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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
一過性脳虚血発作	X			X

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	MALE	WHITE

Medical History	Onset Year
VALVULAR HEART DISEASE: LIGHT AORTIC STEATOSIS	19[redacted]
DEGENERATIVE DISC DISEASE: HERNIATED DISC L5-S1	19[redacted]
OSTEOARTHRITIS: LUMBAR	20[redacted]
CARDIAC ARRHYTHMIA: ATRIAL FIBRILLATION	20[redacted]
HYPERTENSION	20[redacted]
OTHER: PLAQUE PSORIASIS (ELBOWS)	20[redacted]
PERIPHERAL NERVE DISORDER: LEFT CARPAL TUNNEL	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
TUBERCULOSIS: LATENT TB	20[redacted]

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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BISOPROLOL	10.00 mg	QD	Y-M: 20
HYDROCHLOROTHIAZIDE	25.0 mg	QD	Y-M: 20
RIVAROXABAN	20.0 mg	QD	Y-M: 20
METHOTREXATE	10.00 mg	EVERY WEEK	Y-M: 20
PREDNISONE	10.0 mg	QD	Y-M: 20
FOLIC ACID	5.0 mg	EVERY WEEK	Y-M: 20
PREDNISONE	7.50 mg	QD	Y-M: 20
PREDNISONE	5.0 mg	QD	Y-M: 20
PREDNISONE	10.0 mg	QD	Y-M: 20 / -357
METHOTREXATE	20.0 mg	EVERY WEEK	Y-M: 20 / -355
PREDNISONE	7.50 mg	QD	Y-M: 20 / -336
PREDNISONE	5.0 mg	QD	Y-M: 20 / -315
PREDNISONE	2.5 mg	QD	Y-M: 20 / -294
PARACETAMOL	1000.00 mg	PRN	Y-M: 20 / -250
PREDNISONE	25.0 mg	QD	Y-M: 20 / -181
METHOTREXATE	25.0 mg	EVERY WEEK	Y-M: 20 / -160
PREDNISONE	2.50 mg	QD	Y-M: 20 / -160
TRIAMCINOLONE	40.0 mg	OTHER: ONCE	Y-M: 20 / -55
ISONIAZID	300.00 mg	QD	Y-M: 20 / -21
PYRIDOXINE	25.00 mg	QD	Y-M: 20 / -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
BISOPROLOL	10.00 mg	QD	Y-M: 20	NOT REPORTED
HYDROCHLOROTHIAZIDE	25.0 mg	QD	Y-M: 20	NOT REPORTED
RIVAROXABAN	20.0 mg	QD	Y-M: 20	NOT REPORTED
PARACETAMOL	1000.00 mg	PRN	Y-M: 20 / -250	NOT REPORTED
PREDNISONE	2.50 mg	QD	Y-M: 20 / -160	Y-M: 20 / 262
ISONIAZID	300.00 mg	QD	Y-M: 20 / -21	Y-M: 20 / 253
PYRIDOXINE	25.00 mg	QD	Y-M: 20 / -21	Y-M: 20 / 253
FOLIC ACID	5.00 mg	EVERY WEEK	Y-M: 20 / 71	NOT REPORTED
METHOTREXATE	25.00 mg	EVERY WEEK	Y-M: 20 / 71	NOT REPORTED
CLOTRIMAZOLE	1 OTHER: APPLICATION	QD	Y-M: 20 / 71	Y-M: 20 / 153
ALLOPURINOL	200.00 mg	QD	Y-M: 20 / 71	Y-M: 20 / 167
COLCHICINE	0.6 mg	QD	Y-M: 20 / 74	Y-M: 20 / 253
DEXLANSOPRAZOLE	60.00 mg	QD	Y-M: 20 / 121	Y-M: 20 / 123
MACROGOL	17 g	QD	Y-M: 20 / 121	Y-M: 20 / 123
ATORVASTATIN	20.00 mg	QD	Y-M: 20 / 122	ONGOING
ACETYLSALICYLIC ACID	80.00 mg	QD	Y-M: 20 / 122	Y-M: 20 / 302

Event #1: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description	TRANSIENT ISCHEMIC ATTACK
Preferred term	一過性脳虚血発作
AE Onset Date / Rx Day	[redacted]20[redacted] / 121
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 121): Basophils: 0.02 [0 - 0.15] 10^9/L; Chloride: 102 [98 - 107] MMOL/L; Creatinine: 45 [64 - 104] UMOL/L; Eosinophils: 0.13 [0.02 - 0.44] 10^9/L; Glucose: 6.9 [4.1 - 5.6] MMOL/L; Hematocrit: 0 [0 - 0.01] FRACTION OF 1; Hemoglobin: 139 [135 - 175] G/L; Leukocytes: 6.4 [4.5 - 11] 10^9/L; Lymphocytes: 1.85 [1 - 4.8] 10^9/L; Monocytes: 0.44 [0.1 - 0.85] 10^9/L; NPTST071-APTT: 37.1 [22.6 - 28.6] SEC; NPTST534-PROTHROMBIN: 23.7 [11 - 13] SEC; NPTST644-TROPONIN: 0.01 [0 - 0.03] UG/L; Neutrophils: 3.9 [1.8 - 7] 10^9/L; Platelets: 149 [140 - 440] 10^9/L; Potassium: 3.7 [3.5 - 5.1] MMOL/L; Prothrombin Intl. Normalized Ratio: 2.03 [0.9 - 1.15] RATIO; Sodium: 138 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 122): Cholesterol: 4.63 [4.2 - 5.2] MMOL/L; Glucose: 4.9 [4.1 - 5.6] MMOL/L; Triglycerides: 2.3 [0.5 - 1.7] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 121): HEAD SCAN: NEGATIF FOR STROKE; [redacted]20[redacted] (RX DAY 122): ANGIO SCAN OF THE CAROTID CEREBRAL: LEFT SIDE STENOSIS 50%; HEAD SCAN: NO LESION

AE Stopped Rx Day	123
Duration of AE	3 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PATIENT TREATED FOR ATRIAL FIBRILLATION
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: M15-572

治験責任医師からの報告。本被験者はカナダの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，一過性脳虚血発作の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，軽微な大動脈脂肪症，椎間板変性疾患（椎間板ヘルニア［L5-S1］），心房細動，高血圧，局面型乾癬（両肘），潜伏結核，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された

皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は一過性脳虚血発作を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，一過性脳虚血発作は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右上肢脱力のため入院した。軽度の右脚脱力及び測定障害以外に症状はなかった。身体的診察の結果，上肢の近位筋力は 4/5 であった。頭部 CT 検査の結果は正常で，被験者は 48 時間以内に急速に回復した。各種検査で左頚動脈の 50%狭窄及び既知の心房細動が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，asa 及びアトルバスタチンであった。

The patient's past medications include:

KENALOG for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CELEBREX for GOUT ([redacted] 20[redacted] - [redacted] 20[redacted])

DEXILANT for GASTRIC PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Transient ischemic attack (10072760) (Transient ischaemic attack (10044390)) [v.22.1] [10072760]

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 TRANSIENT ISCHEMIC ATTACK

- Investigator: The patient was treated for atrial fibrillation.

- AbbVie: Risk factors include subject's age, pre-existing atrial fibrillation, hypertension, and obesity (BMI 33).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANGIOSCAN OF THE CEREBRAL CAROTIDS:** 50% stenosis at the origin of the left internal carotid with a small, short stenosis of approximately 50% at the origin of the left vertebral also noted.

[redacted] **20[redacted] APTT:** 37.1 SEC (normal 22.6 to 28.6)

[redacted] **20[redacted] CHLORIDE:** 102 MMOL/L (normal 98 to 107)

[redacted] **20[redacted] CHOLESTEROL:** 4.639 MMOL/L

[redacted] **20[redacted] CRANIAL CT SCAN WITHOUT CONTRAST:**: No signs of ischemia or other acute intracranial anomaly.

[redacted] **20[redacted] CREATININE:** 45 MMOL/L (normal 64 to 104)

[redacted] **20[redacted] EKG:** Screening-Atrial Fibrillation. Abnormal rhythm.

[redacted] **20[redacted] ERYTHROCYTES:** 4.1 X10**12/L (normal 4.5 to 5.9)

[redacted] **20[redacted] EVF:** 15.8 no units (normal 11.5 to 14.5)

[redacted] **20[redacted] GLUCOSE:** 6.9 MMOL/L

[redacted] **20[redacted] GLUCOSE:** 4.9 MMOL/L (normal 4.1 to 5.6)

[redacted] **20[redacted] HDL:** 0.569 MMOL/L

[redacted] **20[redacted] HEAD SCAN:** Negative for stroke

[redacted] **20[redacted] HEMATOCRIT:** 0.379 no units (normal 0.410 to 0.530)

[redacted] **20[redacted] HEMOGLOBIN:** 139 G/L (normal 135 to 175)

[redacted] **20[redacted] INR:** 2.03 no unit (normal 0.90 to 1.15)

[redacted] **20[redacted] LDL:** 9 MMOL/L

[redacted] **20[redacted] LEUCOCYTES:** 6.4 X10**9/L (normal 4.5 to 11.0)

[redacted] **20[redacted] MCH:** 34 PG (normal 27 to 33)

[redacted] **20[redacted] MCHC:** 367 G/L (normal 325 to 370)

[redacted] **20[redacted] MPV:** 9.6 FL (normal 7.0 to 10.4)

[redacted] **20[redacted] PLATELETS:** 149 X10**9/L (normal 140 to 440)

[redacted] 20[redacted] **POTASSIUM:** 3.7 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **PT:** 23.7 SEC (normal 11.0 to 13.0)

[redacted] 20[redacted] **SODIUM:** 138 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] **TRIGLYCERIDES:** 2.309 MMOL/L (normal 0.50 to 1.70)

[redacted] 20[redacted] **TROPONIN:** 0.010 UG/L (normal <0.030)

[redacted] 20[redacted] **TROPONIN I:** 0.010 MCG/L (normal 0.00 to 0.30)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	3[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: CHICKEN POX AFFECTING CUTANEOUS ONLY	19[redacted]
OTHER: PSORIASIS PLAQUE	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 167	167
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 168	[redacted]20[redacted] / 292	125

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DICLOFENAC	50 mg	TID	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
NORGESIC	2 OTHER: TABLET	TID	Y-M: 20[redacted]
CELECOXIB	200 mg	BID	Y-M: 20[redacted]
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted]
MOMETASONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted] / -148
CELECOXIB	200 mg	OTHER: 3 TIMES PER WEEK	Y-M: 20[redacted] / -112

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted] / -148	ONGOING
CELECOXIB	200 mg	OTHER: 3 TIMES PER WEEK	Y-M: 20[redacted] / -112	Y-M: 20[redacted] / 300
NORGESIC	2 OTHER: TABLET	QD	Y-M: 20[redacted] / 290	Y-M: 20[redacted] / 293
ACICLOVIR	800 mg	OTHER: 5 TIMES/DAY	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 294
FAMOTIDINE	200 mg	BID	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 294
IBUPROFEN	400 mg	TID	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 294
PARACETAMOL	1000 mg	TID	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 294
TRAMADOL	500 mg	TID	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 294
ACICLOVIR	900 mg	QD	Y-M: 20[redacted] / 294	Y-M: 20[redacted] / 294
POTASSIUM PERMANGANATE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 294	Y-M: 20[redacted] / 309
TEARS NATURAL FREE	1 OTHER: DROP TO BOTH	QID	Y-M: 20[redacted] / 294	Y-M: 20[redacted] / 309
ACICLOVIR	1000 mg	OTHER: EVERY 8 HOUR	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 300
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 298
ONDANSETRON	4 mg	QD	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 299

SODIUM CHLORIDE	1.5 L	OTHER: INFUSE OVER 24 HOUR	Y-M: 20[redacted]-[redacted] / 300	Y-M: 20[redacted]-[redacted] / 302

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

Event Description	CUTANEOUS DISSEMINATED HERPES ZOSTER
Preferred term	皮膚播種性帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 286
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 294): Alanine Aminotransferase: 40 [6 - 66] U/L; Albumin: 46 [40 - 51] G/L; Alkaline Phosphatase: 81 [39 - 99] U/L; Aspartate Aminotransferase: 35 [12 - 42] U/L; Basophils: 0.03 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.6 [0 - 1] %; Bicarbonate: 26 [19 - 29] MMOL/L; Bilirubin: 6 [7 - 32] UMOL/L; Chloride: 103 [100 - 107] MMOL/L; Creatinine: 91 [54 - 101] UMOL/L; Eosinophils: 0.01 [0.04 - 0.44] 10^9/L; Eosinophils/Leukocytes: 0.2 [0 - 6] %; Erythrocytes: 4.2 [4.5 - 6.3] 10^12/L; Hematocrit: 0.36 [0.38 - 0.52] FRACTION OF 1; Hemoglobin: 127 [140 - 180] G/L; Leukocytes: 5.1 [4 - 10] 10^9/L; Lymphocytes: 1.67 [1 - 3] 10^9/L; Lymphocytes/Leukocytes: 32.9 [15 - 41] %; Monocytes: 0.79 [0.2 - 0.8] 10^9/L; Monocytes/Leukocytes: 15.6 [2 - 10] %; NPTST131-C-REATIVE PROTEIN: 3.8 [0.2 - 9.1] MG/L; NPTST291-GAMMA-GLUTAMYL TRANSFERASE: 36 [14 - 94] U/L; NPTST427-MCH: 30.5 [27 - 32] PG; NPTST428-MCHC: 35.4 [32 - 36] G/DL; NPTST429-MCV: 86.3 [78 - 98] FL; NPTST437-MEAN PLATELET VOLUME: 9.2 [7.2 - 11.1] FL; NPTST560-RBC DISTRIBUTION WIDTH: 13 [10.9 - 15.7] %; NPTST662-UREA: 4.4 [2.7 - 6.9] MMOL/L; Neutrophils: 2.57 [2 - 7.5] 10^9/L; Neutrophils/Leukocytes: 50.7 [40 - 75] %; Platelets: 290 [140 - 440] 10^9/L; Potassium: 4.1 [3.6 - 5] MMOL/L; Protein: 75 [68 - 85] G/L; Sodium: 138 [136 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 295): Bicarbonate: 25 [19 - 29] MMOL/L; Chloride: 105 [100 - 107] MMOL/L; Creatinine: 91 [54 - 101] UMOL/L; NPTST662-UREA: 3.7 [2.7 - 6.9] MMOL/L; Potassium: 4 [3.6 - 5] MMOL/L; Sodium: 140 [136 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 296): Basophils: 0.02 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.4 [0 - 1] %; Bicarbonate: 26 [19 - 29] MMOL/L; Chloride: 105 [100 - 107] MMOL/L; Creatinine: 75 [54 - 101] UMOL/L; Eosinophils: 0.06 [0.04 - 0.44] 10^9/L; Eosinophils/Leukocytes: 1.1 [0 - 6] %; Erythrocytes: 4.1 [4.5 - 6.3] 10^12/L; Hematocrit: 0.36 [0.38 - 0.52] FRACTION OF 1; Hemoglobin: 124 [140 - 180] G/L; Leukocytes: 5.5 [4 - 10] 10^9/L; Lymphocytes: 1.03 [1 - 3] 10^9/L; Lymphocytes/Leukocytes: 18.9 [15 - 41] %; Monocytes: 0.44 [0.2 - 0.8] 10^9/L; Monocytes/Leukocytes: 8.1 [2 - 10] %; NPTST427-MCH: 30.6 [27 - 32] PG; NPTST428-MCHC: 34.3 [32 - 36] G/DL; NPTST429-MCV: 89.1 [78 - 98] FL; NPTST437-MEAN PLATELET VOLUME: 8.9 [7.2 - 11.1] FL; NPTST560-RBC DISTRIBUTION WIDTH: 12.9 [10.9 - 15.7] %; NPTST662-UREA: 2.8 [2.7 - 6.9] MMOL/L; Neutrophils: 3.91 [2 - 7.5] 10^9/L; Neutrophils/Leukocytes: 71.5 [40 - 75] %; Platelets: 297 [140 - 440] 10^9/L; Potassium: 3.9 [3.6 - 5] MMOL/L; Sodium: 140 [136 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 300): Alanine Aminotransferase: 22 [6 - 66] U/L; Albumin: 42 [40 - 51] G/L; Alkaline Phosphatase: 72 [39 - 99] U/L; Aspartate Aminotransferase: 21 [12 - 42] U/L; Basophils: 0.03 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.4 [0 - 1] %; Bicarbonate: 25 [19 - 29] MMOL/L; Bilirubin: 14 [7 - 32] UMOL/L; Chloride: 102 [100 - 107] MMOL/L; Creatinine: 197 [54 - 101] UMOL/L; Eosinophils: 0.01 [0.04 - 0.44] 10^9/L; Eosinophils/Leukocytes: 0.1 [0 - 6] %; Erythrocytes: 0 [0 - 16.85] /HPF; Erythrocytes: 3.7 [4.5 - 6.3] 10^12/L; Hematocrit: 0.33 [0.38 - 0.52] FRACTION OF 1; Hemoglobin: 114 [140 - 180] G/L; Leukocytes: 0 [0 - 33.71] /HPF; Leukocytes: 8.5 [4 - 10] 10^9/L; Lymphocytes: 1.09 [1 - 3] 10^9/L; Lymphocytes/Leukocytes: 12.8 [15 - 41] %; Monocytes: 1.21 [0.2 - 0.8] 10^9/L; Monocytes/Leukocytes: 14.2 [2 - 10] %; NPTST143-CALCIUM TOTAL: 2.3 [2.09 - 2.46] MMOL/L; NPTST249-EPITHELIAL CELL: 3 [0 - 4] /UL; NPTST422-MAGNESIUM: 0.78 [0.74 - 0.97] MMOL/L; NPTST427-MCH: 30.6 [27 - 32] PG; NPTST428-MCHC: 35.1 [32 - 36] G/DL; NPTST429-MCV: 87.1 [78 - 98] FL; NPTST437-MEAN PLATELET VOLUME: 9 [7.2 - 11.1] FL; NPTST560-RBC DISTRIBUTION WIDTH: 12.7 [10.9 - 15.7] %; NPTST662-UREA: 4.8 [2.7 - 6.9] MMOL/L; Neutrophils: 6.16 [2 - 7.5] 10^9/L; Neutrophils/Leukocytes: 72.5 [40 - 75] %; Phosphate: 1.28 [0.94 - 1.5] MMOL/L; Platelets: 309 [140 - 440] 10^9/L; Potassium: 3.8 [3.6 - 5] MMOL/L; Protein: 70 [68 - 85] G/L; Sodium: 138 [136 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 301): Bicarbonate: 24 [19 - 29] MMOL/L; Chloride: 102 [100 - 107] MMOL/L; Creatinine: 192 [54 - 101] UMOL/L; NPTST662-UREA: 4.5 [2.7 - 6.9] MMOL/L; Potassium: 4 [3.6 - 5] MMOL/L; Sodium: 137 [136 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 302): Bicarbonate: 24 [19 - 29] MMOL/L; Chloride: 104 [100 - 107] MMOL/L; Creatinine: 173 [54 - 101] UMOL/L; NPTST662-UREA: 4.4 [2.7 - 6.9] MMOL/L; Potassium: 4.2 [3.6 - 5] MMOL/L; Sodium: 140 [136 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 304): Bicarbonate: 25 [19 - 29] MMOL/L; Chloride: 102 [100 - 107] MMOL/L; Creatinine: 160 [54 - 101] UMOL/L; NPTST662-UREA: 4.1 [2.7 - 6.9] MMOL/L; Potassium: 4.2 [3.6 - 5] MMOL/L; Sodium: 141 [136 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 307): Bicarbonate: 27 [19 - 29] MMOL/L; Chloride: 103 [100 - 107] MMOL/L; Creatinine: 133 [54 - 101] UMOL/L; NPTST662-UREA: 3 [2.7 - 6.9] MMOL/L; Potassium: 4.3 [3.6 - 5] MMOL/L; Sodium: 141 [136 - 146] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 294): OTHER SWAB NPTST456-MRSA PCR SCREENING TEST: Negative
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 300): IV HYDRATION: ACUTE KIDNEY INJURY AS A RESULT OF IV ACYCLOVIR. ACUTE RISE IN CREATININE LEVEL FROM 75 UMOL/L ([redacted] [redacted] 20[redacted]) TO 197 UMOL/L ([redacted] [redacted] 20[redacted]) [NORMAL RANGE: 54-101 UMOL/L]. HENCE, ACYCLOVIR WAS STOPPED ON[redacted] [redacted] 20[redacted], AND HIS CREATININE HAS BEEN IMPROVING WITH IV HYDRATION. (KINDLY REFER TO SUPPLEMENTAL LAB FOR CREATININE LAB RESULTS) PATIENT RETURNED ON [redacted] [redacted] 20[redacted] FOR TRIAL?S PREMATURE DISCONTINUATION (PD) VISIT. HIS CREATININE CONTINUED TO IMPROVE TO 130 UMOL/L [NORMAL RANGE: 40-110 UMOL/L] BUT NOT NORMALIZED YET.

