最悪のかゆみの NRS がベースラインから 4 以上改善（低下）した被験者の割合
投与 16 週時に EASI スコアのベースラインからの 90%以上の低下（以下「EASI 90」）を達成した被験者の割合	投与 16 週時に EASI 90 を達成した被験者の割合
投与 4 週時に最悪のかゆみの NRS がベースラインから 4 以上改善（低下）した被験者の割合	投与 16 週時の最悪のかゆみの NRS のベースラインからの変化率
投与 4 週時に EASI 75 を達成した被験者の割合	投与 16 週時の EASI スコアのベースラインからの変化率
投与 2 週時に EASI 75 を達成した被験者の割合	投与 4 週時に最悪のかゆみの NRS がベースラインから 4 以上改善（低下）した被験者の割合
投与 4 週時に EASI 90 を達成した被験者の割合	投与 4 週時に EASI 75 を達成した被験者の割合
投与 16 週時に EASI スコアのベースラインからの 100%以上の低下（以下「EASI 100」）を達成した被験者の割合（30 mg 群のみ）	投与 2 週時に EASI 75 を達成した被験者の割合
投与 1 週時に最悪のかゆみの NRS がベースラインから 4 以上改善（低下）した被験者の割合	投与 4 週時に EASI 90 を達成した被験者の割合
	投与 16 週時に EASI 100 を達成した被験者の割合（30 mg 群のみ）
	投与 1 週時に最悪のかゆみの NRS がベースラインから 4 以上改善（低下）した被験者の割合

その他の評価項目には，投与 16 週時及び他の規定来院時に得られた EASI 75 を達成した被験者の副腎皮質ステロイド外用薬を中断した日数，EASI 75 を達成した被験者が初めてすべての副腎皮質ステロイド外用薬を中断するまでの期間，並びに健康関連の生活の質（以下「QOL」）などが含まれた。

安全性：

試験期間を通して，有害事象，バイタルサインの変動，臨床検査（血液学的検査，血液生化学検査，尿検査）及び製品苦情のデータを評価した。

統計手法：

有効性：

主試験の ITT 集団（以下「ITT_M 集団」）は，主試験のすべてのランダム化された被験者から構成され，すべての有効性解析に用いた。ITT_M 集団の被験者の解析は，実際に受けた投与に関わらず，主試験でランダム化

された投与群に基づいて実施した。二重盲検投与期にプラセボ群にランダム化され，盲検継続投与期に移行しなかった被験者は，盲検継続投与期の解析に含めなかった。盲検継続投与期（投与 52 週時まで）の主要評価項目及び副次評価項目について，カテゴリー変数は記述的に要約し，連続変数は混合効果・反復測定モデル（以下「MMRM」）を用いて解析した。EASI 75 を達成した被験者の割合，vIGA-AD スコアが 0 又は 1 であり，かつベースラインと比較して 2 グレード以上改善した被験者の割合，及び最悪のかゆみの NRS がベースラインから 4 以上改善した被験者の割合は，新型コロナウイルス感染症（以下「COVID-19」）による来院中止・延期を考慮したノンレスポンダーインピュテーション（以下「NRI-C」）法又は多重補完（以下「MI」）法を用いて解析した。長期有効性は，NRI-C 法，MI 法，MMRM 法又は OC 法を用いて要約した。

安全性：

主試験の盲検継続投与期の安全性解析対象集団は，主試験の盲検継続投与期に治験薬投与を 1 回以上受けたすべてのランダム化された被験者から構成された（主試験の盲検継続投与期の安全性解析対象集団は，臨床検査の解析にのみ用いた）。盲検継続投与期の安全性解析対象集団は，主試験又は青少年サブスタディの盲検継続投与期に治験薬投与を 1 回以上受けたすべてのランダム化された被験者から構成された。主試験の全ウパダシチニブ投与集団は，主試験でウパダシチニブ投与を 1 回以上受けたすべての被験者から構成された。

安全性は，有害事象，身体検査，臨床検査及びバイタルサインにより評価した。有害事象が発現した被験者の数及び割合並びに曝露期間で調整した有害事象の発現率を，ICH 国際医薬用語集（以下「MedDRA」）の器官別大分類及び基本語を用いて投与群ごとに示した。また，重篤な有害事象の要約，並びに重症度別及び治験責任（担当）医師が評価した治験薬との因果関係別の有害事象の要約も示した。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を一覧表に示した。各来院時のバイタルサイン，身体検査及び臨床検査の変化を要約した。規定の時点での臨床検査値のベースラインからの変動を表に示した。