AE Stopped Rx Day	309 (17 DAYS AFTER LAST TREATMENT)
Duration of AE	24 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はシンガポールの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，皮膚の播種性帯状疱疹の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，非喫煙者，現飲酒者（1 日 2 杯未満）及び小児期の水疱瘡の罹患であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は皮膚の播種性帯状疱疹を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，背部痛が出現した。20[redacted] 年 [redacted] 月 [redacted] 日，発熱を伴い，前額部及び右側腹部に発疹が出現した。20[redacted] 年 [redacted] 月 [redacted] 日及び 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は外来クリニックを受診し帯状疱疹と診断された。被験者はアシクロビルを経口投与され，併せて帯状疱疹による疼痛の治療薬を投与された。20[redacted] 年 [redacted] 月 [redacted] 日，熱が引いた。20[redacted] 年 [redacted] 月 [redacted] 日，ヘルペスの臨床的特徴は，右側腹部及び前額部に生じた播種性帯状疱疹によるものであるとわかった。被験者の両眼には，

症状は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はアシクロビル静脈内投与のため入院した。播種性帯状疱疹感染は，右半身 T6/7 皮膚分節及び両側第 5 脳神経に及んでいた。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日までアシクロビルを静脈内投与され，病変は痂皮化した。20[redacted] 年 [redacted] 月 [redacted] 日に発現した急性腎障害（非重篤）のためアシクロビルが中止された。被験者は輸液の静脈内投与を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は安定状態で退院した。被験者の状態は改善し続けた。

本事象により治験薬の投与が完全に中止された。

被験者に帯状疱疹の既往歴や帯状疱疹ワクチンの接種歴はなかったが，水疱瘡の既往歴があった。

投与された薬剤は，anarex，アシクロビル，アセトアミノフェン，イブプロフェン，ファモチジン及びトラマドールであった。

The patient's past medications include:

DICLOFENAC SODIUM EC for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LEFLUNOMIDE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MOMETASONE FUROATE 0.1% CREAM for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BETAMETASONE (DIPROPIONATE) 0.05% CREAM for PSORIASIS ([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.22.1] [10074297]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of CUTANEOUS DISSEMINATED HERPES ZOSTER

- Investigator: Not applicable.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CREATININE:** 91 umol/L (normal 54 to 101)

[redacted] **20[redacted] CREATININE:** 75 umol/L (normal 54 to 101)

[redacted] **20[redacted] CREATININE:** 197 umol/L (normal 54 to 101)

[redacted] **20[redacted] CREATININE:** 192 umol/L (normal 54 to 101)

[redacted] **20[redacted] CREATININE:** 173 umol/L (normal 54 to 101)

[redacted] **20[redacted] CREATININE:** 160 umol/L (normal 54 to 101)

[redacted] **20[redacted] CREATININE:** 130 umol/L (normal 54 to 101)

[redacted] **20[redacted] HGB:** 12.7 G/DL (normal 14.0 to 18.0)

[redacted] **20[redacted] HGB:** 11.4 G/DL (normal 14.0 to 18.0)

[redacted] **20[redacted] MPHOCYTES:** 32.9 % (normal 15 to 41)

[redacted] **20[redacted] LYMPHOCYTES:** 12.8 % (normal 15 to 41)

[redacted] **20[redacted] MRSA SWAB PCR:** Negative

[redacted] **20[redacted] NEUTROPHILS:** 50.7 % (normal 40 to 75)

[redacted] **20[redacted] NEUTROPHILS:** 72.5 % (normal 40 to 75)

[redacted] **20[redacted] UREA:** 4.8 MMOL/L (normal 2.7 to 6.9)

[redacted] **20[redacted] UREA:** 4.4 MMOL/L (normal 2.7 to 6.9)

[redacted] **20[redacted] WBC:** 5.07 X10**9/L (normal 4.0 to 10.0)

[redacted] **20[redacted] WBC:** 8.50 X10**9/L (normal 4.0 to 10.0)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	4[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
DIABETES MELLITUS	20[redacted]
OTHER: FATTY LIVER	20[redacted]
OTHER: HYPERCHOLESTEROLAEMIA	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
HYPERTHYROIDISM	20[redacted]
TUBERCULOSIS: LATENT TUBERCULOSIS	20[redacted]

Prior Procedures	Procedure Year
INCREASED CREATINE PHOSPHOKINASE: BLOOD TEST	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	3 PACK	30	
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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 172	172
ADA	40MG	SC	EOW	[redacted]20[redacted] / 173	[redacted]20[redacted] / 392	220
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETORICOXIB	90 mg	PRN	Y-M: 20[redacted] / -187
FOLIC ACID	5 mg	BID	Y-M: 20[redacted] / -187
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -187
OMEPRAZOLE	20 mg	PRN	Y-M: 20[redacted] / -187
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -187
LEKOVIT CA	2 OTHER: TABLETS	QD	Y-M: 20[redacted] / -167
RIFAMPICIN	600 mg	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
FOLIC ACID	5 mg	BID	Y-M: 20[redacted] / -187	NOT REPORTED
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -187	NOT REPORTED
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -187	NOT REPORTED
LEKOVIT CA	2 OTHER: TABLETS	QD	Y-M: 20[redacted] / -167	NOT REPORTED
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / 22	NOT REPORTED
CARBIMAZOLE	10 mg	QD	Y-M: 20[redacted] / 85	NOT REPORTED
OTHER OPHTHALMOLOGICALS	1 OTHER: WIPE	BID	Y-M: 20[redacted] / 173	NOT REPORTED
TEARS NATURALE	1 OTHER: DROP	OTHER: EVERY 3 HOURS	Y-M: 20[redacted] / 173	NOT REPORTED
PARACETAMOL	UNKNOWN OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / 370	Y-M: 20[redacted] / 370

Event #1: Serious Adverse Event

Event Description FEVER OF UNKNOWN ORIGIN
Preferred term 発熱
AE Onset Date / Rx Day [redacted]20[redacted] / 370
Age at AE Onset 4[redacted]
Laboratory Testing
NOT REPORTED
Microbiology
[redacted]20[redacted] (RX DAY 371): OTHER NASAL SWAB NPTST022-ADENOVIRUS GENE: Negative; OTHER NASAL SWAB NPTST118-BORD PERTUSSIS: Negative; OTHER NASAL SWAB NPTST119-BORDETELLA PARAPERTU: Negative; OTHER NASAL SWAB NPTST132-C. PNEUMONIAE: Negative; OTHER NASAL SWAB NPTST190-CORONAVIRUS 229E: Negative; OTHER NASAL SWAB NPTST191-CORONAVIRUS HKU1: Negative; OTHER NASAL SWAB NPTST192-CORONAVIRUS NL63: Negative; OTHER NASAL SWAB NPTST193-CORONAVIRUS OC43: Negative; OTHER NASAL SWAB NPTST383-INFLUENZA A GENE: Negative; OTHER NASAL SWAB NPTST387-INFLUENZA B GENE: Negative; OTHER NASAL SWAB NPTST443-METAPNEUMOVIRU: Negative; OTHER NASAL SWAB NPTST460-MYCO PNEUMONIAE: Negative; OTHER NASAL SWAB NPTST493-PARAINFLUENZA V 1: Negative; OTHER NASAL SWAB NPTST494-PARAINFLUENZA V 2: Negative; OTHER

NASAL SWAB NPTST495-PARAINFLUENZA V 3: Negative; OTHER NASAL SWAB NPTST496-PARAINFLUENZA V 4: Negative; OTHER NASAL SWAB NPTST573-RESPIRATOY SYNCYTIAL VIRUS: Negative; OTHER NASAL SWAB NPTST579-RHINO/ENTEROVIRUS: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 370): CHEST X RAY, ERECT: NORMAL; [redacted]20[redacted] (RX DAY 371): CT BRAIN: NORMAL

AE Stopped Rx Day	372
Duration of AE	3 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	THIS SAE HAS NO REASONABLE POSSIBILITY OF BEING CAUSED BY STUDY IP--PATIENT WORKS IN A CAFE ENVIRONMENT AND IS AT RISK OF CONTRACTING VIRAL INFECTIONS FROM CUSTOMERS AND STAFF
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: M15-572

治験責任医師からの報告。本被験者はシンガポールの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，原因不明の発熱の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，2 型糖尿病，乾癬性関節炎，現紙巻タバコ喫煙者（1 日 3 箱を 30 年間）及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は原因不明の発熱を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，原因不明の発熱は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 37.7°C まで発熱し入院した。拍動性頭痛並びに両肩と両膝の関節痛が認められた。入院時，治験薬の投与は中止された。その他の薬剤はすべて入院中も継続された。一晩で解熱した。パラセタモールを 1 回内服後，肩と膝の疼痛も消失した。臨床検査及び診断検査が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，頭痛は軽度となった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退

院した。報告によると，被験者はカフェで働いており，客や従業員からの伝播によるウイルス感染のリスクがあった。

投与された薬剤は，アセトアミノフェンであった。

The patient's past medications include:

ETORICOXIB for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Fever of unknown origin (1006563) (Pyrexia (10037660)) [v.23.0] [10016563]

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 FEVER OF UNKNOWN ORGIN

- Investigator: This SAE has no reasonable possibility of being caused by study IP--Patient works in a café environment and is at risk of contracting viral infections from customers and staff.

- AbbVie: Event with multiple etiologies and common in the general population.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ADENOVIRUS GENE TEST (NASAL SWAB):** Negative

[redacted] 20[redacted] **BORD PERTUSSIS TEST (NASAL SWAB):** Negative

[redacted] 20[redacted] **BORDETELLA PARAPERTU TEST (NASAL SWAB):** Negative

[redacted] 20[redacted] **C REACTIVE PROTEIN:** 7.2 MG/L (normal <3)

[redacted] **20[redacted] C. PNEUMONIAE TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] CHEST X RAY, ERECT:** Normal

[redacted] **20[redacted] CORONAVIRUS 229E TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] CORONAVIRUS HKU1 TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] CORONAVIRUS NL63 TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] CORONAVIRUS OC43 TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] CT BRAIN:** Normal

[redacted] **20[redacted] HEMATOCRIT:** 50.2 % (normal 38 to 52)

[redacted] **20[redacted] HEMOGLOBIN:** 17.4 G/DL (normal 13 to 17)

[redacted] **20[redacted] INFLUENZA A GENE TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] INFLUENZA B GENE TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.8 X10**3/MCL (normal 1 to 3)

[redacted] **20[redacted] MCV:** 90.6 FL (normal 76 to 96)

[redacted] **20[redacted] METAPNEUMOVIRUS TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] MONOCYTES ABS:** 1.0 X10**3/MCL (normal 0.2 to 0.8)

[redacted] **20[redacted] MYCO PNEUMONIAE TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] NEUTROPHILS ABS:** 15.5 X10**3/MCL (normal 2 to 7.5)

[redacted] **20[redacted] PARAINFLUENZA V 1 TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] PARAINFLUENZA V 2 TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] PARAINFLUENZA V 3 TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] PARAINFLUENZA V 4 TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] PLATELET COUNT:** 167 X10**3/MCL (normal 150 to 450)

[redacted] **20[redacted] RESPIRATOY SYNCYTIAL VIRUS TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] RHINO/ENTEROVIRUS TEST (NASAL SWAB):** Negative

[redacted] **20[redacted] TEMPERATURE:** 37.7 Degrees C

[redacted] **20[redacted] WEIGHT (SCREENING):** 69.7 KG

[redacted] **20[redacted] WHITE BLOOD CELLS:** 17.3 X10**3/MCL (normal 4 to 10)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	5[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: UTERINE MYOMA	20[redacted]
OTHER: MENOPAUSE	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: IMPAIRED GLUCOSE TOLERANCE	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.5 PACK	30	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted] / 1	[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted] / 169	[redacted] / 196	28

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / -222
VALSARTAN	40 mg	QD	Y-M: 20[redacted] / -222
CELECOXIB	100 mg	BID	Y-M: 20[redacted] / -168

CICLOSPORIN	100 mg	QD	Y-M: 20[redacted] / -168
PREDNISOLONE	1 mg	BID	Y-M: 20[redacted] / -168
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -131
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -130
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted] / -75

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-M: 20[redacted] / -222	ONGOING
VALSARTAN	40 mg	QD	Y-M: 20[redacted] / -222	ONGOING
CELECOXIB	100 mg	BID	Y-M: 20[redacted] / -168	ONGOING
PREDNISOLONE	1 mg	BID	Y-M: 20[redacted] / -168	ONGOING
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -130	Y-M: 20[redacted] / 193
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted] / -75	Y-M: 20[redacted] / 108
PA	1 g	TID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 31
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / 115	Y-M: 20[redacted] / 192
SUVOREXANT	15 mg	PRN	Y-M: 20[redacted] / 232	Y-M: 20[redacted] / 240
FENTANYL	0.1 mL	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
REMIFENTANIL	2 mg	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
SOLUTIONS AFFECTING THE ELECTROLYTE BALANCE	1 mL	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
FENTANYL	0.1 mg	PRN	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 237
ROPIVACAINE	2 %	PRN	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 237
FLOMOXEF	1 g	TID	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 239
VEEN D	1 OTHER: PACK	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 239
DAIKENCHUTO	2.5 g	TID	Y-M: 20[redacted] / 234	ONGOING
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 234	ONGOING
MAGNESIUM OXIDE	330 mg	TID	Y-M: 20[redacted] / 234	ONGOING
REBAMIPIDE	100 mg	PRN	Y-M: 20[redacted] / 234	ONGOING

PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 236
POSTERISAN F	1 OTHER: OTHER	PRN	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 237
WHITE SOFT PARAFFIN	1 OTHER: OTHER	PRN	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 237

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 CANCER SARCOMA (UTERINE)

Preferred term 子宮癌

AE Onset Date / Rx Day [redacted] / 32

Age at AE Onset 5[redacted]

Laboratory Testing

[redacted] (RX DAY 197): NPTST160-CEA: 6.9 [NOT REPORTED - 5] MG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted] (RX DAY 169): ENDOMETRIAL CYTOLOGY: UTERINE CANCER CLASS5; [redacted] (RX DAY 197): CYTOLOGY: THE SECTION SHOWS PROLIFERATION OF ATYPICAL EPITHELIAL CELLS ARRANGED IN IRREGULAR GLANDULAR STRUCYURES, FUSED GLANDULAR STRUCTURES, AND PAPILLARY STRUCTURES, ACCOMPANIED BY FIBROUS STROMA AND FOCI OFNECROSIS. ENDOMETRIOID CARCINOMA, GRADE 1 IS CONSIDERED.; [redacted] (RX DAY 233): ABDOMINAL TYPE EXTENSIVE HYSTERECTOMY...: SUCCESS; ADNEXECTOMY(BOTH) LYMPH NODEDISSECTION(PELVIC) PARA-AORTIC LYMPH NODES BIOPSY BILATERAL: PATHOLOGY REVEALED "CANCER SARCOMA" AND THE DIAGNOSIS CHANGED TO THIS. NO OTHER METASTASIS FOUND; URETERAL STENT PLACEMENT.: SUCCESS; [redacted] (RX DAY 261): CT SCAN(CHEST~ABDOMINAL): NO METASTASIS

AE Stopped Rx Day 263 (80 DAYS AFTER LAST TREATMENT)

Duration of AE 232 DAYS

Severity Severe

Relation to Study Drug by Investigator No Reasonable Possibility

Investigator Alternative Etiology CONSISTENT WITH GENERAL RISK FACTORS SUCH AS AGE, FEMALE, MENOPAUSE, FIRST BIRTH, AND LESS CHILDBIRTH EXPERIENCE.

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: M15-572

治験責任医師からの報告。本被験者は日本の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，癌肉腫（子宮）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，子宮筋腫，閉経，乾癬性関節炎，現喫煙者（1 日 0.5 箱を 30 年間）及び現飲酒者であった。

20[redacted] 年 [redacted] 月，被験者は癌肉腫（子宮）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，癌肉腫（子宮）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，白帯下の増加が見られていた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はクリニックを受診し，細胞診を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，細胞診の結果はクラス IV であった。詳細な検査が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，検査結果が得られ，被験者は子宮癌と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は子宮摘出のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，腹式広汎子宮摘出術，両側子宮付属器切除，リンパ節郭清術（骨盤部），両側傍大動脈リンパ節生検及び両側尿管ステント留置が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，経過良好により被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は病理組織学的検査及び CT 検査の結果を聞くため，予約していた受診日に来院した。結果は癌肉腫で，その他の転移は認められなかった。

この被験者の治験は中止された。

投与された薬剤はベルソムラであった。

The patient's past medications include:

PL COMBINATION GRANULES for COMMON COLD ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

NEORAL for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Carcino-sarcoma uterus (10007261) (Uterine cancer (10046766)) [v.22.1] [10007261]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of CANCER SARCOMA (UTERINE)

- Investigator: consistent with general risk factors such as age, female, menopause, first birth, and less childbirth experience.

- AbbVie: Weak temporal association. Only two months of study drug exposure prior to onset of symptoms and less than 7 months of study drug exposure prior to diagnosis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CEA:** 6.9 mg/ml upper range 5.0

[redacted] **20[redacted] CT SCAN:** Chest - abdominal: No metastasis.

[redacted] **20[redacted] CYTOLOGY:** endometrial: uterine class V

[redacted] **20[redacted] CYTOLOGY:** THE SECTION SHOWS PROLIFERATION OF ATYPICAL EPITHELIAL CELLS ARRANGED IN IRREGULAR GLANDULAR STRUCYURES, FUSED GLANDULAR STRUCTURES, AND PAPILLARY STRUCTURES, ACCOMPANIED BY FIBROUS STROMA AND FOCI OF NECROSIS. ENDOMETRIOID CARCINOMA, GRADE 1 IS CONSIDERED.

[redacted] **20[redacted] HISTOPATHOLOGY:** para-aortic lymph nodes biopsy from hysterectomy: cancer sarcoma

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	3[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
HYPERTENSION	20[redacted]
DRUG ALLERGIES/REACTIONS: ITCHINESS DUE TO SULPHASALAZINE	20[redacted]

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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 385	217
ADA	40MG	SC	EOW	[redacted]20[redacted] / 386		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMLODIPINE	10 mg	QD	Y-M: 20[redacted] / -333
PERINDOPRIL	4 mg	QD	Y-M: 20[redacted] / -333
CALCITRIOL	0.25 ug	QD	Y-M: 20[redacted] / -277
ETORICOXIB	90 mg	PRN	Y-M: 20[redacted] / -277
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -277
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted] / -277
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -263
AQUEOUS	30% EMULSIFYING OINTMENT %	BID	Y-M: 20[redacted] / -257
BETAMETHASONE	0.05 %	BID	Y-M: 20[redacted] / -257
BETAMETHASONE	0.1 %	BID	Y-M: 20[redacted] / -257
CETRIMIDE	1 %	BID	Y-M: 20[redacted] / -257
CLOBETASONE	0.05 %	BID	Y-M: 20[redacted] / -257
COAL TAR	3 %	BID	Y-M: 20[redacted] / -257
COAL TAR	4 %	BID	Y-M: 20[redacted] / -257
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted] / -249
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -186
SULFASALAZINE	1 g	BID	Y-M: 20[redacted] / -186

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	10 mg	QD	Y-M: 20[redacted] / -333	ONGOING
PERINDOPRIL	4 mg	QD	Y-M: 20[redacted] / -333	ONGOING
CALCITRIOL	0.25 ug	QD	Y-M: 20[redacted] / -277	NOT REPORTED
ETORICOXIB	90 mg	PRN	Y-M: 20[redacted] / -277	NOT REPORTED
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -277	NOT REPORTED
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -186	NOT REPORTED
TRAMADOL	50 mg	TID	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 250

Event #1: Serious Adverse Event

Event Description	HEADACHE WITH VOMITING
Preferred term	頭痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 240
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 248): Alanine Aminotransferase: 23 [0 - 33] U/L; Aspartate Aminotransferase: 22 [0 - 32] U/L; Creatinine: 52 [44 - 80] UMOL/L; Hemoglobin: 128 [115 - 160] G/L; Leukocytes: 8 [4 - 11] 10^9/L; Platelets: 331 [150 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 248): BLOOD PRESSURE READINGS: 132/78MMHG; CT BRAIN: NORMAL; ECG: NORMAL

AE Stopped Rx Day	250
Duration of AE	11 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	HEADACHE WITH VOMITING
Preferred term	嘔吐
AE Onset Date / Rx Day	[redacted]20[redacted] / 240
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 248): Alanine Aminotransferase: 23 [0 - 33] U/L; Aspartate Aminotransferase: 22 [0 - 32] U/L; Creatinine: 52 [44 - 80] UMOL/L; Hemoglobin: 128 [115 - 160] G/L; Leukocytes: 8 [4 - 11] 10^9/L; Platelets: 331 [150 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 248): BLOOD PRESSURE READINGS: 132/78MMHG; CT BRAIN: NORMAL; ECG: NORMAL

AE Stopped Rx Day	250
Duration of AE	11 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はマレーシアの 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が投与され，嘔吐を伴う頭痛の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，高血圧，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は嘔吐を伴う頭痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，嘔吐を伴う頭痛は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頭痛及び嘔吐で入院した。脳 CT 検査，心電図検査及び臨床検査の結果はすべて正常であった。20[redacted] 年 [redacted] 月 [redacted] 日，頭痛はトラマドールで軽減された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頭痛もなく退院した。

投与された薬剤はトラマドールであった。

Causality for UPADACITINIB (Blinded)

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1) Vomiting (10047700) (Vomiting (10047700)) [v.22.1] [10047700]

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) Headache (10019211) (Headache (10019211)) [v.22.1] [10019211]

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 HEADACHE WITH VOMITING

- Investigator: Not applicable

- AbbVie: Event is common in the general population. Additionally, all diagnostics are within normal limits.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ALANINE AMINO TRANSFERASE:** 23 U/L (normal 0 to 33)

[redacted] **ASPARTATE AMINO TRANSFERASE:** 22 U/L (normal 0 to 32)

[redacted] **BLOOD PRESSURE:** During event: 132/78 mmHg

Unknown date BLOOD PRESSURE: Prior to event: 121/89 mmHg

[redacted] **CREATININE:** 52 MCMOL/L (normal 44 to 80)

[redacted] **CT BRAIN:** NORMAL

[redacted] **ECG:** NORMAL

[redacted] **HEMOGLOBIN:** 12.8 G/DL (normal 11.5 to 16)

[redacted] **PLATELET COUNT:** 331 X10**9/L (normal 150 to 400)

[redacted] **WHITE BLOOD CELLS:** 8 X10**9/L (normal 4 to 11)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	4[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: PSORIASIS VULGARIS	19[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	8	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BETAMETHASONE	APPLICABLE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
DEXAMETHASONE	APPLICABLE OTHER: APPLICATION	PRN	Y-M: 20[redacted]

HEPARINOID	APPLICABLE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
PREDNISOLONE	APPLICABLE OTHER: APPLICATION	PRN	Y-M: 20[redacted]
CELECOXIB	200 mg	BID	Y-M: 20[redacted] / -238
LANSOPRAZOLE	15 mg	QD	Y-M: 20[redacted] / -238
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -210
METHOTREXATE	8 mg	EVERY WEEK	Y-M: 20[redacted] / -210
CELECOXIB	100 mg	BID	Y-M: 20[redacted] / -173
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -173

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -210	Y-M: 20[redacted] / 545
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -173	Y-M: 20[redacted] / 537
PA	1 g	TID	Y-M: 20[redacted] / 540	Y-M: 20[redacted] / 543
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 540	Y-M: 20[redacted] / 543
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 541	Y-M: 20[redacted] / 543
AMOXICILLIN	250 mg	TID	Y-M: 20[redacted] / 543	Y-M: 20[redacted] / 549
AUGMENTIN	375 mg	TID	Y-M: 20[redacted] / 543	Y-M: 20[redacted] / 549
BETAMETHASONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 547	Y-M: 20[redacted] / 585
METHOTREXATE	6 mg	EVERY WEEK	Y-M: 20[redacted] / 604	Y-M: 20[redacted] / 617
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / 606	Y-M: 20[redacted] / 617
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 616	Y-M: 20[redacted] / 646
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 617	Y-M: 20[redacted] / 617
GUAIAZULENE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 617	Y-M: 20[redacted] / 621
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 617	Y-M: 20[redacted] / 623
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 617	Y-M: 20[redacted] / 646

TERRA-CORTRIL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 617	Y-M: 20[redacted] / 646
PREGABALIN	25 mg	BID	Y-M: 20[redacted] / 619	Y-M: 20[redacted] / 623
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / 631	NOT REPORTED
METHOTREXATE	6 mg	EVERY WEEK	Y-M: 20[redacted] / 631	NOT REPORTED

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

Event Description	BRONCHITIS
Preferred term	気管支炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 543
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 540): Alanine Aminotransferase: 12 [10 - 42] U/L; Aspartate Aminotransferase: 25 [13 - 30] U/L; Leukocytes: 3.9 [3.3 - 8.6] 10^9/L; Lymphocytes: 1.9 [NOT REPORTED - NOT REPORTED] 10^8/L; NPTST209-CRP: 1.66 [0 - 0.14] MG/DL; NPTST239-E-GFR: 85.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 33.0 [NOT REPORTED - NOT REPORTED] 10^8/L; [redacted]20[redacted] (RX DAY 541): Alanine Aminotransferase: 11 [10 - 42] U/L; Aspartate Aminotransferase: 26 [13 - 30] U/L; Leukocytes: 3.2 [3.3 - 8.6] 10^9/L; Lymphocytes: 3.8 [NOT REPORTED - NOT REPORTED] 10^8/L; NPTST209-CRP: 7.81 [0 - 0.14] MG/DL; NPTST242-EGFR: 84.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 23.6 [NOT REPORTED - NOT REPORTED] 10^8/L; [redacted]20[redacted] (RX DAY 543): Alanine Aminotransferase: 11 [10 - 42] U/L; Aspartate Aminotransferase: 26 [13 - 30] U/L; Leukocytes: 4.5 [3.3 - 8.6] 10^9/L; Lymphocytes: 7.6 [NOT REPORTED - NOT REPORTED] 10^8/L; NPTST209-CRP: 13.03 [0 - 0.14] MG/DL; NPTST242-EGFR: 85.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 31.4 [NOT REPORTED - NOT REPORTED] 10^8/L; [redacted]20[redacted] (RX DAY 548): Alkaline Phosphatase: 12 [10 - 42] U/L; Aspartate Aminotransferase: 16 [13 - 30] U/L; Leukocytes: 2.1 [3.3 - 8.6] 10^9/L; Lymphocytes: 7.1 [NOT REPORTED - NOT REPORTED] 10^8/L; NPTST209-CRP: 1.11 [0 - 0.14] MG/DL; Neutrophils: 8.3 [NOT REPORTED - NOT REPORTED] 10^8/L

Microbiology

[redacted]20[redacted] (RX DAY 541): SPUTUM NPTST617-STREPTOCOCCUS PNEUMONIAE: Positive-3+; [redacted]20[redacted] (RX DAY 543): URINE NPTST665-URINARY LEGIONELLA: Negative; URINE NPTST666-URINARY PNEUMOCOCCI: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 540): CHEST X-RAY: SUSPECTED UPPER RESPIRATORY INFLAMMATION; [redacted]20[redacted] (RX DAY 541): CHEST X-RAY: SUSPECTED UPPER RESPIRATORY INFLAMMATION; [redacted]20[redacted] (RX DAY 543): CHEST CT: NO ABNORMAL FINDING.DIAGNOSED AS BRONCHITIS

AE Stopped Rx Day	568
Duration of AE	26 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 614
Age at AE Onset	5[redacted]

Laboratory Testing
[redacted]20[redacted] (RX DAY 616): NPTST389-INFLUENZA TEST: NEGATIVE [NOT REPORTED - NOT REPORTED] ONCE
Microbiology
[redacted]20[redacted] (RX DAY 617): OTHER VESICULAR FLUID NPTST230-DERMAQUICK: Positive-SHINGLES
SAE Supplemental Procedure
NOT REPORTED

AE Stopped Rx Day	729
Duration of AE	116 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は日本の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，気管支炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，尋常性乾癬，元紙巻タバコ喫煙者（1 日 1 箱を 8 年間），乾癬性関節炎及び現飲酒者（1 日 2～4 杯）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年[redacted] 月[redacted] 日であった。

20[redacted] 年[redacted] 月[redacted] 日，被験者は気管支炎を発現した。20[redacted] 年[redacted] 月[redacted] 日，気管支炎は消失した。

20[redacted] 年[redacted] 月[redacted] 日の事象発現前，被験者は上気道炎（非重篤）と診断された。被験者は咳嗽，痰及び鼻汁の症状を呈していた。20[redacted] 年[redacted] 月[redacted] 日，約 38°C の発熱及び頭痛が出現し，治験薬は中止された。20[redacted] 年[redacted] 月[redacted] 日，被験者は来院し，胸部 X 線検査及び血液検査が行われた。上気道炎症が疑われ，薬剤が処方された。20[redacted] 年[redacted] 月[redacted] 日，被験者は外来を再受診した。胸部 X

線検査，血液検査及び喀痰検査が行われた。ここでも上気道炎症が疑われ，ジスロマックが追加で処方された。喀痰検査で肺炎連鎖球菌が認められ，被験者は気管支炎と診断された。20[redacted]年[redacted]月[redacted]日，被験者は入院し，投与された薬剤は抗生物質であった。20[redacted]年[redacted]月[redacted]日，被験者は退院した。

投与された薬剤は，アモキシシリン水和物，PL 顆粒，カロナール，ジスロマック及びオーグメンチン配合錠であった。

The patient's past medications include:

ANTEBATE for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

HIRUDOID for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

LIDOMEXKOWA for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

METHADERM for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

CELECOX for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

TAKEPRON for NSAIDS SIDE EFFECTS PREVENTION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Bronchitis (10006451) (Bronchitis (10006451)) [v.22.1] [10006451]

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 BRONCHITIS

- Investigator: Not applicable

- AbbVie: Event isa common occurrence in the general population.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ALANINE AMINO TRANSFERASE:** 12 U/L (normal 10 to 12)

[redacted] **ALANINE AMINO TRANSFERASE:** 11 U/L (normal 10 to 12)

[redacted] **ALKALINE PHOSPHATASE:** 12 U/L (normal 10 to 42)

[redacted] **ASPARATATE AMINO TRANSFERASE:** 25 U/L (normal 13 to 30)

[redacted] **ASPARATATE AMINO TRANSFERASE:** 26 U/L (normal 13 to 30)

[redacted] **ASPARATATE AMINO TRANSFERASE:** 16 U/L (normal 13 to 30)

[redacted] **CHEST CT:** NO ABNORMAL FINDING. DIAGNOSED AS BRONCHITIS

[redacted] **CHEST X-RAY:** SUSPECTED UPPER RESPIRATORY INFLAMMATION

[redacted] **CHEST X-RAY:** SUSPECTED UPPER RESPIRATORY INFLAMMATION

[redacted] **CHEST X-RAY (SCREENING):** Normal

[redacted] **CHEST X-RAY (WEEK 56):** Normal

[redacted] **CHEST XRAY:** no change

[redacted] **CRP:** 1.66 mg/dL (normal 0 to 0.14)

[redacted] **CRP:** 7.81 mg/dL (normal 0 to 0.14)

[redacted] **CRP:** 13.03 mg/dL (normal 0 to 0.14)

[redacted] **CRP:** 1.11 mg/dL (normal 0 to 0.14)

[redacted] **E-GFR:** 85.2 no units

[redacted] **E-GFR:** 85.2 no units

[redacted] **LYMPHOCYTES ABS:** 1.9 x10*2/uL

[redacted] **LYMPHOCYTES ABS:** 3.8 x10*2/uL

[redacted] **LYMPHOCYTES ABS:** 7.6 x10*2/uL

[redacted] **LYMPHOCYTES ABS:** 7.1 x10*2/uL

[redacted] **NEUTROPHILS ABS:** 33.0 x10*2/uL

[redacted] **NEUTROPHILS ABS:** 23.6 x10*2/uL

[redacted] 20[redacted] **NEUTROPHILS ABS:** 31.4 x10*2/uL

[redacted] 20[redacted] **NEUTROPHILS ABS:** 8.3 x10*2/uL

[redacted] 20[redacted] **SPUTUM TEST:** STREPTOCOCCUS PNEUMONIAE: Positive, 3+

[redacted] 20[redacted] **TEMPERATURE:** About 38 degrees C

[redacted] 20[redacted] **URINARY LEGIONELLA TEST:** Negative

[redacted] 20[redacted] **URINARY PNEUMOCOCCI TEST:** Negative

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.86 X10**3/MCL (normal 3.3 to 8.6)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.20 X10**3/MCL (normal 3.3 to 8.6)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 4.49 X10**3/MCL (normal 3.3 to 8.6)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 2.05 X10**3/MCL (normal 3.3 to 8.6)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は日本の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，帯状疱疹の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，乾癬性関節炎，元紙巻タバコ喫煙者（1 日 1 箱を 8 年間，1996 年から禁煙）及び現飲酒者（1 日 2～4 杯）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頭部に発疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，38°C の発熱及び頚部・体幹・臀部に発疹が出現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，抗ウイルス治療を受けた。ヘルペスは播種性で，皮膚のみに見られた。治験責任医師によると，被験者に水疱瘡及び帯状疱疹の既往歴はなく，帯状疱疹ワクチン接種歴もなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

試験の盲検解除の情報を得た。

投与された薬剤は，リリカ，カロナール，アシクロビル，リンデロン，テラ・コートリル及びアズノールであった。

The patient's past medications include:

ANTEBATE for PSORIATIC ARTHRITIS and DRUG ERUPTION (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HIRUDOID for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

LIDOMEXKOWA for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

METHADERM for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted])

CELECOX for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.23.0] [10019974]

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 HERPES ZOSTER

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY TEMPERATURE:** 38 Degrees C

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

[redacted] **20[redacted] VESICULAR FLUID DERMAQUICK:** Positive- Shingles

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
冠動脈疾患	X			

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	5[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: LEFT ELBOW SOFT TISSUE TUMOR; PATHOLOGY REPORT SCHWANNOMA	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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ADA	40MG	SC	EOW	[redacted]20[redacted] / 170	[redacted]20[redacted] / 392	223
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ATENOLOL	50 mg	QD	Y-M: 20[redacted]
SULINDAC	200 mg	QD	Y-M: 20[redacted]
DAIVOBET	1 OTHER: OINTMENT	OTHER: HS	Y-M: 20[redacted]
FOLIC ACID	5 mg	OTHER: BIW	Y-M: 20[redacted]

LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted]
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted]
MOMETASONE	1 OTHER: CREAM	QD	Y-M: 20[redacted]
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: UVA	OTHER: BIW	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
CHLORZOXAZONE	200 mg	PRN	Y-M: 20[redacted] / -218
SULINDAC	200 mg	BID	Y-M: 20[redacted] / -218
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -134
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted] / -106
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -49

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
ATENOLOL	50 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	5 mg	OTHER: BIW	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
SULINDAC	200 mg	BID	Y-M: 20[redacted] / -218	NOT REPORTED
CHLORZOXAZONE	200 mg	PRN	Y-M: 20[redacted] / -218	Y-M: 20[redacted] / 560
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -134	NOT REPORTED
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted] / -106	NOT REPORTED
FUSIDIC ACID	1 OTHER: TOPICAL	TID	Y-M: 20[redacted] / 309	NOT REPORTED
BENZONATATE	100 mg	TID	Y-M: 20[redacted] / 528	Y-M: 20[redacted] / 530
CHLORPHENAMINE	2 mg	TID	Y-M: 20[redacted] / 528	Y-M: 20[redacted] / 530
CODEPINE	5 mg	TID	Y-M: 20[redacted] / 528	Y-M: 20[redacted] / 530
DEXTROMETHORPHAN	30 mg	TID	Y-M: 20[redacted] / 528	Y-M: 20[redacted] / 530
PROCATEROL	25 OTHER: MCG	TID	Y-M: 20[redacted] / 528	Y-M: 20[redacted] / 530
BENZONATATE	100 mg	TID	Y-M: 20[redacted] / 541	Y-M: 20[redacted] / 543
CHLORPHENAMINE	2 mg	TID	Y-M: 20[redacted] / 541	Y-M: 20[redacted] / 543
CODEPINE	5 mg	TID	Y-M: 20[redacted] / 541	Y-M: 20[redacted] / 543
DEXTROMETHORPHAN	30 mg	TID	Y-M: 20[redacted] / 541	Y-M: 20[redacted] / 543
PROCATEROL	25 OTHER: MCG	TID	Y-M: 20[redacted] / 541	Y-M: 20[redacted] / 543
BENZONATATE	100 mg	TID	Y-M: 20[redacted] / 551	Y-M: 20[redacted] / 553
CHLORPHENAMINE	2 mg	TID	Y-M: 20[redacted] / 551	Y-M: 20[redacted] / 553
CODEPINE	5 mg	TID	Y-M: 20[redacted] / 551	Y-M: 20[redacted] / 553
DEXTROMETHORPHAN	30 mg	TID	Y-M: 20[redacted] / 551	Y-M: 20[redacted] / 553
PROCATEROL	25 OTHER: MCG	TID	Y-M: 20[redacted] / 551	Y-M: 20[redacted] / 553
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted] / 554	NOT REPORTED
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 554	NOT REPORTED
PROPRANOLOL	10 mg	BID	Y-M: 20[redacted] / 554	NOT REPORTED
CHLORZOXAZONE	200 mg	QID	Y-M: 20[redacted] / 554	Y-M: 20[redacted] / 557
PARACETAMOL	500 mg	QID	Y-M: 20[redacted] / 554	Y-M: 20[redacted] / 557
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted] / 589	NOT REPORTED
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 589	NOT REPORTED

SERTACONAZOLE	1 OTHER: UNIT	BID	Y-M: 20[redacted] / 813	NOT REPORTED

Event #1: Serious Adverse Event

Event Description	CORONARY ARTERY DISEASE
Preferred term	冠動脈疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 553
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 553): NPTST168-CK-MB: 14 [0 - 24] U/L; NPTST198-CPK: 140 [20 - 170] IU/L; [redacted]20[redacted] (RX DAY 554): NPTST168-CK-MB: 22 [0 - 24] U/L; NPTST198-CPK: 141 [20 - 170] IU/L; [redacted]20[redacted] (RX DAY 613): NPTST168-CK-MB: 13 [0 - 24] U/L; NPTST198-CPK: 178 [20 - 170] IU/L; NPTST652-TROPONIN-T: 5.4 [0 - 14] NG/L; [redacted]20[redacted] (RX DAY 614): NPTST168-CK-MB: 23 [0 - 24] U/L; NPTST198-CPK: 164 [20 - 170] IU/L; NPTST652-TROPONIN-T: 8.2 [0 - 14] NG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 554): TREADMILL EXERCISE TEST (TET): 6MIN32SEC, 85% (141/165), II, II, AVF, V4-6.; [redacted]20[redacted] (RX DAY 561): ECG REPORT: NORMAL SINUS RHYTHM NORMAL ECG; [redacted]20[redacted] (RX DAY 562): ULTRASOUND CARDIOGRAM(UCG): LVEF 65 % BY M-MODE, NO REGIONAL WALL MOTION ABNORMALITY.; [redacted]20[redacted] (RX DAY 583): THALLIUM SPECT, DIPYRIDAMOLE RESTING: 1.MILD STRESS INDUCIBLE ISCHEMIA AT INFERIOR AND BASAL INFEROSEPTAL WALL, 2.NORMAL LV SYSTOLIC FUNCTION, 3. STRESS-INDUCED LV DILATION.; [redacted]20[redacted] (RX DAY 613): CARDIAC CATHETERIZATION: CORONARY ARTERY DISEASE, 3 VESSEL DISEASE (VD) (LEFT ANTERIOR DESCENDING MID: 70%, LEFT ANTERIOR DESCENDING DISTAL: 70%, LEFT CIRCUMFLEX DISTAL :90% STENOSIS, RIGHT CORONARY ARTERY-M/3:60% STENOSIS RCA HYPOPLASIA. S/P PLAIN OLD BALLOON ANGIOPLASTY WITH STENT (POBAS) TO DISTAL TO MID LEFT ANTERIOR DESCENDING (LAD) WITH 2 DRUG-ELUTING STENTS (DES) AND TO DISTAL LEFT CIRCUMFLEX (LCX) WITH ONE DRUG-ELUTING STENT (DES).