要約 / 結論：

有効性の結果：

副腎皮質ステロイド外用薬併用下でのウパダシチニブ 15 mg 及び 30 mg QD の有効性は，中等症から重症の青少年（12 歳以上 17 歳以下）及び成人（18 歳以上 75 歳以下）アトピー性皮膚炎患者に対し，盲検継続投与期の投与 52 週時まで，ウパダシチニブ継続投与群では，おおむね維持され，プラセボ投与からウパダシチニブ投与に切り替えた被験者群では，改善が続いた。また，投与 16 週時に EASI 75 を達成し，vIGA-AD スコアが 0 又は 1 であり，かつベースラインと比較して 2 グレード以上改善した被験者のうち，投与 52 週時までに，治験実施計画書で事前に規定した治療効果の喪失が認められた被験者は，ごくわずかであった（ウパダシチニブ 15 mg 群 8 名，ウパダシチニブ 30 mg 群 5 名）。治療効果は，ウパダシチニブ 15 mg 群と比較してウパダシチニブ 30 mg 群で数値的に高く維持された。

プラセボ投与からウパダシチニブ投与に切り替えた被験者のうち，EASI 75 を達成した被験者の割合，及び vIGA-AD スコアが 0 又は 1 であり，かつベースラインと比較して 2 グレード以上改善した被験者の割合は，ウパダシチニブ継続投与群での結果と類似しており，投与 52 週時まで両被験者群間で類似した結果が維持された。

皮膚症状の改善及び疾患活動性，かゆみの軽減，皮膚の痛み及び全般的症状，睡眠，アトピー性皮膚炎の影響，健康関連の QOL，並びにアトピー性皮膚炎の患者評価のいずれの評価項目の結果も，副腎皮質ステロイド外用薬併用下でウパダシチニブの投与を受けた成人被験者及び青少年被験者の両集団で，投与 52 週時まで長期的に改善効果が維持されたことを示している。

安全性の結果：

副腎皮質ステロイド外用薬併用下でのウパダシチニブの長期投与は，中等症から重症のアトピー性皮膚炎患者に対し，データカットオフ日まで，おおむね安全で忍容性も良好であった。ウパダシチニブの他の適応症（関節リウマチ及び乾癬性関節炎）の試験と比較して，新たな重大な安全性の懸念は認められなかった。しかし，本試験でウパダシチニブの投与を受けた被験者のざ瘡の発現率は，関節リウマチを適応症とした試験と比較して著しく高かった。

データカットオフ日までに，重篤な感染症の発現率はウパダシチニブ 30 mg 群及びウパダシチニブ 15 mg 群で類

似していた。報告された日和見感染は，ヘルペス性状湿疹（カポジ水痘様発疹と同義）であった。ヘルペス性状湿疹は，アトピー性皮膚炎患者集団でよく認められるウイルス性の合併症である。帯状疱疹はヤヌスキナーゼ（以下「JAK」）阻害薬では予期される有害事象であり，その発現リスクの増加がウパダシチニブの投与を受けた被験者で認められ，ウパダシチニブ 15 mg 群と比較してウパダシチニブ 30 mg 群で高かった。大部分の帯状疱疹が単一の皮節のみに認められた。

悪性腫瘍は，ウパダシチニブの投与を受けた被験者でほとんど報告されなかった（0.5 件 / 100 人年以下）。判定された主要心血管事象（非致死性脳卒中）が，ウパダシチニブ 15 mg 群及びウパダシチニブ 30 mg 群で各 1 件報告され，いずれの被験者も心血管疾患に関連する既往歴を有していた。判定された静脈血栓塞栓症（肺塞栓症）が，ウパダシチニブ 15 mg 群の高コレステロール血症の既往歴を有する被験者で 1 件報告され，腎機能障害（急性腎障害）がウパダシチニブ 15 mg 群の被験者で 1 件報告された。本試験では，死亡例は認められなかった。クレアチンホスホキナーゼ増加，貧血及び好中球減少症の発現率は，ウパダシチニブ 15 mg 群と比較してウパダシチニブ 30 mg 群で高かった。肝障害（大部分が無症候性の肝酵素増加）の発現率は，ウパダシチニブ 30 mg 群と比較してウパダシチニブ 15 mg 群で高かった。JAK 阻害薬では，これらの臨床検査異常に対するウパダシチニブの用量依存性は予期されている。

成人被験者及び青少年被験者の両集団でわずかな体重増加が認められた。体重増加は成長期の青少年では予期されている。

データカットオフ日までに，判定された消化管穿孔，活動性結核及びリンパ腫は報告されなかった。青少年被験者数は成人被験者数よりも少なかったが，青少年被験者集団の安全性の結果は，好中球減少症及びざ瘡の発現率にわずかな上昇が認められたことを除き，全体集団の結果と一貫していた。

結論：

副腎皮質ステロイド外用薬併用下での，ウパダシチニブ 30 mg 及び 15 mg 投与の長期的な有効性及び安全性の評価の結果，中等症から重症のアトピー性皮膚炎患者に対して，投与 52 週時まで持続的な有効性が示された。全体として，ウパダシチニブ 30 mg 及び 15 mg の安全性プロファイルは，長期曝露によっても変化しなかった。青少年被験者集団は，様々な皮膚症状の改善及びかゆみなどの反応の基準値に関する評価項目で，全体集団と一貫した有効性を継続的に示した。本試験の結果は，中等症から重症の青少年及び成人アトピー性皮膚炎患者に対し，ウパダシチニブは有効で忍容性が良好な治療の選択肢であることを支持している。