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は台湾の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，冠動脈疾患の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，高血圧，乾癬性関節炎，非喫煙者，非飲酒者及び冠動脈バイパス移植（CABG）の家族歴（父親）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は冠動脈疾患を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者より，冷汗及び全身脱力を伴う胸部絞扼感が 3 回出現したとの訴えがあった。被験者は救急治療室を受診した。心電図検査が行われ，不整脈が認められた。CPK 値は正常であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は施設から血管狭窄の疑いがあると知らされた。その後，心カテーテル検査が予定された。検査前に治験薬の投与が中止された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は予定されていた心カテーテル検査のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，心カテーテル検査と単純旧式バルーン血管形成ステント留置術（POBAS）が行われ，左前下行枝（LAD）遠位部から中央部に薬剤溶出ステントが 2 本，左回旋枝遠位部に薬剤溶出ステントが 1 本留置された。手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は安定状態で退院した。

治験責任医師によると，高脂血症が危険因子であったと考えられた。

投与された薬剤は，アトルバスタチン，アスピリン，cardolol 及びクロピドグレルであった。

The patient's past medications include:

ARHEUMA for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Coronary artery disease (10011078) (Coronary artery disease (10011078)) [v.22.1] [10011078]

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 CORONARY ARTERY DISEASE

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing hypertension, pre-existing psoriasis, family history of father with coronary artery bypass graft, and hyperlipidemia as noted by PI

Relevant Laboratory & Other Diagnostic Tests

[redacted] **CK-MB:** 13 U/L (normal 0 to 24)

[redacted] **CK-MB:** 14 U/L (normal 0 to 24)

[redacted] **CK-MB:** 23 U/L (normal 0 to 24)

[redacted] **CK-MB:** 22 U/L (normal 0 to 24)

[redacted] **CPK:** 178 IU/L (normal 20 to 170)

[redacted] **CPK:** 140 GBq (normal 20 to 170)

[redacted] **CPK:** 164 IU/L (normal 20 to 170)

[redacted] **CPK:** 141 IU/L (normal 20 to 170)

[redacted] **ECG:** Arrhythmia

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

[redacted] **THALLIUM SPECT, DYPIRIDAMOLE RESTING:** 1. Mild stress inducible ischemia at inferior and basal inferoseptal wall 2. Normal LV systolic function 3. stress-induced LV dilation

[redacted] **TREADMILL EXERCISE TEST (TET):** 6 min 32 sec, 85% (141/165) II, II aVF, V4-6

[redacted] **TROPONIN-T:** 5.4 NG/L (normal 0 to 14)

[redacted] **TROPONIN-T:** 8.2 NG/L (normal 0 to 14)

[redacted] **ULTRASOUND CARDIOGRAM:** LVEF 65% by M-mode; no regional wall motion abnormality

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
冠動脈疾患	X			X
骨壊死	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	6[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: CHICKEN POX	19[redacted]
HYPERTENSION	20[redacted]
OTHER: HYPERLIPIDEMIA	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
PERIPHERAL NERVE DISORDER: ESSENTIAL TREMOR	20[redacted]
OSTEOPOROSIS	20[redacted]
OTHER: RIB FRACTURE, MULTIPLE RIB, LEFT	20[redacted]
PNEUMONIA: BRONCHITIS	20[redacted]
DEGENERATIVE DISC DISEASE: DEGENERATIVE SPONDYLOSIS, NTERVERTEBRAL DISC DISORDERS WITH MYELOPATHY,	20[redacted]
OTHER: MYOFASCIAL PAIN SYNDROMEMYELOPATHY (RELATED PSORIATIC ARTHRITIS)	20[redacted]
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE	20[redacted]
OSTEOARTHRITIS	20[redacted]
OTHER: MYCOPLASMA INFECTION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY & UNILATERAL SALPINGO-OOPHORECTOMY	19[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.5 PACK	36	
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)
ABT-494	30 MG	ORAL	QD	[redacted] / 1	[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted] / 169	[redacted] / 392	224
ABT-494	30 MG	ORAL	QD	[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: TOPICAL	BID	Y-M: 20[redacted] / -245
CLOBETASOL	7.5 mL	PRN	Y-M: 20[redacted] / -245
BISOPROLOL	1.25 mg	QD	Y-M: 20[redacted] / -139
PIRACETAM	1200 mg	QD	Y-M: 20[redacted] / -139

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
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
PIRACETAM	1200 mg	QD	Y-M: 20[redacted] / -139	NOT REPORTED
BISOPROLOL	1.25 mg	QD	Y-M: 20[redacted] / -139	Y-M: 20[redacted] / 213
TEARS NATURALE	1 gtt	OTHER: ONCE	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 128
ATORVASTATIN	10 mg	OTHER: HS	Y-M: 20[redacted] / 129	Y-M: 20[redacted] / 156
NICAMETATE	50 mg	BID	Y-M: 20[redacted] / 162	NOT REPORTED
PARAFON	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 162	NOT REPORTED
PARACETAMOL	500 mg	QID	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 197
ATORVASTATIN	20 mg	OTHER: HS	Y-M: 20[redacted] / 178	Y-M: 20[redacted] / 184
TEARS NATURALE	1 gtt	QID	Y-M: 20[redacted] / 213	ONGOING
CARTEOLOL	1 gtt	QD	Y-M: 20[redacted] / 213	Y-M: 20[redacted] / 244
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted] / 214	NOT REPORTED
ATORVASTATIN	20 mg	OTHER: HS	Y-M: 20[redacted] / 214	NOT REPORTED
NICORANDIL	5 mg	BID	Y-M: 20[redacted] / 214	NOT REPORTED

SENNOSIDE A+B	25 mg	OTHER: HS	Y-M: 20[redacted] / 218	Y-M: 20[redacted] / 219
DEXTROSE AND SODIUM CHLORIDE INJECTION	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 219	Y-M: 20[redacted] / 219
ENOXAPARIN	1 OTHER: SYRG	OTHER: STAT	Y-M: 20[redacted] / 219	Y-M: 20[redacted] / 219
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 220	NOT REPORTED
CALCIDO	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 225	NOT REPORTED
CELECOXIB	200 mg	QD	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 308
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 308
LATANOPROST	1 gtt	OTHER: HS	Y-M: 20[redacted] / 245	ONGOING
TRIAMCINOLONE	1 mL	OTHER: STAT	Y-M: 20[redacted] / 284	Y-M: 20[redacted] / 284
TRIAMCINOLONE	1 mL	OTHER: STAT	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 298
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 419
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 477
CLONAZEPAM	0.25 mg	OTHER: HS	Y-M: 20[redacted] / 311	Y-M: 20[redacted] / 317
PARACETAMOL	500 mg	QID	Y-M: 20[redacted] / 311	Y-M: 20[redacted] / 324
PARACETAMOL	500 mg	QID	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 392
CHLORZOXAZONE	200 mg	TID	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 477
ULTRACET	1 OTHER: TABLT	TID	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 419
SERTACONAZOLE	1 OTHER: UNIT	BID	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 419
ULTRACET	1 OTHER: TAB	QD	Y-M: 20[redacted] / 420	Y-M: 20[redacted] / 477
SERTACONAZOLE	1 OTHER: UNIT	BID	Y-M: 20[redacted] / 477	Y-M: 20[redacted] / 729
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / 725	Y-M: 20[redacted] / 730
DICLOFENAC	100 mg	QD	Y-M: 20[redacted] / 730	NOT REPORTED
FENTICONAZOLE	1 OTHER: PUFF	QD	Y-M: 20[redacted] / 730	NOT REPORTED

Event #1: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description	CORONARY ARTERIAL DISEASE
Preferred term	冠動脈疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 157

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 218): Alanine Aminotransferase: 25 [0 - 41] U/L; Blood Urea Nitrogen: 6 [2.5 - 8.9] MMOL/L; Cholesterol: 3.8 [0 - 5.17] MMOL/L; Creatinine: 0.6 MG/DL [0.6 - 1.3] mg/dL; HDL Cholesterol: 40 [40 - NOT REPORTED] mg/dL; Hemoglobin: 122 [108 - 149] G/L; LDL Cholesterol: 86 [NOT REPORTED - 130] mg/dL; Leukocytes: 10.8 [3.5 - 9.1] 10^9/L; NPTST242-EGFR: 106.0 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; Platelets: 452 [150 - 361] 10^9/L; Triglycerides: 0.85 [0 - 1.7] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 157): CT-CORONARY ANGIOGRAPHY: AGATSTON SCORE: 646.91 CORONARY ARTERY: SEVERE (70%-99%) STENOSIS IN LEFT ANTERIOR DESCENDING ARTERY. MILD (25%-49%) STENOSIS IN RIGHT CORONARY ARTERY. VENTRICULAR FUNCTION: NORMAL.; [redacted]20[redacted] (RX DAY 218): CHEST X RAY SHOWS: NORMAL HEART SIZE. MILD AORTIC WALL CALCIFICATION. BILATERAL APICAL PLEURAL THICKENING. SHARP BILATERAL COSTOPHRENIC ANGLES.; ECG: SINUS RHYTHM WITH PREMATURE VENTRICULAR COMPLEXES; [redacted]20[redacted] (RX DAY 219): CORONARY ANGIOGRAM: CORONARY ANGIOGRAM S/P PLAIN OLD BALLOON ANGIOPLASTY WITH STENT (POBAS) TO LAD(LEFT ANTERIOR DESCENDING ARTERY).CORONARY ANGIOGRAPHY: LM: PATENT LAD: PROXIMAL STENOSIS 70 %, MIDDLE STENOSIS 70 %LCX: OSTIAL STENOSIS 50 %, HYPOPLASIA RCA: DISTAL STENOSIS 20 %; ECG: NORMAL SINUS RHYTHM ST & T WAVE ABNORMALITY, CONSIDER INFERIOR ISCHEMIA ABNORMAL ECG

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	IN THE JUDGMENT OF THE PRINCIPAL INVESTIGATOR, THE EVENT WAS NOT RELATED TO THE STUDY DRUG AND ANGIOGRAPHY IS A PROCEDURE AND NOT A SURGERY BECAUSE NO INCISION AND SUTURE WAS NEEDED.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	AVASCULAR NECROSIS OF BILATERAL HIP JOINTS
Preferred term	骨壊死
AE Onset Date / Rx Day	[redacted]20[redacted] / 378
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 392): Eosinophils/Leukocytes: 0.4 [0.3 - 7.9] %; Erythrocyte Sedimentation Rate: 12 [NOT REPORTED - 20] mm/h; Hemoglobin: 131 [110 - 152] G/L; Leukocytes: 5.4 [3.3 - 9.2] 10^9/L; Lymphocytes/Leukocytes: 28.8 [18 - 48.8] %; NPTST353-HSCRP: 0.05 [0.1 - 0.3] MG/DL; Neutrophils/Leukocytes: 64.5 [41.6 - 74.4] %; Platelets: 358 [150 - 378] 10^9/L; [redacted]20[redacted] (RX DAY 408): Basophils/Leukocytes: 0.5 [0 - 1] %; Blood Urea Nitrogen: 2.6 [2.1 - 7.5] MMOL/L; Creatinine: 42 [39 - 88] UMOL/L; Eosinophils/Leukocytes: 1.6 [0 - 5] %; Hemoglobin: 120 [120 - 160] G/L; Leukocytes: 4.3 [3.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 21.8 [20 - 56] %; Monocytes/Leukocytes: 7.4 [0 - 12] %; NPTST018-ACTIVATED PARTIAL THROMBOPLASTI: 26.5 [NOT REPORTED - 33.8] sec; NPTST345-HIGH SENSITIVE CRP: 6.8 [0 - 3] MG/L; NPTST537-PROTHROMBIN TIME: 11.8 [8 - 12] SEC; Neutrophils/Leukocytes: 68.7 [42 - 74] %; Platelets: 241 [150 - 400] 10^9/L; Potassium: 4.2 [3.6 - 5] MMOL/L; Prothrombin Intl. Normalized Ratio: 1.1 [0 - 1.2] RATIO; Sodium: 142 [134 - 148] MMOL/L; [redacted]20[redacted] (RX DAY 492): Erythrocyte Sedimentation Rate: 18 [0 - 30] MM/H; Hemoglobin: 106 [120 - 160] G/L; NPTST352-HS-CRP: 14.12 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 225): X RAY, PELVIS FOR THR: PHLEBOLITHS IN THE PELVIC CAVITY. DEGENERATIVE ARTHROSIS OF BILATERAL SACROILIAC AND HIP JOINTS.; [redacted]20[redacted] (RX DAY 251): PELVIS MRI: (1) A SYNOVIAL HERNIATION PIT AT THE RIGHT FEMORAL HEAD-NECK JUNCTION.(2) DEGENERATIVE CHANGE(S) AT BILATERAL HIP JOINTS. MILD SYNOVITIS AT THE RIGHT HIP JOINT.; [redacted]20[redacted] (RX DAY 303): X RAY, PELVIS FOR THR: NO VISIBLE GROSS FRACTURE. MILD OSTEOARTHRITIS. SUGGEST CLINICAL CORRELATION.SHOWED LOSS OF BIL HIP CARTILAGE (THICKNESS ONLY HALF OF CARTILAGE WHICH COMPARE WITH IMAGE ON [redacted] 20[redacted]); [redacted]20[redacted] (RX DAY 309): MRI OF THE LUMBER SPINE: SPINAL STENOSIS, L1 COMPRESSION FRACTURE; L4-5 HIVD; L2-3 RETROLISTHESIS.; [redacted]20[redacted] (RX DAY 372): SKELETAL MUSCLE SYSTEM ULTRASONIC EXAMINATION: 1.CORTICAL DESTRUCTION OF LEFT FEMORAL HEAD AND NECK. 2.AMORPHOUS HYPERECHOIC LESION WITH PARTIAL ACOUSTIC SHADOW AND HYPOECHOIC BULGING OF LEFT ANTERIOR HIP RECESS, WITHOUT GR.IIIVASCULARITY. PERIARTICULAR SOFT TISSUE CALCIFICATION WITH INFLAMMATION IS MOST LIKELY. HOWEVER MALIGNANCY SHOULD BE EXCLUDED FIRST.; [redacted]20[redacted] (RX DAY 378): PELVIS OF MRI: (1) STAGE III AVASCULAR NECROSIS AT RIGHT FEMORAL HEAD WITH MILD REACTIVE SYNOVITIS IN RIGHT HIP JOINT. A SYNOVIAL HERNIATION PIT AT THE RIGHT FEMORAL HEAD-NECK JUNCTION. (2) STAGE III-IV AVASCULAR NECROSIS AT THE LEFT FEMORAL HEAD WITH REACTIVE SYNOVITIS IN LEFT HIP JOINT. HOWEVER, SUPERIMPOSED SEPTIC ARTHRITIS IN LEFT HIP JOINT CAN NOT BE EXCLUDED.; [redacted]20[redacted] (RX DAY 392): X RAY,PELVIS FOR THR: MODERATE OSTEOARTHRITIS CHANGE WITH MARGINAL SPUR FORMATION AND JOINT SPACE NARROWING AT RIGHT HIP JOINT. DEFORMED LEFT FEMORAL HEAD, SUGGEST CLINICAL CORRELATION. MODERATE DEGENERATIVE CHANGE WITH MARGINAL SPUR FORMATION.; [redacted]20[redacted] (RX DAY 408): ECG: NORMAL SINUS RHYTHM.; RADIOGRAPHY OF CHEST P-A VIEW: NO DEFINITE ACTIVE LUNG LESION NORMAL HEART SIZE AND CONFIGURATION CLEAR BILATERAL COSTOPHRENIC ANGLES; RADIOGRAPHY OF LEFT HIP LATERAL: COLLAPSE OF LEFT FEMORAL HEAD DIMINISHED BILATERAL HIP JOINTS SPACE; RADIOGRAPHY OF LEFT PELVIS A-P VIEW: COMPRESSION FRACTURE OF LUMBAR1 BLUNTING OF RIGHT COSTOPHRENIC ANGLE; [redacted]20[redacted] (RX DAY 409): LEFT FEMORAL HEAD BONE PATHOLOGY REPORT: SHOW FIBRILLATION AND EROSION OF ARTICULAR CARTILAGE. ALSO SEEN A FEW NECROTIC BONY TRABECULAE. THE BONE MARROW SPACES SHOW FIBROSIS.; LEFT HIP JOINT REPLACEMENT SURGERY: TOTAL LEFT HIP JOINT REPLACEMENT FINDING: SYNOVIUM HYPERTROPHY, ARTICULAR CARTILAGE DESTRUCTION ON ACETABULUM AND FEMORAL HEAD. SUBCHONDRAL NECROSIS AND COLLAPSE ON FEMORAL HEAD.OSTEOPOROSIS; LEFT HIP JOINT SYNOVIUM PATHOLOGY REPORT: SHOW SYNOVIAL TISSUE WITH MILD CHRONIC INFLAMMATION.; [redacted]20[redacted] (RX DAY 492): CHEST POSTERIOR TO ANTERIOR VIEW, PLEVIS ANTERIOR TO POSTERIOR VIEW, RIGHT HIP LATERAL VIEW: SUSPECTED NODULAR OPACITY AT BILATERAL LOWER LUNG FIELD, DIFFERENTIAL DIAGNOSIS(DDX): LUNG NODULES.NO COSTOPHRENIC (C-P) ANGLE BLUNTING.NORMAL SIZE OF CARDIAC SHADOW. ATHEROSCLEROTIC CALCIFICATION OFAORTIC KNOB.MILD PLEURAL THICKENING AT BILATERAL APICAL LUNGS DIFFUSE OSTEOPENIA OF THE VISIBLE BONY STRUCTURE POST -SURGICAL(S/P) LEFT TOTAL HIP ARTHROPLASTY SURGERY.OSTEOARTHRITIS CHANGE AT RIGHTHIP JOINT SMALLCALCIFIED DENSITY AT BILATERAL PLEVIC CAVITY,RULE IN (R/I) VASCULAR CALCIFICATION OR URETERAL STONES; ECG RESTING: SINUS RHYTHM WITH OCCASIONAL PREMATURE VENTRICULAR COMPLEXES; [redacted]20[redacted] (RX DAY 493): RIGHT HIP JOINT REPLACEMENT: SYNOVIUM HYPERTROPHY, ARTICULAR CARTILAGE DESTRUCTION ON ACETABULUM AND FEMORAL HEAD, SUBCHONDRAL NECROSIS AND COLLAPSE ON FEMORAL HEAD AND ACETABULUM,OSTEOARTHRITIS; RIGHT HIP SYNOVIAL TISSUE PATHOLOGY REPORT: SYNOVIAL TISSUE WITH MILD HYPERPLASIA

AE Stopped Rx Day	493
Duration of AE	116 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SMOKING AND RECEIVING LOCAL TRIAMCINOLONE INJECTION WERE CONSIDERED AS CAUSE OF THE EVENT.
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: M15-572

治験責任医師からの報告。本被験者は台湾の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，冠動脈疾患の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，高血圧，高脂血症，肺気腫／慢性閉塞性肺疾患，マイコプラズマ感染及び現紙巻タバコ喫煙者（1 日 0.5 箱を 36 年間）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は冠動脈疾患を発現した。

被験者に冠動脈疾患の強い家族歴があったため，20[redacted] 年 [redacted] 月 [redacted] 日に CT 血管造影検査が行われた。被験者より，2 人の兄弟及び 1 人の姉妹に急性心筋梗塞の病歴があると報告された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。CT 血管造影検査所見は，重度の LAD 70%～99%狭窄であった。被験者はいつもどおりの健康状態にあり，胸痛，胸部絞扼感及び呼吸困難はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，冠血管造影が完了し，被験者は LAD（左下行前動脈）に対する単純旧式バルーン血管形成ステント留置術（POBAS）後の状態にあった。術後回復室にて，左肩に放射状に拡がる急性胸痛が出現した。心電図検査及び心エコー検査が行われ，ST 波及び T 波の異常が明らかとなった。同日，経過観察のために行われた心電図の再検査でも，同じ所見が認められた。放射状に拡がる胸痛は 1 時間以内に改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は安定状態で退院した。

投与された薬剤は，bokey EM 及びプラビックスであった。

The patient's past medications include:

DERMOVATE OINT for PSORIASIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Coronary artery disease (10011078) (Coronary artery disease (10011078)) [v.22.1] [10011078]

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 CORONARY ARTERIAL DISEASE

- Investigator: The event was not related to the study drug and angiography is a procedure and not a surgery because no incision and suture was needed.

- AbbVie: Event is more likely related to pre-existing hypertension, dyslipidemia and subject is a current smoker (0.5 ppd x 36 years).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ALANINE AMINO TRANSFERASE:** 25 U/L (normal 0 to 41)

[redacted] **BLOOD UREA NITROGEN:** 16.8 mg/dL (normal 7 to 25)

[redacted] **CHEST X-RAY:** NORMAL HEART SIZE. MILD AORTIC WALL CALCIFICATION. BILATERAL APICAL PLEURAL THICKENING. SHARP BILATERAL COSTOPHRENIC ANGLES.

[redacted] **CHOLESTEROL:** 147 mg/dL (normal 0 to 200)

[redacted] **CORONARY ANGIOGRAM:** CORONARY ANGIOGRAM S/P PLAIN OLD BALLOON ANGIOPLASTY WITH STENT (POBAS) TO LAD(LEFT ANTERIOR DESCENDING ARTERY).CORONARY ANGIOGRAPHY: LM: PATENT LAD: PROXIMAL STENOSIS 70 %, MIDDLE STENOSIS 70 % LCX: OSTIAL STENOSIS 50 %, HYPOPLASIA RCA: DISTAL STENOSIS 20 %

[redacted] **CREATININE:** 0.6 mg/dL (normal 0.6 to 1.3)

[redacted] **CT ANGIOGRAM:** AGATSTON SCORE: 646.91 CORONARY ARTERY: SEVERE (70%-99%) STENOSIS IN LEFT ANTERIOR DESCENDING ARTERY. MILD (25%-49%) STENOSIS IN RIGHT CORONARY ARTERY. VENTRICULAR FUNCTION: NORMAL.

[redacted] **ECG:** SINUS RHYTHM WITH PREMATURE VENTRICULAR COMPLEXES

[redacted] **ECG:** NORMAL SINUS RHYTHM ST & T WAVE ABNORMALITY, CONSIDER INFERIOR ISCHEMIA ABNORMAL ECG

[redacted] 20[redacted] **ECHOCARDIOGRAM:** MILD TO MODERATE MITRAL REGURGITATION AND MILD TRICUSPID REGURGITATION

[redacted] 20[redacted] **EGFR:** 106.0 ML/MIN/1.73 M^2

[redacted] 20[redacted] **EKG:** Normal

[redacted] 20[redacted] **HDL CHOLESTEROL:** 40 mg/dL (normal >40)

[redacted] 20[redacted] **HEMOGLOBIN:** 12.2 MG/L (normal 10.8 to 14.9)

[redacted] 20[redacted] **LDL CHOLESTEROL:** 86 mg/dL (normal <130)

[redacted] 20[redacted] **PLATELET COUNT:** 452 no units (normal 150 to 361)

[redacted] 20[redacted] **TRIGLYCERIDES:** 75 mg/dL (normal 0 to 150)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 10.79 k/µL (3.54~90.6
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は台湾の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，両側股関節の無腐性壊死の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，子宮摘出及び片側卵管卵巣摘除，高血圧，高脂血症，本態性振戦，末梢神経障害，本態性振戦，骨粗鬆症，肋骨骨折，変性脊椎症，脊髄症を伴う椎間板障害，筋膜疼痛症候群，脊髄症，マイコプラズマ感染，乾癬性関節炎，喫煙者（1 日 0.5 箱を 36 年間）並びに禁酒であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両側股関節の無腐性壊死を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，両側股関節の無腐性壊死は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日より被験者は左股関節痛を訴えており，捻挫及び徒手リハビリテーションによるものと報告された。状態が悪化し，両側股関節痛が出現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，X 線検査及び診察後，整形外科医により右股関節変形性関節症と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，骨盤 MRI 検査が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はトリアムシノロンの右股関節内注射を受

けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はトリアムシノロンの左股関節内注射を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，THR の骨盤 X 線の再検査が行われ，両側股関節軟骨消失が認められた（軟骨厚が 20[redacted] 年 [redacted] 月 [redacted] 日の画像と比べて半分しかなかった）。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はリウマチ専門医を受診した。股関節乾癬性関節炎が考えられた。同日，別の病院で腰椎 MRI 検査が行われ，脊柱管狭窄症，L1 の圧迫骨折，L4～L5 の HIVD 及び L2～L3 の後方すべり症が認められた。手術が勧められたが，被験者は手術を拒否し，整形外科及びリハビリテーションクリニックで治療を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は別の神経外科医を受診し，神経伝導検査が予定された。検査結果は正常で，手術は勧められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は骨格筋系の診察を受けるためリハビリテーション医を受診した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は整形外科医により股関節の無腐性壊死と診断され，左股関節置換術を受けることに同意した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は予定されていた手術のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，左股関節全置換術が行われた。この手術で，滑膜肥大，寛骨臼及び大腿骨頭の関節軟骨破壊，大腿骨頭崩壊，肋軟骨下壊死並びに骨粗鬆症が明らかとなった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日の骨盤 MRI 検査結果を受けて，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に右股関節手術のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，右股関節置換術が行われた。この手術で，滑膜肥大，寛骨臼及び大腿骨頭の関節軟骨破壊，肋軟骨下壊死，大腿骨頭及び寛骨臼の崩壊並びに変形性関節症が明らかとなった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は安定状態で退院した。

投与された薬剤は ultracet であった。

The patient's past medications include:

CLOBEX SHAMPOO 500 MCG/1 G for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DERMOVATE OINT 0.05% for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CONCOR for HYPERTENSION ([redacted] 20[redacted] - [redacted] 20[redacted])

ANCOGEN for LEFT HIP PAIN (Started [redacted] 20[redacted])

MIKELAN LA OPH SOLN 2% for BILATERAL GLAUCOMA ([redacted] 20[redacted] - [redacted] 20[redacted])

DEXT-SALINE 2.5%:0.45%(OTSUKA) for CORONARY ARTERIAL DISEASE S/P ([redacted] 20[redacted] - [redacted] 20[redacted])

POLICE CLEXANE 6000ANTI-XA for CORONARY ARTERIAL DISEASE S/P ([redacted] 20[redacted] - [redacted] 20[redacted])

SENNAPUR for CONSTIPATION (Stopped [redacted] 20[redacted])

CELEBREX for WORSENING LEFT HIP PAIN ([redacted] 20[redacted] - [redacted] 20[redacted])

WEIMOK F.C. for PROPHYLAXIS PAINKILLER SIDE EFFECT ([redacted] 20[redacted] - [redacted] 20[redacted])

TRIAMCINOLONE for WORSENING OSTEOARTHRITIS and BILATERAL HIP JOINTS DEGENERATE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

RIVOTRIL for WORSENING MYOFASCIAL PAIN ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Avascular necrosis (10066480) (Osteonecrosis (10031264)) [v.22.1] [10066480]

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 AVASCULAR NECROSIS OF BILATERAL HIP JOINTS

- Investigator: Smoking and receiving local triamcinolone injection were considered as cause of the event.

- AbbVie: Risk factor includes pre-existing psoriatic arthritis and intra-articular triamcinolone.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ACTIVATED PARTIAL THROMBOPLASTIN TIME:** 26.5 SEC (normal 24.6 to 33.8)

[redacted] **20[redacted] BASOPHILS %:** 0.5 % (normal 0 to 1)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 7.4 mg/dL (normal 6 to 21)

[redacted] **20[redacted] CREATININE:** 0.48 mg/dL (normal 0.44 to 1.0)

[redacted] **20[redacted] CRP:** 0.05 mg/dL (normal 0.1 to 0.3)

[redacted] **20[redacted] CRP:** 6.8 MG/L (normal 0 to 3)

[redacted] **20[redacted] CRP:** 14.12 MG/L (normal 0 to 5)

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

[redacted] **20[redacted] ECG:** resting: sinus rhythm with occasional premature ventricular complexes

[redacted] **20[redacted] EOSINOPHILS %:** 0.4 % (normal 0.3 to 7.9)

[redacted] **20[redacted] EOSINOPHILS %:** 1.6 % (normal 0.3 to 7.9)

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 12 mm/h (normal <20)

[redacted] **20[redacted] ESR:** 18 mm/h (normal 0 to 30)

[redacted] **20[redacted] HEMOGLOBIN:** 13.1 G/DL (normal 11.0 to 15.2)

[redacted] **20[redacted] HEMOGLOBIN:** 12..0 G/DL (normal 11.0 to 15.2)

[redacted] **20[redacted] HEMOGLOBIN:** 10.6 G/DL (normal 12 to 16)

[redacted] **20[redacted] INTERNATIONAL NORMALIZED RATIO:** 1.1 Ratio (normal 0 to 1.2)

[redacted] **20[redacted] LEFT FEMORAL HEAD BONE PATHOLOGY:** Fibrillation and erosion of articular cartilage. Also seen a few necrotic bony trabeculae. The bone marrow spaces show fibrosis.

[redacted] **20[redacted] LEFT HIP JOINT SYNOVIUM PATHOLOGY:** Synovial tissue with mild chronic inflammation.

[redacted] **20[redacted] LUMBAR MRI:** Spinal stenosis, L1 compression fracture; L4-5 herniated intervertebral disk; L2-3 retrolisthesis.

[redacted] **20[redacted] LYMPHOCYTES %:** 28.8 % (normal18.0 to 48.8)

[redacted] **20[redacted] LYMPHOCYTES %:** 21.8 % (normal 18.0 to 48.8)

[redacted] **20[redacted] MONOCYTES %:** 7.4 % (normal 0 to 12)

[redacted] **20[redacted] MRI OF PELVIS:** 1. A synovial herniation pit at the right femoral head-neck junction. Degenerative change(s) at bilateral hip joints. 2. Mild synovitis at the right hip joint.

[redacted] **20[redacted] MRI OF PELVIS:** 1) Stage III avascular necrosis at right femoral head with mild reactive synovitis in right hip joint. A synovial herniation pit at the right femoral head-neck junction. 2) Stage III-IV avascular necrosis at the left femoral head with reactive synovitis in left hip joint. However, superimposed septic arthritis in left hip joint can not be excluded.

[redacted] **20[redacted] NEUTROPHILS %:** 64.5 % (normal 41.6 to 74.4)

[redacted] **20[redacted] NEUTROPHILS %:** 68.7 % (normal 41.6 to 74.4)

[redacted] **20[redacted] PLATELET COUNT:** 358 X10**3/MCL (normal 150 to 378)

[redacted] **20[redacted] PLATELET COUNT:** 241 X10**3/MCL (normal 150 to 378)

[redacted] **20[redacted] POTASSIUM:** 4.2 MEQ/L (normal 3.6 to 5.0)

[redacted] **20[redacted] PROTHROMBIN TIME:** 11.8 SEC (normal 8 to 12)

[redacted] **20[redacted] RADIOGRAPHY OF CHEST PA VIEW:** No definite active lung lesion; Normal heart size and configuration; Clear bilateral costophrenic angles.

[redacted] **20[redacted] RADIOGRAPHY OF LEFT HIP:** Collapse of left femoral head diminished bilateral hip joints space.

[redacted] **20[redacted] RADIOGRAPHY OF LEFT PELVIS AP VIEW:** Compression fracture of lumbar1 blunting of right costophrenic angle.

[redacted] **20[redacted] RIGHT HIP SYNOVIAL TISSUE PATHOLOGY:** synovial tissue with mild hyperplasia

[redacted] **20[redacted] SKELETAL MUSCLE SYSTEM ULTRASONIC EXAMINATION:** 1. Cortical destruction of left femoral head and neck. 2.amorphous hyperechoic lesion with partial acoustic shadow and hypoechoic bulging of left anterior hip recess, without GR.IIIVASCULARITY. Periarticular soft tissue calcification with inflammation is most likely. However, malignancy should be excluded first.

[redacted] **20[redacted] SODIUM:** 142 MEQ/L (normal 134 to 148)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.42 X10**3/MCL (normal 3.25 to 9.16)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.3 X10**3/MCL (normal 3.25 to 9.16)

[redacted] **20[redacted] X RAY, PELVIS FOR THR:** Phleboliths in the pelvic cavity. Degenerative arthrosis of bilateral sacroiliac and hip joints. **A synovial Herniation pit at the right femoral head-neck junction. Degenerative change(s) at bilateral hip joints. 2.mild synovitis at the right hip joint.

[redacted] **20[redacted] X RAY, PELVIS FOR THR:** NO VISIBLE GROSS FRACTURE. MILD OSTEOARTHRITIS. SUGGEST CLINICAL CORRELATION. Showed loss of bil hip cartilage (thickness only half of cartilage which compare with image on [redacted] 20[redacted]).

[redacted] **20[redacted] X-RAY:** Chest Posterior to Anterior View, pelvis Anterior to Posterior view, right hip lateral view: suspected nodular opacity at bilateral lower lung field, differential diagnosis(DDx): lung nodules. No costophrenic (C-P) angle blunting. Normal size of cardiac shadow. Atherosclerotic calcification of aortic knob. Mild pleural thickening at bilateral apical lungs diffuse osteopeniaof the visible bony structure Post - surgical(S/P) left total hip arthroplasty surgery. Osteoarthritis change at right hip joint Small calcified density at bilateral pelvic cavity, rule in (R/I) vascular calcification or ureteral stones

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	6[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: CHICKEN POX	19[redacted]
CLOTTING/BLEEDING PROBLEMS: VON WILLEBRAND'S DISEASE	20[redacted]
OTHER: TENDINITIS	20[redacted]
OTHER: THROMBOCYTOPENIA	20[redacted]
OTHER: BRONCHITIS	20[redacted]
OTHER: LEUKOCYTOCLASTIC VASCULITIS	20[redacted]
OTHER: TINEA CORPORIS	20[redacted]
OTHER: ECZEMA	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: TINEA CRURIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: COUGH	20[redacted]
OTHER: SORE THROAT	20[redacted]

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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 167	167

ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / [redacted]20[redacted] / 391	224	
				168		
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 392		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CILOSTAZOL	50 mg	BID	Y-M: 20[redacted]
GINKGO BILOBA	9.6 mg	BID	Y-M: 20[redacted]
DIFLUCORTOLONE	0.1 %	BID	Y-M: 20[redacted] / -232
BETAMETHASONE	0.06 %	BID	Y-M: 20[redacted] / -225
BETAMETHASONE	0.64 OTHER: MG/G	QD	Y-M: 20[redacted] / -218
DICLOFENAC	75 mg	QD	Y-M: 20[redacted] / -147
BETAMETHASONE W/CALCIPOTRIOL	0.05/0.005 OTHER: %/%	QD	Y-M: 20[redacted] / -127
CELECOXIB	200 mg	QD	Y-M: 20[redacted] / -127
CLOBETASOL	0.5 OTHER: MG/GM	QD	Y-M: 20[redacted] / -127
BETAMETHASONE	0.06 %	BID	Y-M: 20[redacted] / -106
BETAMETHASONE W/CALCIPOTRIOL	50/500 OTHER: MCG/MCG	QD	Y-M: 20[redacted] / -106
CELECOXIB	200 mg	OTHER: BIDPRN	Y-M: 20[redacted] / -106
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -106
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -106
METHYLPREDNISOLONE	4 mg	BID	Y-M: 20[redacted] / -71
ULTRACET	37.5/325 OTHER: MG/MG	BID	Y-M: 20[redacted] / -71
BETAMETHASONE	0.06 %	BID	Y-M: 20[redacted] / -57
BETAMETHASONE W/CALCIPOTRIOL	50/500 OTHER: MCG/MCG	QD	Y-M: 20[redacted] / -57
CLOBETASOL	0.5 OTHER: MG/GM	QD	Y-M: 20[redacted] / -57
DIFLUCORTOLONE	0.1 %	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
CILOSTAZOL	50 mg	BID	Y-M: 20[redacted]	NOT REPORTED
GINKGO BILOBA	9.6 mg	BID	Y-M: 20[redacted]	NOT REPORTED
CELECOXIB	200 mg	OTHER: BIDPRN	Y-M: 20[redacted] / -106	NOT REPORTED
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -106	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -106	NOT REPORTED
BUTENAFINE	1/10 OTHER: %/G	QD	Y-M: 20[redacted] / 224	NOT REPORTED
METHYLPREDNISOLONE	4 mg	OTHER: QDPRN	Y-M: 20[redacted] / 252	NOT REPORTED
ACETYLCYSTEINE	66.7 mg	OTHER: TIDPRN	Y-M: 20[redacted] / 308	NOT REPORTED

ULTRACET	37.5/325 OTHER: MG/MG	OTHER: BIDPRN	Y-M: 20[redacted] / 308	NOT REPORTED
AZELAIC ACID	20 %	BID	Y-M: 20[redacted] / 343	NOT REPORTED
CHLORAMPHENICOL	0.25 %	QID	Y-M: 20[redacted] / 343	NOT REPORTED
MINOCYCLINE	200 mg	OTHER: Q12H	Y-M: 20[redacted] / 350	NOT REPORTED
ETOFENAMATE	10 %	TID	Y-M: 20[redacted] / 392	NOT REPORTED
DEXTROMETHORPHAN;LYSOZYME;POTASSIUM CRESOLSUL	20/90/20 OTHER: MG/MG/MG	TID	Y-M: 20[redacted] / 532	Y-M: 20[redacted] / 534
ACICLOVIR	500 mg	OTHER: Q8H	Y-M: 20[redacted] / 532	Y-M: 20[redacted] / 537
SODIUM CHLORIDE	0.9 %	QD	Y-M: 20[redacted] / 532	Y-M: 20[redacted] / 537
ULTRACET	37.5/325 OTHER: MG/MG	OTHER: Q6HPRN	Y-M: 20[redacted] / 532	Y-M: 20[redacted] / 537
ACETYLCYSTEINE	200 mg	TID	Y-M: 20[redacted] / 534	Y-M: 20[redacted] / 537
PREGABALIN	75 mg	OTHER: BIDPRN	Y-M: 20[redacted] / 537	Y-M: 20[redacted] / 540
VALACICLOVIR	1000 mg	OTHER: Q8H	Y-M: 20[redacted] / 537	Y-M: 20[redacted] / 540
ALUMINIUM HYDROXIDE	300 mg	TID	Y-M: 20[redacted] / 541	NOT REPORTED
CHLORPHENAMINE;GLYCYRRHIZA SPP.;OROTIC ACID	2.5/50/30 OTHER: MG/MG/MG	TID	Y-M: 20[redacted] / 541	NOT REPORTED
PARACETAMOL	500 mg	TID	Y-M: 20[redacted] / 541	NOT REPORTED
TETRACYCLINE	250 mg	TID	Y-M: 20[redacted] / 541	NOT REPORTED
CALAMINE	375 mL	TID	Y-M: 20[redacted] / 544	Y-M: 20[redacted] / 545
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted] / 545	NOT REPORTED
OPIUM ALKALOIDS AND DERIVATIVES	0.24/0.5/0.15/15 OTHER: MG/MG/MG/MG	QID	Y-M: 20[redacted] / 545	Y-M: 20[redacted] / 589
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / 546	Y-M: 20[redacted] / 549
METHYLPREDNISOLONE	4 mg	BID	Y-M: 20[redacted] / 546	Y-M: 20[redacted] / 549
BROEN-C	20000/20 OTHER: U/L/MG	TID	Y-M: 20[redacted] / 553	NOT REPORTED

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

Event Description	HERPES ZOSTER(RIGHT SIDE CHEST WALL)(RIGHT T4-T6 DERMATOME)
Preferred term	帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 528
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 532): CHEST X-RAY: NO INTERVAL CHANGE COMPARED TO CXR, PERFORMED ON 2019.07.03

AE Stopped Rx Day	553
Duration of AE	26 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は台湾の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，帯状疱疹（右側胸壁）（右 T4～T6 の皮膚分節）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎及び帯状疱疹であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹（右側胸壁）（右 T4～T6 の皮膚分節）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹（右側胸壁）（右 T4～T6 の皮膚分節）は消失した。

本事象発現前，20[redacted] 年 [redacted] 月，被験者は単純ヘルペス（非重篤な事象）（下唇及び左口角）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，右胸部の水疱を伴う皮疹のため 5 日間入院した。発熱はなく，病変部のかゆみや痛みもなかった。水疱を伴う皮疹は右 T4～T6 の皮膚分節に及んでおり，病歴及び身体的診察の結果に基づき帯状疱疹と診断された。本事象によりメトトレキサート及び治験薬が中止され，診断のための臨床検査及び画像検査が行われた。アシクロビルの静脈内投与が行われ，右 T4～T5 の紅斑性丘疹は治まり，小水疱の集まりがいくつか形成され，色素沈着が見られた。このほかにも軽度の右胸痛が出現し，帯状疱疹後神経痛に対して必要に応じて服用するリリカが追加で処方された。被験者は状態が改善し，20[redacted] 年 [redacted] 月 [redacted] 日に退院した。被験者に帯状疱疹ワクチン接種歴はなかった。

投与された薬剤は，アシクロビル，塩化ナトリウム，バラシクロビル，プレガバリン，アセトアミノフェン，weil，テトラサイクリン及び orotoretin であった。

The patient's past medications include:

STEROIDS for LEUKOCYTOCLASTIC VASCULITIS (20[redacted] - 20[redacted])

NERISONE for PSORIASIS and PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON-V for PSORIASIS and PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

SEPTON SOL-GEL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MEITIFEN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BETAMETHASONE/CALCIPOTRIOL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CLOBESTASOL SHAMPOO for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

BETAMETHASONE DIPROPIONATE W/CALCIPOTRIOL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ACYCLOVIR for HERPES SIMPLEX (LOWER LIP & LEFT MOUTH ANGLE) ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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 HERPES ZOSTER(RIGHT SIDE CHEST WALL)(RIGHT T4-T6 DERMATOME)

- Investigator: Not applicable.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CXR:** NO INTERVAL CHANGE COMPARED TO CXR, PERFORMED ON 20[redacted].[redacted].[redacted]

[redacted] **20[redacted] SKIN BIOPSY:** Leukocytoclastic vasculitis

[redacted] **20[redacted] SKIN BIOPSY:** Psoriasis

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
出血性十二指腸潰瘍	X			
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	6[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: POST-MENOPAUSAL	20[redacted]
DIABETES MELLITUS	20[redacted]
HYPERTENSION	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 399	231
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 400		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LOSARTAN	50 mg	OTHER: HS	Y-M: 20[redacted]
VELMETIA	50/500 OTHER: MG/MG	QD	Y-M: 20[redacted]
BETAMETHASONE W/CALCIPOTRIOL	50/0.5 OTHER: MCG/MG	QD	Y-M: 20[redacted] / -217
BETAMETHASONE W/CALCIPOTRIOL	50/0.5 OTHER: UG/MG	QD	Y-M: 20[redacted] / -217
CLOBETASOL	500 OTHER: UG/G	QD	Y-M: 20[redacted] / -217
DESLORATADINE	5 mg	QD	Y-M: 20[redacted] / -217
DIFLUCORTOLONE	0.1 %	BID	Y-M: 20[redacted] / -217
ETORICOXIB	60 mg	QD	Y-M: 20[redacted] / -168
ETORICOXIB	60 mg	OTHER: QDPRN	Y-M: 20[redacted] / -133
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -133
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -133
ULTRACET	37.5/325 OTHER: MG/MG	OTHER: BIDPRN	Y-M: 20[redacted] / -105
BETAMETHASONE	0.64 OTHER: MG/G	QD	Y-M: 20[redacted] / -77