表 1. ウパダシチニブ投与期間中に有害事象を発現した被験者数及び発現割合：MedDRA 器官別大分類及び基本語別（全ウパダシチニブ投与集団）

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=443) n (%)	UPA 30 mg QD + TCS (N=436) n (%)	Total (N=879) n (%)
Any adverse event	356 (80.4)	375 (86.0)	731 (83.2)
*** Not coded ***	1 (0.2)	0	1 (0.1)
*** Not coded ***	1 (0.2)	0	1 (0.1)
血液およびリンパ系障害	15 (3.4)	25 (5.7)	40 (4.6)
貧血	3 (0.7)	5 (1.1)	8 (0.9)
大球性貧血	0	1 (0.2)	1 (0.1)
皮膚病性リンパ節症	1 (0.2)	0	1 (0.1)
好酸球増加症	1 (0.2)	1 (0.2)	2 (0.2)
赤血球減少症	0	1 (0.2)	1 (0.1)
内出血発生の増加傾向	0	2 (0.5)	2 (0.2)
鉄欠乏性貧血	0	1 (0.2)	1 (0.1)
白血球増加症	2 (0.5)	0	2 (0.2)
白血球減少症	0	4 (0.9)	4 (0.5)
リンパ節石灰化	1 (0.2)	0	1 (0.1)
リンパ節症	4 (0.9)	3 (0.7)	7 (0.8)
リンパ球増加症	0	1 (0.2)	1 (0.1)
リンパ組織過形成	0	1 (0.2)	1 (0.1)

Note: Treatment-emergent adverse events are defined as any adverse events with an onset or worsening date on or after the first dose of upadacitinib and no more than 30 days after the last dose of upadacitinib in the study.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=443) n (%)	UPA 30 mg QD + TCS (N=436) n (%)	Total (N=879) n (%)
血液およびリンパ系障害 (Cont.)			
リンパ球減少症	1 (0.2)	1 (0.2)	2 (0.2)
大赤血球症	1 (0.2)	0	1 (0.1)
単球減少症	0	1 (0.2)	1 (0.1)
好中球減少症	1 (0.2)	6 (1.4)	7 (0.8)
汎血球減少症	0	1 (0.2)	1 (0.1)
血小板減少症	0	1 (0.2)	1 (0.1)
血小板増加症	0	1 (0.2)	1 (0.1)
心臓障害	6 (1.4)	8 (1.8)	14 (1.6)
急性冠動脈症候群	0	1 (0.2)	1 (0.1)
心房細動	0	1 (0.2)	1 (0.1)
第一度房室ブロック	1 (0.2)	0	1 (0.1)
徐脈	0	1 (0.2)	1 (0.1)
うっ血性心不全	0	1 (0.2)	1 (0.1)
左室肥大	1 (0.2)	0	1 (0.1)
僧帽弁閉鎖不全症	0	1 (0.2)	1 (0.1)
動悸	1 (0.2)	3 (0.7)	4 (0.5)
洞性徐脈	2 (0.5)	1 (0.2)	3 (0.3)

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Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

MedDRA 22.1 System Organ Class Preferred Term	UPA 15 mg QD + TCS (N=443) n (%)	UPA 30 mg QD + TCS (N=436) n (%)	Total (N=879) n (%)
心臓障害 (Cont.)			
頻脈	2 (0.5)	0	2 (0.2)
心室性頻脈	0	1 (0.2)	1 (0.1)
先天性、家族性および遺伝性障害	3 (0.7)	2 (0.5)	5 (0.6)
先天性メラノサイト性母斑	0	1 (0.2)	1 (0.1)
表皮母斑	1 (0.2)	0	1 (0.1)
ジルベール症候群	0	1 (0.2)	1 (0.1)
色素性網膜炎	1 (0.2)	0	1 (0.1)
2a 型高脂血症	1 (0.2)	0	1 (0.1)
耳および迷路障害	7 (1.6)	7 (1.6)	14 (1.6)
難聴	0	1 (0.2)	1 (0.1)
耳の障害	1 (0.2)	0	1 (0.1)
耳痛	3 (0.7)	2 (0.5)	5 (0.6)
耳垢分泌過多	1 (0.2)	0	1 (0.1)
聴力低下	0	1 (0.2)	1 (0.1)
耳鳴	0	2 (0.5)	2 (0.2)
回転性めまい	2 (0.5)	2 (0.5)	4 (0.5)
頭位性回転性めまい	1 (0.2)	0	1 (0.1)

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Subjects are counted once in each row, regardless of the number of events they may have had.

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