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LOSARTAN	50 mg	OTHER: HS	Y-M: 20[redacted]	NOT REPORTED
VELMETIA	50/500 OTHER: MG/MG	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -133	Y-M: 20[redacted] / 46
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -133	Y-M: 20[redacted] / 46
ULTRACET	37.5/325 OTHER: MG/MG	OTHER: BIDPRN	Y-M: 20[redacted] / -105	Y-M: 20[redacted] / 46
PROPRANOLOL	10 mg	OTHER: TIDPRN	Y-M: 20[redacted] / 15	NOT REPORTED
ACETYLCYSTEINE	200 mg	TID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 36
BROWN MIXTURE	0.12/0.12/0.24 OTHER: ML/ML/MG	TID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 36
CEFTRIAXONE	1000 mg	OTHER: Q6H	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
DEXTROMETHORPHAN	30 mg	QID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
IPRATROPIUM	0.5 mg	TID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
MEFENAMIC ACID	500 mg	PRN	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52
TERBUTALINE	5 mg	TID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 52

ACETYLCYSTEINE	100 mg	QID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 53
ACTIFED	2.5 mg	QID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 53
ALPRAZOLAM	0.5 mg	OTHER: STAT	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 53
CODEINE W/TERPIN HYDRATE	5/10 OTHER: MG/MG	QID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 55
FENOFIBRATE	160 mg	QD	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 55
MUCITERAN	200/2.8 OTHER: MG/G	QID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 55
THEOPHYLLINE	125 mg	TID	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 55
EPRAZINONE	20 mg	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
LEVOCETIRIZINE	5 mg	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
MEFENAMIC ACID	250 mg	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
MEQUITAZINE	2.5 mg	BID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
OXOLAMINE	100 mg	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
PARACETAMOL	500 mg	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
PREDNISOLONE	2.5 mg	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
STOMACAIN	5/100 OTHER: MG/MG	TID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
CLARITHROMYCIN	250 mg	BID	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 75
ACETYLCYSTEINE	200 mg	TID	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 168
ULTRACET	37.5/325 OTHER: MG/MG	OTHER: BIDPRN	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 168
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 308
SALACTOL	167/167 OTHER: MG/G	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 141
LEFLUNOMIDE	10 mg	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 399
HUMAN MIXTARD	8 OTHER: U	QD	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 337
DEXTROSE AND SODIUM CHLORIDE INJECTION	1000 mg	QD	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 339
PANTOPRAZOLE	40 mg	OTHER: Q6H	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 339
GLUCOSE	500 mg	QD	Y-M: 20[redacted] / 338	Y-M: 20[redacted] / 338
HUMAN MIXTARD	10 OTHER: U	QD	Y-M: 20[redacted] / 338	Y-M: 20[redacted] / 338

DEXTROSE AND SODIUM CHLORIDE INJECTION	500 mg	QD	Y-M: 20[redacted] / 338	Y-M: 20[redacted] / 340
HUMAN MIXTARD	4 OTHER: U	QD	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 340
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted] / 340	NOT REPORTED
RABEPRAZOLE	20 mg	OTHER: QDAC	Y-M: 20[redacted] / 400	NOT REPORTED
LEFLUNOMIDE	10 mg	OTHER: QOD	Y-M: 20[redacted] / 400	Y-M: 20[redacted] / 483
LEFLUNOMIDE	10 mg	OTHER: BIW	Y-M: 20[redacted] / 484	NOT REPORTED

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

Event Description	ACUTE PNEUMOIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 52
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 52): Glucose: 3+ [82.8724 - 115.3008] mg/dL; NPTST129-C-REACTIVE PROTEIN: 3.4 [0 - 1] MG/DL; NPTST181-COLD HEMAGGLUTININ: 128 X [NOT REPORTED - NOT REPORTED] NA; NPTST251-EPSTEIN-BARR VIRUS CAPSID ANTIG: + [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST516-PNEUMOCOCCUS RAPID SCREEN: - [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 53): NPTST462-MYCOPLASMA PNEUMONIA AB TEST: + [NOT REPORTED - NOT REPORTED] NA

Microbiology

[redacted]20[redacted] (RX DAY 52): BLOOD NPTST026-AEROBIC BLOOD CULTURE: Negative-NA; SPUTUM NPTST607-SPUTUM CULTURE: Positive-KLEBSIELLA TERRIGENA

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 52): BLOOD PRESSURE: 159/88MMHG; CHEST X-RAY: PROMINENT LUNG MARKINNG.; TEMPERATURE: 37.7C

AE Stopped Rx Day	92
Duration of AE	41 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #4: Serious Adverse Event

Event Description	DUODENAL ULCER WITH BLEEDING
Preferred term	出血性十二指腸潰瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 336
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 336): Blood: 4+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 112 [108 - 149] G/L; [redacted]20[redacted] (RX DAY 337): Hemoglobin: 90 [108 - 149] G/L; [redacted]20[redacted] (RX DAY 338): Hemoglobin: 109 [108 - 149] G/L; [redacted]20[redacted] (RX DAY 342): Hemoglobin: 106 [108 - 149] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 336): KINEY URETERAL BLADDER X-RAY: STOOL IMPACTION OVER SMALL BOWEL AND ASCENDING COLON.; PENDOSCOPE: DUODENAL ULCERS; [redacted]20[redacted] (RX DAY 337): BLOOD PRESSURE: 116/75 MMHG; BLOOD TRANSFUSION: BLOOD TRANSFUSION WITH PRBC WAS APPLIED, HB 10.9

AE Stopped Rx Day	342
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PEPTIC ULCERS
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: M15-572

治験責任医師からの報告。本被験者は台湾の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性肺炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，閉経後，糖尿病，高血圧，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

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

本事象発現前，咳嗽が 3 ヵ月間にわたって出現と消失を繰り返していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性呼吸器感染（非重篤）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，急性呼吸器感染により治験薬の投与が休止された。

20[redacted] 年 [redacted] 月 [redacted] 日，出現と消失を繰り返す咳嗽及び発熱を伴って，黄色痰が認められた。症状が持続して悪化したため，被験者は外来診療科に搬送された。その他の所見は，咽喉痛，両

側ラ音，心拍正常で雑音なし，腹部軟，腸音正常，急性症状ありであった。今回は，被験者はさらなる治療及び管理のため同日入院した。20[redacted] 年 [redacted] 月 [redacted] 日，マイコプラズマ肺炎 AB 検査の結果は陽性であった。静脈内輸液が投与されたほか，高熱，脱力及び摂取不足に対し B12 補給が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は周囲の騒音を訴え，医師の指示に反して退院した。

投与された薬剤は，コデイン酸塩／terpin hydrate，アセチルシステイン／精製白糖，テオフィリン，クラリスロマイシン，プレドニゾロン，panadol，メフェナム酸，エプラジノン塩酸塩，oxolamine，オキセサゼイン／ケイ酸アルミニウム，レボセチリジン塩酸塩，ロセフィン，メジコン，fluimucil，actifed，scanol，ponstan F.C.，butanyl，ビタミン B12，アトロベントネブライザー，xanax，lipanthyl，カンゾウエキス/opiumtincture／antimony potassium tartrate，cardolol 及びメキタジンであった。

The patient's past medications include:

ARCOXIA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] Jun 20[redacted], [redacted] Jun 20[redacted] - [redacted] 20[redacted])

TRAMADOL HCL/ACETAMINOPHEN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute pneumonia (10066724) (Pneumonia (10035664)) [v.22.1] [10066724]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE PNEUMONIA

- Investigator: Not Applicable.

- AbbVie: Not Applicable.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] BLOOD EPSTEIN-BARR VIRUS CAPSID ANTIGEN IGG:** Positive

[redacted] **20[redacted] BLOOD PRESSURE:** 159/88 mmHg

[redacted] **20[redacted] BODY TEMPERATURE:** 37.7 Degrees C

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 3.4 mg/dL (normal 0 to 1)

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

[redacted] **20[redacted] CHEST X-RAY:** prominent lung marking

[redacted] **20[redacted] COLD HEMAGGLUTININ:** 128 X (normal 0 X to 16 X)

[redacted] **20[redacted] MYCOPLASMA PNEUMONIA AB TEST:** positive

[redacted] **20[redacted] PNEUMOCOCCUS RAPID SCREEN:** Negative

[redacted] **20[redacted] SPUTUM CULTURE:** Klebsiella Terrigena - Positive

[redacted] **20[redacted] URINE GLUCOSE:** 3 + mg/dL
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は台湾の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，出血を伴う十二指腸潰瘍の事象を発現した。

Event 4 の臨床経過：

関連する病歴は，閉経後，糖尿病，高血圧，局面型乾癬，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年[redacted] 月[redacted] 日であった。

20[redacted] 年[redacted] 月[redacted] 日，被験者は出血を伴う十二指腸潰瘍を発現した。20[redacted] 年[redacted] 月[redacted] 日，出血を伴う十二指腸潰瘍は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，心窩部痛，タール様便，浮動性めまい及び冷汗のため救急治療室に搬送された。被験者によればコーヒー残渣様吐物は見られなかった。被験者はさらなる評価のため入院した。腎，尿管，膀胱 X 線検査，内視鏡検査及び臨床検査が行われた。胃腸専門医による治療は，急性出血状態下での絶食（NPO）及び静脈内輸液投与であった。20[redacted] 年 [redacted] 月 [redacted] 日，胃腸出血を抑えるため，高用量プロトンポンプ阻害薬（Pantoloc）3 日間の投与が開始された。同日，貧血（非重篤）のため輸血（濃厚赤血球）も行われた。胃腸症状が治まった後，20[redacted] 年 [redacted] 月 [redacted] 日に清澄流動食が開始され，その翌日には軟食が開始された。被験者はこの食事に十分耐えることができた。胃腸症状を抑えるための Pantoloc 静脈内投与がタケプロン経口投与に変更された。退院時，患者によると腹痛並びにタール便及び／又は黒色便はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は比較的安定した状態で退院した。

投与された薬剤は，ヒューマリン，濃厚赤血球，ブドウ糖 5%／塩化ナトリウム 0.45%，タケプロン，pantoloc 及びブドウ糖 5%であった。

The patient's past medications include:

CALCIPOTRIOL /BETAMETHASONE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CLOBETASOL PROPIONATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DENOSIN FC for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DIFLUCORTOLONE VALERATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ARCOXIA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

FOLIC ACID for PROPHYLAXIS TO MTX TOXICITY ([redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TRAMADOL HCL/ACETAMINOPHEN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BETAMETHASONE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Duodenal ulcer bleeding (10071802) (Duodenal ulcer haemorrhage (10013839)) [v.22.1] [10071802]

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 DUODENAL ULCER WITH BLEEDING

- Investigator: PEPTIC ULCERS

- AbbVie: Event is not consistent with study drug's mechanism of action.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BLOOD PRESSURE:** 116/75 mmHg

[redacted] **BODY TEMPERATURE:** 35.7 Degrees C

[redacted] **ENDOSCOPY:** duodenal ulcers, Forrest Ib status post endoscopic hemostasis

[redacted] **GLASGOW COMA SCALE:** 4/5/6

[redacted] **HEART RATE:** 110 /min

[redacted] **HEMOGLOBIN:** 11.2 G/DL (normal 10.8 to 14.9)

[redacted] **HEMOGLOBIN:** 9.0 G/DL (normal 10.8 to 14.9)

[redacted] **HEMOGLOBIN:** 10.9 G/DL (normal 10.8 to 14.9)

[redacted] **HEMOGLOBIN:** 10.6 G/DL (normal 10.8 to 14.9)

[redacted] **KUB X-RAY:** stool impaction over small bowel and ascending colon

[redacted] **OXYGEN SATURATION:** 99 %

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

[redacted] **STOOL ANALYSIS:** Blood - 4+

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
粉砕骨折	X			
上腕骨骨折	X			
発熱	X	X		

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	5[redacted]	MALE	ASIAN

Medical History	Onset Year
EYE DISEASE/DISORDER: IRITIS	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
HYPERTENSION	20[redacted]
OSTEOARTHRITIS: OSTEOARTHRITIS KNEES	20[redacted]
OTHER: CERVICO-LUMBAR SYNDROME	20[redacted]
OTHER: HYPOPROTEINEMIA	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
BENIGN PROSTATIC HYPERPLASIA	20[redacted]
NEPHROLITHIASIS	20[redacted]
OTHER: CERVICAL SPINE BONE HYPERPLASIA	20[redacted]
OTHER: FATTY LIVER	20[redacted]
OTHER: HYPERURICEMIA	20[redacted]
OTHER: TB LATENT INFECTION	20[redacted]
OTHER: HEMATURIA	20[redacted]
OTHER: PROTEINURIA	20[redacted]

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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted] / 1	[redacted] / 166	166
ABT-494	30 MG	ORAL	QD	[redacted] / 167	[redacted] / 283	117

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DEXAMETHASONE	NOT REPORTED	PRN	Y-M: [redacted]
CALCIPOTRIOL	NOT REPORTED	QD	Y-M: [redacted]
FLUTICASONE	NOT REPORTED	QD	Y-M: [redacted]
POLICRESULEN	NOT REPORTED	QD	Y-M: [redacted]
CELECOXIB	0.2 g	BID	Y-M: [redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: [redacted]
VALSARTAN	80 mg	QD	Y-M: [redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: [redacted]
CELECOXIB	0.2 g	OTHER: QN	Y-M: [redacted] / -39
LEVAMLODIPINE	2.5 mg	QD	Y-M: [redacted] / -24
ISONIAZID	0.3 g	QD	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
FOLIC ACID	5 mg	EVERY WEEK	Y-M: [redacted]	Y-M: [redacted] / 285
METHOTREXATE	15 mg	EVERY WEEK	Y-M: [redacted]	Y-M: [redacted] / 285
CELECOXIB	0.2 g	OTHER: QN	Y-M: [redacted] / -39	Y-M: [redacted] / 285
LEVAMLODIPINE	2.5 mg	QD	Y-M: [redacted] / -24	Y-M: [redacted] / 285
ISONIAZID	0.3 g	QD	Y-M: [redacted] / -14	Y-M: [redacted] / 285
BUPRENORPHINE	5 mg	OTHER: ST	Y-M: [redacted] / 136	Y-M: [redacted] / 136
FLURBIPROFEN	5 mL	BID	Y-M: [redacted] / 136	Y-M: [redacted] / 139
UNSPECIFIED HERBAL	25 mL	OTHER: QOD	Y-M: [redacted] / 136	Y-M: [redacted] / 142
ESCIN	15 mg	QD	Y-M: [redacted] / 136	Y-M: [redacted] / 146
HEPARIN	0.6 mL	QD	Y-M: [redacted] / 136	Y-M: [redacted] / 146
LEKOVIT CA	3 g	BID	Y-M: [redacted] / 136	Y-M: [redacted] / 288
LEKOVIT CA	0.6 g	QD	Y-M: [redacted] / 146	ONGOING

UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	0.15 g	QD	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 167
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	0.5 g	QD	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 167
PIPERACILLIN W/SULBACTAM	3.0 g	BID	Y-M: 20[redacted] / 285	Y-M: 20[redacted] / 289
IBUPROFEN	0.3 g	OTHER: ST	Y-M: 20[redacted] / 289	Y-M: 20[redacted] / 289
SULFAMETHOXAZOLE	2 OTHER: TABLETS	OTHER: ONCE	Y-M: 20[redacted] / 289	Y-M: 20[redacted] / 289
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / 289	Y-M: 20[redacted] / 297
SOLUTIONS AFFECTING THE ELECTROLYTE BALANCE	500 mL	QD	Y-M: 20[redacted] / 289	Y-M: 20[redacted] / 321
ATORVASTATIN	20 mg	OTHER: QN	Y-M: 20[redacted] / 290	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 290	ONGOING
SODIUM BICARBONATE	0.5 g	TID	Y-M: 20[redacted] / 290	ONGOING
BACTRIM	3 OTHER: PILL	OTHER: Q6H	Y-M: 20[redacted] / 290	Y-M: 20[redacted] / 305
SODIUM BICARBONATE	0.5 g	TID	Y-M: 20[redacted] / 290	Y-M: 20[redacted] / 321
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 290	Y-M: 20[redacted] / 371
IBUPROFEN	0.3 g	OTHER: ST	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 291
BATILOL	40 mg	TID	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 310
LEUCOGEN	20 mg	TID	Y-M: 20[redacted] / 291	Y-M: 20[redacted] / 310
GLYCYRRHIZA GLABRA	40 mL	QD	Y-M: 20[redacted] / 293	Y-M: 20[redacted] / 302
AMINO ACIDS	250 mL	QD	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 321
DOMPERIDONE	10 mg	TID	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 321
GRANULOCYTE COLONY STIMULATING FACTOR	0.5 mL	OTHER: ST	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 298
SODIUM CHLORIDE	1 OTHER: CAPSULE	PRN	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 310
SUCRALFATE	1 g	BID	Y-M: 20[redacted] / 300	Y-M: 20[redacted] / 364
TRAMADOL	0.1 g	OTHER: ST	Y-M: 20[redacted] / 302	Y-M: 20[redacted] / 302
ESCIN	10 mg	QD	Y-M: 20[redacted] / 302	Y-M: 20[redacted] / 303
ISONIAZID	0.3 g	QD	Y-M: 20[redacted] / 303	ONGOING
GRANULOCYTE COLONY STIMULATING FACTOR	200 ug	OTHER: ST	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 303

INOSINE	0.2 g	TID	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 308
INTRALIPID	250 mL	QD	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 312
SULFAMETHOXAZOLE	2 OTHER: TABLETS	QD	Y-M: 20[redacted] / 306	ONGOING
GRANULOCYTE COLONY STIMULATING FACTOR	200 ug	OTHER: ST	Y-M: 20[redacted] / 306	Y-M: 20[redacted] / 306
SULFAMETHOXAZOLE	2 OTHER: TABLE	OTHER: PO QOD	Y-M: 20[redacted] / 306	Y-M: 20[redacted] / 351
GRANULOCYTE COLONY STIMULATING FACTOR	200 ug	OTHER: ST	Y-M: 20[redacted] / 307	Y-M: 20[redacted] / 307
ETHAMBUTOL	0.75 g	QD	Y-M: 20[redacted] / 308	ONGOING
GLYCYRRHIZIC ACID	100 mg	TID	Y-M: 20[redacted] / 308	ONGOING
GRANULOCYTE COLONY STIMULATING FACTOR	0.5 mL	OTHER: ST	Y-M: 20[redacted] / 308	Y-M: 20[redacted] / 308
RIFAMPICIN	450 mg	QD	Y-M: 20[redacted] / 308	Y-M: 20[redacted] / 309
IBUPROFEN	7 mL	OTHER: ST	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 309
SULFAMETHOXAZOLE	2 OTHER: TABLETS	OTHER: Q6H	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 310
RIFAMPICIN	0.6 g	QD	Y-M: 20[redacted] / 310	ONGOING
ALBUMIN HUMAN	50 mL	OTHER: ST	Y-M: 20[redacted] / 310	Y-M: 20[redacted] / 312
LEVOFLOXACIN	0.5 g	QD	Y-M: 20[redacted] / 310	Y-M: 20[redacted] / 332
IBUPROFEN	7 mL	OTHER: ST	Y-M: 20[redacted] / 311	Y-M: 20[redacted] / 311
LIDOCAINE	5 mL	OTHER: ST	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 312
ALBUMIN HUMAN	50 mL	OTHER: ST	Y-M: 20[redacted] / 315	Y-M: 20[redacted] / 315
ASCORBIC ACID	0.1 g	TID	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 333
CALCIUM DOBESILATE	1 g	BID	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 339
TROXERUTIN	120 mg	TID	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 339
CALCITRIOL	0.25 ug	QD	Y-M: 20[redacted] / 323	ONGOING
DIGNOWELL	UN OTHER: UN	OTHER: UN	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 333
CALCIPOTRIOL	UN OTHER: UN	BID	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 345
YIN XIE JIAO NANG	1.8 g	TID	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 350
PYRAZINAMIDE	1.5 g	QD	Y-M: 20[redacted] / 333	ONGOING

BENZBROMARONE	50 mg	QD	Y-M: 20[redacted] / 357	Y-M: 20[redacted] / 388
INOSINE	0.2 g	TID	Y-M: 20[redacted] / 371	ONGOING

Event #1: Serious Adverse Event

Event Description	MIDDLE AND LOWER COMMINUTED FRACTURE OF THE RIGHT TIBIA (AO43-A1 TYPE), MIDDLE RIGHT UPPER HUMERUS FRACTURE (AO 41-A1 TYPE)
Preferred term	粉砕骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 135
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 136): Eosinophils: 0.04 [0.05 - 0.5] 10^9/L; Hematocrit: 0.37 [0.37 - 0.5] FRACTION OF 1; Hemoglobin: 128 [120 - 160] G/L; Leukocytes: 7.4 [4 - 10] 10^9/L; Lymphocytes: 0.75 [1.5 - 4] 10^9/L; Lymphocytes/Leukocytes: 10.1 [20 - 40] %; Monocytes: 0.68 [0 - 0.45] 10^9/L; Monocytes/Leukocytes: 9.2 [3 - 8] %; NPTST511-PHOSPHORUS: 0.9 [0.97 - 1.62] MMOL/L; NPTST513-PLATELET DISTRIBUTION WIDTH: 9.1 [10 - 18.5] %; NPTST561-RBC VOLUME DISTRIBUTING WIDTH-S: 48.6 [39 - 46] FL; NPTST624-THE RATIO OF ASPARTATE AMINO TR: 1.7 [0.5 - 1.5] NA; NPTST633-TOTAL BILE ACID: 10.8 [0 - 10] UMOL/L; Neutrophils/Leukocytes: 79.8 [50 - 70] %; Protein: TRACE [NOT REPORTED - NOT REPORTED] NA; Urate: 454 [125 - 410] UMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 135): THE X-RAY TESTS: COMMINUTED FRACTURE OF THE LOWER RIGHT TIBIA.; THE X-RAY TESTS: OBLIQUE FRACTURE OF THE UPPER RIGHT FIBULA.; [redacted]20[redacted] (RX DAY 136): GYPSUM TO HOLD FIXEDLY TO TREAT: GYPSUM TO HOLD FIXEDLY TO TREAT,REST IN BED; [redacted]20[redacted] (RX DAY 144): X-RAY: RIGHT TIBIOFIBULAR SHOWED THAT THE UPPER RIGHT FIBULA FRACTURE AND THE LOWER RIGHT TIBIA COMMINUTED FRACTURE ON .; [redacted]20[redacted] (RX DAY 167): X-RAY: RIGHT TIBIOFIBULAR SHOWED THAT THE UPPER RIGHT FIBULA FRACTURE AND THE LOWER RIGHT TIBIA COMMINUTED FRACTURE ON .; [redacted]20[redacted] (RX DAY 228): B ULTRASONIC TESTING: NO OBVIOUS ABNORMALITIES WERE OBSERVED IN THE DEEP ARTERIES AND VEINS OF THE RIGHT LOWER EXTREMITY

AE Stopped Rx Day	228
Duration of AE	94 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	FELL DOWN THE LOWER STEP
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	MIDDLE AND LOWER COMMINUTED FRACTURE OF THE RIGHT TIBIA (AO43-A1 TYPE), MIDDLE RIGHT UPPER HUMERUS FRACTURE (AO 41-A1 TYPE)
Preferred term	上腕骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 135
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 136): Eosinophils: 0.04 [0.05 - 0.5] 10^9/L; Hematocrit: 0.37 [0.37 - 0.5] FRACTION OF 1; Hemoglobin: 128 [120 - 160] G/L; Leukocytes: 7.4 [4 - 10] 10^9/L; Lymphocytes: 0.75 [1.5 - 4] 10^9/L; Lymphocytes/Leukocytes: 10.1 [20 - 40] %; Monocytes: 0.68 [0 - 0.45] 10^9/L; Monocytes/Leukocytes: 9.2 [3 - 8] %;

NPTST511-PHOSPHORUS: 0.9 [0.97 - 1.62] MMOL/L; NPTST513-PLATELET DISTRIBUTION WIDTH: 9.1 [10 - 18.5] %; NPTST561-RBC VOLUME DISTRIBUTING WIDTH-S: 48.6 [39 - 46] FL; NPTST624-THE RATIO OF ASPARTATE AMINO TR: 1.7 [0.5 - 1.5] NA; NPTST633-TOTAL BILE ACID: 10.8 [0 - 10] UMOL/L; Neutrophils/Leukocytes: 79.8 [50 - 70] %; Protein: TRACE [NOT REPORTED - NOT REPORTED] NA; Urate: 454 [125 - 410] UMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 135): THE X-RAY TESTS: COMMINUTED FRACTURE OF THE LOWER RIGHT TIBIA.; THE X-RAY TESTS: OBLIQUE FRACTURE OF THE UPPER RIGHT FIBULA.; [redacted]20[redacted] (RX DAY 136): GYPSUM TO HOLD FIXEDLY TO TREAT: GYPSUM TO HOLD FIXEDLY TO TREAT,REST IN BED; [redacted]20[redacted] (RX DAY 144): X-RAY: RIGHT TIBIOFIBULAR SHOWED THAT THE UPPER RIGHT FIBULA FRACTURE AND THE LOWER RIGHT TIBIA COMMINUTED FRACTURE ON .; [redacted]20[redacted] (RX DAY 167): X-RAY: RIGHT TIBIOFIBULAR SHOWED THAT THE UPPER RIGHT FIBULA FRACTURE AND THE LOWER RIGHT TIBIA COMMINUTED FRACTURE ON .; [redacted]20[redacted] (RX DAY 228): B ULTRASONIC TESTING: NO OBVIOUS ABNORMALITIES WERE OBSERVED IN THE DEEP ARTERIES AND VEINS OF THE RIGHT LOWER EXTREMITY

AE Stopped Rx Day	228
Duration of AE	94 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	FELL DOWN THE LOWER STEP
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	FEVER
Preferred term	発熱
AE Onset Date / Rx Day	[redacted]20[redacted] / 282
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 1): Erythrocytes: 4.6 [4.5 - 6.4] 10^12/L; Leukocytes: 7 [3.8 - 10.7] 10^9/L; Lymphocytes: 1.07 [0.91 - 4.28] 10^9/L; Neutrophils: 5.56 [1.96 - 7.23] 10^9/L; Platelets: 320 [140 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 2): Hemoglobin: 141 [127 - 181] G/L; [redacted]20[redacted] (RX DAY 289): Erythrocyte Sedimentation Rate: 47 [0 - 15] MM/H; Hemoglobin: 108 [120 - 160] G/L; Leukocytes: 2.2 [4 - 10] 10^9/L; Lymphocytes: 0.25 [1.5 - 4] 10^9/L; NPTST224-D-DIMER: 7.93 [0 - 0.5] UG/ML; NPTST261-FDP: 28 [0 - 5] UG/ML; NPTST400-LACTATE DEHYDROGENASE: 435 [85 - 250] IU/L; Neutrophils: 1.73 [2 - 7] 10^9/L; Sodium: 133 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 290): Alanine Aminotransferase: 86 [0 - 40] U/L; Albumin: 34 [35 - 55] G/L; Aspartate Aminotransferase: 92 [0 - 40] U/L; Hemoglobin: 113 [120 - 160] G/L; Leukocytes: 2.2 [4 - 10] 10^9/L; Lymphocytes: 0.22 [1.5 - 4] 10^9/L; NPTST020-ADENOSINE DEAMINASE: 54 [0 - 20] U/L; NPTST209-CRP: 149.4 [0 - 10] MG/L; NPTST298-GGT: 92 [0 - 50] IU/L; NPTST353-HSCRP: 42.98 [0 - 3] MG/L; NPTST591-SERUM FERRITIN: 1681.83 [21.8 - 274.66] NG/ML; Neutrophils: 1.74 [2 - 7] 10^9/L; [redacted]20[redacted] (RX DAY 291): NPTST096-BETA D GLUCAN: 16 [0 - 100] PG/ML; NPTST350-HIV: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; NPTST620-TB-AB-IGG: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; NPTST621-TB-AB-IGM: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; [redacted]20[redacted] (RX DAY 293): Alanine Aminotransferase: 80 [0 - 40] U/L; Aspartate Aminotransferase: 102 [0 - 40] U/L; Chloride: 94 [96 - 108] MMOL/L; NPTST209-CRP: 97.5 [0 - 10] U/L; NPTST298-GGT: 110 [0 - 50] IU/L; NPTST523-PREALBUMIN: 94 [160 - 450] MG/L; NPTST662-UREA: 2.49 [3.3 - 7.1] MMOL/L; Protein: 55 [60 - 85] G/L; Sodium: 133 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 303): NPTST662-UREA: 2.96 [3.3 - 7.1] MMOL/L; Urate: 158 [208 - 428] UMOL/L; [redacted]20[redacted] (RX DAY 347): Urate: 782 [149 - 494] UMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 290): SPUTUM NPTST088-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; BLOOD NPTST088-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; [redacted]20[redacted] (RX DAY 297): STOOL NPTST188-CONVENTIONAL STOOL OCCULT BLOOD: Negative; [redacted]20[redacted] (RX DAY 301): SPUTUM NPTST087-BACTERIAL CULTURE AND CHEMOSENS: Negative; [redacted]20[redacted] (RX DAY 305): CEREBROSPINAL FLUID

NPTST088-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; [redacted]20[redacted] (RX DAY 310): BLOOD NPTST088-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; [redacted]20[redacted] (RX DAY 311): SPUTUM NPTST088-BACTERIAL CULTURE+CHEMOSENSITIV: Positive-STOMATOCCUS++ STREPTOCOCCUS VIRIDANS++; [redacted]20[redacted] (RX DAY 313): CEREBROSPINAL FLUID NPTST043-ANAEROBIC CULTURE: Negative; CEREBROSPINAL FLUID NPTST088-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; [redacted]20[redacted] (RX DAY 317): BLOOD NPTST088-BACTERIAL CULTURE+CHEMOSENSITIV: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 290): B-MODE ULTRASOUND: GALLBLADDER STONE, CHOLECYSTITIS CAN, ACCESSORY SPLEEN; CARDIAC AND VERTEBRAL ARTERY COLOR DOPPLER IMAGE: NO OBVIOUS ABNORMALITY WAS OBSERVED IN HEART STRUCTURE. LEFT VENTRICULAR SYSTOLIC FUNCTION IS NORMAL. DIASTOLIC FUNCTION WAS REDUCED SLIGHTLY. RIGHT CAROTID ATHEROSCLEROTIC PLAQUE FORMATION, THE VESSELS STENOSIS < 50% IN PLAQUE. ATHEROSCLEROTIC PLAQUE FORMATION AT THE BEGINNING OF THE RIGHT SUBCLAVIAN ARTERY, THE VESSELS STENOSIS < 50% IN PLAQUE.; [redacted]20[redacted] (RX DAY 291): LUNG CT: 1) MULTIPLE GRINDING GLASS DENSITY FOCI IN BOTH LUNGS, INFECTIOUS LESION UNDER CONSIDERATION; 2) MULTIPLE LYMPH NODES IN HILUM AND MEDIASTINUM, PARTIALLY TUMEFACTION; 3) SMALL PLEURAL EFFUSION ON BOTH SIDES; 4) ESOPHAGEAL HIATUS HERNIA WAS NOT EXCLUDED.; [redacted]20[redacted] (RX DAY 295): B ULTRASOUND OF PROSTATE: PROSTATE ENLARGEMENT AND CALCIFICATION OF THE FORMATION OF LESIONS, PROSTATE CYSTS; [redacted]20[redacted] (RX DAY 296): ABDOMEN CT: 1.CONSIDER MULTIPLE INTRAPERITONEAL INFARCTS; 2,PROSTATE CALCIFICATION; 3,PARTIAL THORACIC VERTEBRA AND RIGHT RIB BONE DESTRUCTION.; [redacted]20[redacted] (RX DAY 299): ECT: 1.BILATERAL RIBS AND SPINE BONE METABOLISM IS ACTIVE; 2.THE RIGHT UPPER FIBULA SEGMENT, LOWER TIBIA SEGMENT AND ANKLE JOINT PART BONE METABOLISM IS ACTIVE.; [redacted]20[redacted] (RX DAY 300): BONE MINERAL DENSIT: OSTEOPOROSIS; GASTROSCOPE: EROSIVE ESOPHAGITIS (LA-B), EROSIVE GASTRITIS, DUODENAL SPHERITIS; [redacted]20[redacted] (RX DAY 301): B-MODE ULTRASONOGRAPHY OF THYROID AND CERVICAL LYMPH NODES: CYSTIC NODULES IN THE RIGHT LOBE OF THE THYROID GLAND, TI-RADS: GRADE 2; CT OF THE BRAIN: SENILE BRAIN ATROPHY; THORACOLUMBAR MR: 1, T2, 8, 10, 11, LI VERTEBRAL BODY AND PART OF THE ADNEXA, T10-11 LEVEL OF PARAVERTEBRAL SOFT TISSUE SIGNAL ABNORMALITIES: CONSIDER THE POSSIBILITY OF MALIGNANCIES, METASTATIC TUMORS?2. COMPRESSION FRACTURES OF THE T6 AND 8 VERTEBRAE ACCOMPANIED BY THE FORMATION OF THE UPPER MARGIN OF THE Y8 VERTEBRAE. 3. THORACOLUMBAR DEGENERATION;L5 SACROIZATION POSSIBILITY;; [redacted]20[redacted] (RX DAY 302): X-RAY OF THE SPINE: 1, CERVICAL SPONDYLOSIS ?2?T6 AND T8 VERTEBRAL BODY SLIGHTLY CHANGE PARTIAL; 3, LUMBAR DEGENERATIVE CHANGES; [redacted]20[redacted] (RX DAY 308): BONE DNA BIOPSY: TB TEST NEGATIVE; EXAMINATION OF THORACIC OSTEOPATHY: (THORACIC 8TH VERTEBRA) THE BONE TISSUE WAS FOUND TO HAVE MORE LYMPHOCYTES, A SMALL AMOUNT OF PLASMA CELL INFILTRATION, A SMALL AMOUNT OF EPITHELIOID CELL HYPERPLASIA IN SOME AREAS, AND DEGENERATION AND NECROSIS OF BONE TISSUE IN SOME AREAS. TUBERCULOSIS DNA TEST WAS PERFORMED.; SCLEROTIN OF DNA TEST: TB NEGATIVE; [redacted]20[redacted] (RX DAY 313): GENETIC TESTING FOR ISONIAZID RESISTANCE: NOT DETECTED; GENETIC TESTING OF MYCOBACTERIUM TUBERCULOSIS: NOT DETECTED; GENETIC TESTING OF RIFAMPIN RESISTANCE: NOT DETECTED; THE POST-ILIAC BONE MARROW BLOOD SMEAR SHOWED: THE BONE MARROW HYPERPLASIA WAS ACTIVE, THE GRANULOCYTES HAD NUCLEI SHIFTED TO THE LEFT, THE PROPORTION OF RED CELLS INCREASED, AND OCCASIONALLY PHAGOCYTIC HISTIOCYTES WERE OBSERVED.; [redacted]20[redacted] (RX DAY 314): T11 BONE PATHOLOGY INSPECTION: (11 THORACIC VERTEBRA) WERE MORE SEE LYMPHOCYTES IN THE BONE TISSUE, A SMALL AMOUNT OF PLASMA CELL INFILTRATION, PARTS OF A SMALL AMOUNT OF EPITHELIOID CELLS, SEE PARTS OF BONE TISSUE DEGENERATION NECROSIS, TB IMMUNOHISTOCHEMICAL DID NOT SEE CLEAR CANCER METASTASIS, DOES NOT EXCLUDE THE POSSIBILITY WITH FUNGAL INFECTION.; THORACIC OSTEOPATHY: (THORACIC 11TH VERTEBRA) THERE WERE MORE LYMPHOCYTES AND A SMALL AMOUNT OF PLASMA CELL INFILTRATION IN THE BONE TISSUE, SOME AREAS SHOWED A SMALL AMOUNT OF EPITHELIOID CELLS, SOME AREAS SHOWED DEGENERATION AND NECROSIS OF BONE TISSUE, NO DEFINITE CANCER METASTASIS IN THE IMMUNOHISTOCHEMISTRY OF HE TUBERCULOSIS, THE POSSIBILITY OF FUNGAL INFECTION WAS NOT RULED OUT.; [redacted]20[redacted] (RX DAY 316): PET/CT WHOLE BODY TOMOGRAPHY: LOW DENSITY LESION IN VERTEBRAL L1, LOW GLUCOSE METABOLISM: MOST LIKELY VERTEBRAL HEMANGIOMA. LIVER AND SPLEEN WERE BIG, GLUCOSE METABOLISM IN THE CENTRAL AXIS BONE INCREASED: MOST

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING

Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は中国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右脛骨中央部・下部の粉砕骨折（AO43-A1 タイプ），上腕骨中央右上の骨折（AO41-A1 タイプ）の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，局面型乾癬，頚部ウエスト症候群，低蛋白血症，乾癬性関節炎，頚椎骨肥大，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右脛骨中央部・下部の粉砕骨折（AO43-A1 タイプ），上腕骨中央右上の骨折（AO41-A1 タイプ）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右脛骨中央部・下部の粉砕骨折（AO43-A1 タイプ），上腕骨中央右上の骨折（AO41-A1 タイプ）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は階段から落ち，右の足首とふくらはぎに激しい痛みを感じた。被験者は直ちに救急治療室を受診した。X 線検査及び関連する検査が行われ，右脛骨中央部・下部と腓骨上部の骨折が確認された。同日，被験者は「右脛骨粉砕骨折」との診断で同病院の整形外科に入院した。20[redacted] 年 [redacted] 月 [redacted] 日，ギプスによる外固定が行われ，被験者は四肢の制動のためベッドで安静にした。何らかの治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日にギプス固定が行われた。右脛腓関節を正側位としたX線検査で，右上腓骨骨折及び右下脛骨粉砕骨折が確認された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。診断は次のとおりであった。1）右脛骨遠位部の粉砕骨折（ao43-a1 タイプ），2）右腓骨中上部の骨折（ao41-a1 タイプ）。

ギプスによる外固定が 20[redacted] 年 [redacted] 月 [redacted] 日に除去された。20[redacted] 年 [redacted] 月 [redacted] 日，右下肢動静脈の B モード超音波検査が行われた。右下肢の深動脈及び静脈に明らかな異常は見られなかった。症状は改善し，被験者は後遺症なく自由に動けるようになった。

投与された薬剤は，sodium aescinate 注射剤，低分子量ヘパリンカルシウム注射剤，フルルビプロフェン アキセチル注射剤，ブプレノルフィン経皮吸収型製剤，henggu gushangyu heji（タイツリオウギ，ニンジン，コウカ）及び炭酸カルシウム D3 粒子製剤であった。

Causality for UPADACITINIB (Blind)

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1) Comminuted fracture (10052614) (Comminuted fracture (10052614)) [v.22.1] [10052614]

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

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

Dechallenge: Not Applicable

2) Humerus fracture (10020462) (Humerus fracture (10020462)) [v.22.1] [10020462]

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 MIDDLE AND LOWER COMMINUTED FRACTURE OF THE RIGHT TIBIA (AO43-A1 TYPE), MIDDLE RIGHT UPPER HUMERUS FRACTURE (AO 41-A1 TYPE

- Investigator: Fell down the lower step.

- AbbVie: Event is more likely related to trauma sustained from fall down the steps.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **AST TO ALT RATIO:** 1.7 No units (normal 0.5 to 1.5)

[redacted] 20[redacted] **EOSINOPHILS ABS:** 0.04 X10**9/L (normal 0.05 to 0.5)

[redacted] 20[redacted] **HEMATOCRIT:** 37.10 % (normal 37 to 50)

[redacted] 20[redacted] **HEMOGLOBIN:** 128 G/L (normal 120 to 160)

[redacted] 20[redacted] **LYMPHOCYTES:** 10.1 % (normal 20 to 40)

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 0.75 X10**9/L (normal 1.5 to 4)

[redacted] 20[redacted] **MONOCYTES:** 9.20 % (normal 3 to 8)

[redacted] 20[redacted] **MONOCYTES ABS:** 0.68 X10**9/L (normal 0 to 0.45)

[redacted] 20[redacted] **NEUTROPHILS:** 79.80 % (normal 50 to 70)

[redacted] 20[redacted] **PHOSPHORUS:** 0.90 MMOL/L (normal 0.97 to 1.62)

[redacted] 20[redacted] **PLATELET DISTRIBUTION WIDTH:** 9.1 % (normal 10 to 18.5)

[redacted] 20[redacted] **RBC VOLUME DISTRIBUTING WIDTH-SD:** 48.6 FL (normal 39 to 46)

[redacted] 20[redacted] **TOTAL BILE ACID:** 10.8 MCMOL/L (normal 0 to 10)

[redacted] 20[redacted] **URIC ACID:** 454 MCMOL/L (normal 125 to 410)

[redacted] 20[redacted] **URINE PROTEIN:** Trace

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 7.42 X10**9/L (normal 4 to 10)

[redacted] 20[redacted] **X-RAY:** Upper fibula fracture and middle and lower right tibia comminuted fracture

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は中国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，発熱の事象を発現した。

Event 3 の臨床経過：

関連する病歴は，局面型乾癬，高血圧，変形性膝関節症，乾癬性関節炎，頚椎骨肥大，高尿酸血症，非喫煙者，現飲酒者（1 日 2 杯未満）及び潜伏結核であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，

盲検化された皮下注製剤の最終投与は20[redacted]年[redacted]月[redacted]日であった。

20[redacted]年[redacted]月[redacted]日，被験者は発熱を発現した。

20[redacted]年[redacted]月[redacted]日，被験者は本治験の規定来院日に来院した。被験者は咳をしており，それに伴う膿性痰，食欲喪失及び体重減少を呈していた。治験責任医師は被験者に ER を受診するよう勧めたが，被験者はこれを拒否し，地域のクリニックを再受診して抗生物質を投与された。被験者の状態は改善しなかった。

20[redacted]年[redacted]月[redacted]日，被験者は 1 週間にわたる発熱で入院した。同日，被験者は当初，肺炎と診断された。被験者には潜在性結核の既往歴があった。診断検査が行われた。被験者は抗感染療法を約 1 ヵ月間受けたが，回復しなかった。PET/CT 検査で胸椎病変に結核や悪性疾患の所見は見られなかった。20[redacted]年[redacted]月[redacted]日，被験者は他院に転院となり，抗生物質及び抗結核薬による治療を受けた。被験者の状態は改善し，20[redacted]年[redacted]月[redacted]日に被験者は退院した。

治験責任医師によると，最終診断は未確定であった。

投与された薬剤は，intralipid，複方スルファメトキサゾール，ヒト血漿由来アルブミン，リファンピシン，エタンブトール，ピラジナミド，diammonium glycyrrhizinate，イノシン，rutinum，calcium dobesilate，スクラルファート，イブプロフェン，leucogen，batilol，複方グリチルリチン，複方アミノ酸，遺伝子組換えヒト G-CSF 製剤，アトルバスタチンカルシウム，クロピドグレル，スルファメトキサゾール・トリメトプリム，モキシフロキサシン，ピペラシリン／スルバクタム注射剤及びイソニアジドであった。

Causality for UPADACITINIB (Blinded)

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1) Fever (10016558) (Pyrexia (10037660)) [v.22.1] [10016558]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of FEVER

- Investigator: Not Applicable

- AbbVie: Fever is common in the general population as a non-specific indicator of acute infectious, inflammatory, or autoimmune disease. Additionally, diagnostic tests for tuberculosis have all been negative thus far.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMEN CT:** 1. CONSIDER MULTIPLE INTRAPERITONEAL INFARCTS; 2. PROSTATE CALCIFICATION; 3. PARTIAL THORACIC VERTEBRA AND RIGHT RIB BONE DESTRUCTION.

[redacted] **B ULTRASOUND OF PROSTATE:** PROSTATE ENLARGEMENT AND CALCIFICATION OF THE FORMATION OF LESIONS, PROSTATE CYSTS

[redacted] **B-MODE ULTRASONOGRAPHY OF THYROID AND CERVICAL LYMPH NODES:** CYSTIC NODULES IN THE RIGHT LOBE OF THE THYROID GLAND, TI-RADS: GRADE 2

[redacted] **B-MODE ULTRASOUND:** GALLBLADDER STONE, CHOLECYSTITIS CAN, ACCESSORY SPLEEN

[redacted] **BLOOD CULTURE:** Negative

[redacted] **BLOOD TEST:** BACTERIAL CULTURE AND CHEMOSENSITIVITY TEST: NEGATIVE

[redacted] **BLOOD TEST:** BACTERIAL CULTURE AND CHEMOSENSITIVITY TEST: NEGATIVE

[redacted] **BLOOD TEST:** BACTERIAL CULTURE AND CHEMOSENSITIVITY TEST: NEGATIVE

[redacted] **BONE DNA BIOPSY:** TB TEST NEGATIVE

[redacted] **BONE MINERAL DENSITY:** Osteoporosis

[redacted] **CARDIAC/VERTERBRAL ARTERY COLOR DOPPLER:** NO OBVIOUS ABNORMALITY WAS OBSERVED IN HEART STRUCTURE. LEFT VENTRICULAR SYSTOLIC FUNCTION IS NORMAL. DIASTOLIC FUNCTION WAS REDUCED SLIGHTLY. RIGHT CAROTID ATHEROSCLEROTIC PLAQUE FORMATION, THE VESSELS STENOSIS < 50% IN PLAQUE. ATHEROSCLEROTIC PLAQUE FORMATION AT THE BEGINNING OF THE RIGHT SUBCLAVIAN ARTERY, THE VESSELS STENOSIS < 50% IN PLAQUE.

[redacted] **CHEST X-RAY (SCREENING):** Normal

[redacted] **CT BRAIN:** Senile brain atrophy

[redacted] 20[redacted] **CT SCAN:** ECT: 1. BILATERAL RIBS AND SPINE BONE METABOLISM IS ACTIVE; 2. THE RIGHT UPPER FIBULA SEGMENT, LOWER TIBIA SEGMENT AND ANKLE JOINT PART BONE METABOLISM IS ACTIVE.

[redacted] 20[redacted] **EXAMINATION OF THORACIC OSTEOPATHY:** (THORACIC 8TH VERTEBRA) THE BONE TISSUE WAS FOUND TO HAVE MORE LYMPHOCYTES, A SMALL AMOUNT OF PLASMA CELL INFILTRATION, A SMALL AMOUNT OF EPITHELIOID CELL HYPERPLASIA IN SOME AREAS, AND DEGENERATION AND NECROSIS OF BONE TISSUE IN SOME AREAS. TUBERCULOSIS DNA TEST WAS PERFORMED.

[redacted] 20[redacted] **FDP:** 28 MCG/ML (normal 0 to 5)

[redacted] 20[redacted] **GASTROSCOPY:** EROSIVE ESOPHAGITIS (LA-B), EROSIVE GASTRITIS, DUODENAL SPHERITIS

[redacted] 20[redacted] **GENETIC TESTING FOR ISONIAZID RESISTANCE:** Not detected

[redacted] 20[redacted] **GENETIC TESTING OF MYCOBACTERIUM TUBERCULOSIS:** Not detected

[redacted] 20[redacted] **GENETIC TESTING OF RIFAMPIN RESISTANCE:** Not detected

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

[redacted] 20[redacted] **LUNG CT:** 1) Multiple grinding glass density foci in both lungs, Infectious lesion under consideration; 2) Multiple lymph nodes in hilum and mediastinum, Partially tumefaction; 3) Small pleural effusion on both sides; 4) Esophageal hiatus hernia was not excluded.

[redacted] 20[redacted] **PET/CT:** AFTER VERTEBRO PLASTY " T8, T11 VERTEBRAL BIOPSY WITH CEMENT FILLING ”MULTIPLE BONE DESTRUCTION WITH PARTIAL SOFT TISSUE MASS AND THE GLUCOSE METABOLISM INCREASED ABNORMALLY. VERTEBRAL T6 COMPRESSED AND BEING FLATTENED: EOSINOPHILIC GRANULOMA? BONE TUBERCULOSIS? MULTIPLE BONE METASTASES WITH UNKNOWN MALIGNANT TUMORS OF THE PRIMARY TUMOR ARE NOT EXCLUDED. LOW DENSITY LESION IN VERTEBRAL L1, LOW GLUCOSE METABOLISM: MOST LIKELY VERTEBRAL HEMANGIOMA. LIVER AND SPLEEN WERE BIG, GLUCOSE METABOLISM IN THE CENTRAL AXIS BONE INCREASED: MOST LIKELY REACTIVITY CHANGE. INCREASED GLUCOSE METABOLISM IN THE ANTERIOR PART OF THE TONGUE, MOST LIKELY PHYSIOLOGICAL INTAKE. BILATERAL INFERIOR LG BASE HAVE LITTER INFLAMMATION: BILATERAL PLEURA HAVE LITTER EFFUSION. MULTIPLE LYMPH NODES IN THE MEDIASTINUM AND BILATERAL HILAR AREA, GLUCOSE METABOLISM INCREASED, MOST LIKELY REACTIVE HYPERPLASIA. BENIGN PROSTATIC HYPERPLASIA AND CALCIFICATION.

[redacted] 20[redacted] **QUANTIFERON TB GOLD TST:** Positive

[redacted] 20[redacted] **SCLEROTIN OF DNA TB:** TB negative

[redacted] 20[redacted] **SPINAL FLUID CULTURE:** Negative

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

[redacted] 20[redacted] **SPUTUM CULTURE:** Positive stomatococcus++, streptococcus viridans++

[redacted] 20[redacted] **SPUTUM TEST:** BACTERIAL CULTURE AND CHEMOSENSITIVITY TEST: NEGATIVE

[redacted] 20[redacted] **SPUTUM TEST:** BACTERIAL CULTURE AND CHEMOSENSITIVITY TEST: NEGATIVE

[redacted] 20[redacted] **SPUTUM TEST:** BACTERIAL CULTURE AND CHEMOSENSITIVITY TEST: NEGATIVE

[redacted] 20[redacted] **STOOL TEST:** CONVENTIONAL STOOL OCCULT BLOOD: NEGATIVE

[redacted] 20[redacted] **T11 BONE PATHOLOGY INSPECTION:** (11 THORACIC VERTEBRA) WERE MORE SEE LYMPHOCYTES IN THE BONE TISSUE, A SMALL AMOUNT OF PLASMA CELL INFILTRATION, PARTS OF A SMALL AMOUNT OF EPITHELIOID CELLS, SEE PARTS OF BONE TISSUE DEGENERATION NECROSIS, TB IMMUNOHISTOCHEMICAL DID NOT SEE CLEAR CANCER METASTASIS, DOES NOT EXCLUDE THE POSSIBILITY WITH FUNGAL INFECTION.

[redacted] 20[redacted] **TB IGM ANTIBODY TEST:** Negative

[redacted] 20[redacted] **TB TEST:** Latent TB

[redacted] 20[redacted] **THE POST-ILIAC BONE MARROW BLOOD SMEAR SHOWED:** THE BONE MARROW HYPERPLASIA WAS ACTIVE, THE GRANULOCYTES HAD NUCLEI SHIFTED TO THE LEFT, THE PROPORTION OF RED CELLS INCREASED, AND OCCASIONALLY PHAGOCYTIC HISTIOCYTES WERE OBSERVED.

[redacted] 20[redacted] **THORACIC OSTEOPATHY CYTOLOGY:** (THORACIC 11TH VERTEBRA) THERE WERE MORE LYMPHOCYTES AND A SMALL AMOUNT OF PLASMA CELL INFILTRATION IN THE BONE TISSUE, SOME AREAS SHOWED A SMALL AMOUNT OF EPITHELIOID CELLS, SOME AREAS SHOWED DEGENERATION AND NECROSIS OF BONE TISSUE, NO DEFINITE CANCER METASTASIS IN THE IMMUNOHISTOCHEMISTRY OF HE TUBERCULOSIS, THE POSSIBILITY OF FUNGAL INFECTION WAS NOT RULED OUT.

[redacted] 20[redacted] **THORACOLUMBAR MR:** 1. T2, 8, 10, 11 L1 VERTEBRAL BODY AND PART OF THE ADNEXA, T10-11 LEVEL OF PARAVERTEBRAL SOFT TISSUE SIGNAL ABNORMALITIES. CONSIDER THE POSSIBILITY OF MALIGNANCIES, EMTASTATIC TUMORS? 2. COMPRESSION FRACTURES OF THE T6 AND 8 VETEBRAE ACCOMPANIED BY THE FORMATION OF THE UPPER MARGIN OF THE Y8 VERTEBRAE 3. THORACOLUMBAR DEGENERATION; L5 SACROIZATION POSIBILITY.

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 2.16 X10**9/L (normal 4 to 10)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	3[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: ACTIVE TB	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: ACTIVE PLAQUE PSORIASIS	20[redacted]
OTHER: ANEMIA	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 414	246
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 415		

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-M: 20[redacted]

CELECOXIB	200 mg	BID	Y-M: 20[redacted] / -106
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -106
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -106
PAEONIA LACTIFLORA	600 mg	BID	Y-M: 20[redacted] / -106
SULFASALAZINE	0.75 g	BID	Y-M: 20[redacted] / -106
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -86
ISONIAZID	0.3 g	QD	Y-M: 20[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
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -106	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -86	ONGOING
AMBROXOL	30 mg	QD	Y-M: 20[redacted] / 311	Y-M: 20[redacted] / 311
AMBROXOL	30 mg	BID	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 318
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 318
UNSPECIFIED HERBAL	20 mL	QD	Y-M: 20[redacted] / 314	Y-M: 20[redacted] / 318
AMMONIA;CAMPHOR;GLYCEROL;GLYCYRRHIZA GLABRA;G	10 mL	TID	Y-M: 20[redacted] / 317	Y-M: 20[redacted] / 324
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 317	Y-M: 20[redacted] / 324
FUDOSTEINE	0.4 g	TID	Y-M: 20[redacted] / 363	Y-M: 20[redacted] / 369
LEVOFLOXACIN	0.5 g	QD	Y-M: 20[redacted] / 363	Y-M: 20[redacted] / 369

Event #1: Serious Adverse Event

Event Description	LEFT SPONTANEOUS PNEUMOTHORAX
Preferred term	自然気胸
AE Onset Date / Rx Day	[redacted]20[redacted] / 311
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 312): Creatine Kinase: 378 [19 - 226] U/L; Erythrocytes: 4 [4.3 - 5.8] 10^12/L; Hematocrit: 0.36 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 120 [130 - 175] G/L; Leukocytes: 8.1 [3.5 - 9.5] 10^9/L; Lymphocytes: 0.85 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 10.5 [20 - 50] %; Monocytes: 0.67 [0.1 - 0.6] 10^9/L; NPTST233-DETERMINATION OF SERUM HYDROXYB: 0.72 [0.02 - 0.27] MMOL/L; NPTST381-INFLUENZA A ANTIGEN TESTING: NEGATIVE [NOT REPORTED - NOT REPORTED] NEGATIVE; NPTST385-INFLUENZA B ANTIGEN DETECTION: NEGATIVE [NOT REPORTED - NOT REPORTED] NEGATIVE; Neutrophils: 6.51 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 80.7 [40 - 75] %; [redacted]20[redacted] (RX DAY 313): Creatine Kinase: 265 [19 - 226] U/L; Erythrocytes: 4 [4.3 - 5.8] 10^12/L; Hematocrit: 0.38 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 122 [130 - 175] G/L; Leukocytes: 6.5 [3.5 - 9.5] 10^9/L; Lymphocytes: 0.84 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 12.9 [20 - 50] %; NPTST080-B B E ANTIBODY SEMI - QUANTITAT: 1.640 [NOT REPORTED - NOT REPORTED] COI; NPTST184-COMBINED DETECTION OF HIV ANTIG: 0.19 [0 - 0.9] COI; NPTST220-D - DIMER: 0.63 [NOT REPORTED - NOT REPORTED] mg/L; NPTST315-HCV: 0.04 [0 - 0.9] COI; NPTST326-HEPATITIS B CORE ANTIBODY SEMI: 2.280 [NOT REPORTED - NOT REPORTED] COI; NPTST329-HEPATITIS B E ANTIGEN SEMI - QU: 0.11 [0 - 1] COI; NPTST333-

HEPATITIS B SURFACE ANTIBODY SE: ?2.000 [0 - 10] IU/L; NPTST335-HEPATITIS B SURFACE ANTIGEN SEM: 0.46 [0 - 0.9] COI; NPTST641-TREPONEMA PALLIDUM ANTIBODY: 0.1 [0 - 1] S/CO; Neutrophils/Leukocytes: 77.4 [40 - 75] %; [redacted]20[redacted] (RX DAY 315): NPTST217-CYTOMEGALOVIRUS ANTIBODY IGG: 125 [NOT REPORTED - NOT REPORTED] 099,U/ML; NPTST218-CYTOMEGALOVIRUS ANTIBODY IGM: 5.10 [NOT REPORTED - NOT REPORTED] 099,AU/ML

Microbiology

[redacted]20[redacted] (RX DAY 312): OTHER NA NPTST580-RHINOVIRUS: Positive-TEST POSITIVE; SPUTUM NPTST599-SMEAR FOR BACTERIA + SMEAR FOR: Positive-SMEAR GRAM STAINING: NO FUNGUS DETECTED MICROSCOPICALLY, SQUAMOUS EPITHELIAL CELLS < 10/LP LEUCOCYTE > 25/LP WERE QUALIFIED MORE G+ STREPTOCOCCUS (+++) LOW G- BACILLUS (+); SPUTUM NPTST599-SMEAR FOR BACTERIA + SMEAR FOR: Positive-SMEAR GRAM STAINING: NO FUNGUS DETECTED LESS G-BACILLI (++) OLIGG + COCCI (+) OLIGG + STREPTOCOCCUS (+); SPUTUM NPTST601-SMEAR FOR MYCOBACTERIA: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE DETECTED; SPUTUM NPTST609-SPUTUM. CULTURE OF PHARYNGEAL B: Negative-NORMAL MIXED FLORA, NO HAEMOPHILUS ISOLATED; [redacted]20[redacted] (RX DAY 315): BLOOD NPTST618-TB ANTIBODY TEST: Negative; [redacted]20[redacted] (RX DAY 316): SPUTUM NPTST214-CULTURE OF SPUTUM FUNGI: Negative-NONFUNGAL GROWTH; SPUTUM NPTST599-SMEAR FOR BACTERIA + SMEAR FOR: Positive-SMEAR GRAM STAINING: NO FUNGUS DETECTED MICROSCOPICALLY, SQUAMOUS EPITHELIAL CELLS < 25/LP AND WHITE BLOOD CELLS 10-25/LP WERE BASICALLY QUALIFIED LOW G- BACILLUS (+); SPUTUM NPTST602-SMEAR MYCOBACTERIUM: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE DETECTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 311): CHEST CT: 1 A SMALL AMOUNT OF LIQUID PNEUMOTHORAX ON THE LEFT SIDE, MULTIPLE PULMONARY BULLAE AT THE TIP OF BOTH LUNGS 2 PULMONARY BRONCHITIS WITH BRONCHIECTASIS, SCATTERED INFECTION IN BOTH LUNGS; [redacted]20[redacted] (RX DAY 316): CYTOPATHOLOGIC REPORT: SAMPLE TYPE: SPUTUM SMEAR AND FLUID BASE PATHOLOGICAL DIAGNOSIS: NO MALIGNANT CELLS WERE FOUND

AE Stopped Rx Day	457
Duration of AE	147 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。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が投与され，左自然気胸の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，活動性結核，抗結核治療，乾癬性関節炎，活動性局面型乾癬，貧血，現喫煙者（1 日 0.5 箱を 10 年間）及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左自然気胸を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左自然気胸は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左胸痛を伴って悪化した咳嗽を発現した。少量の白色泡沫様喀痰を伴う有効な咳嗽が見られた。胸部絞扼感を伴う持続的な鈍痛が発現した。鈍痛は午前中によりひどく，午後や夕方には消失した。また，労作後に tight air の感覚があった。身体的診察後，被験者に明らかな異常は見られず，胸部 CT 検査を行ったところ左気胸及び肺感染（非重篤）が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左気胸の治療のため入院した。被験者は著しく改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者はその後の実施医療機関への来院で，気胸は 20[redacted] 年 [redacted] 月 [redacted] 日に消失したと述べた。

投与された薬剤は，アンブロキソール塩酸塩，モキシフロキサシン塩酸塩，tanreqing 及び酸素補給であった。

The patient's past medications include:

CELECOXIB for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SULFASALAZINE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TOTAL GLUCOSIDES OF PAEONY CAPSULES for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ISONIAZID for TUBERCULOSIS PREVENTION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pneumothorax spontaneous (10035763) (Pneumothorax spontaneous (10035763)) [v.23.0] [10035763]

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 LEFT SPONTANEOUS PNEUMOTHORAX

- Investigator: Not applicable.

- AbbVie: Risk factors includes active pulmonary infection with multiple pulmonary bullae, current tobacco use and history of 0.5 packs per day for the past 10 years, pre-existing pleural abnormality on screening chest X-ray, and past history of active tuberculosis. Spontaneous pneumothorax is also three to six times higher in men than in women.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] B B E ANTIBODY SEMI-QUANTITATIVE:** 1.640 COI (Normal 1.0)

[redacted] **20[redacted] BLOOD PRESSURE:** 110/74 mmHg

[redacted] **20[redacted] CHEST CT:** 1. A small amount of liquid pneumothorax on the left side, multiple pulmonary bullae at the tip of both lungs. 2. Pulmonary bronchitis with bronchiectasis, scattered infection in both lungs.

[redacted] **20[redacted] CHEST X-RAY:** Screening: Abnormal - Parietal pleural thickening in bilateral lung and scattered nodules in upper fields of the lung

[redacted] **20[redacted] COMBINED DETECTION OF HIV ANTIGEN AND ANTIBODY:** 0.185 COI (Normal 0-0.9)

[redacted] **20[redacted] CREATINE KINASE:** 378 IU/L (normal 19 to 226)

[redacted] **20[redacted] CREATINE KINASE:** 265 IU/L (normal 19 to 226)

[redacted] **20[redacted] CYTOMEGALOVIRUS ANTIBODY IGG:** 125 U/ML (normal 14 to 14)

[redacted] **20[redacted] CYTOMEGALOVIRUS ANTIBODY IGM:** 5.10 AU/ML (Normal 22)

[redacted] **20[redacted] CYTOPATHOLOGIC REPORT:** Sample type: sputum and fluid base pathological diagnosis: No malignant cells were found.

[redacted] **20[redacted] D-DIMER:** 0.63 mg/L (Normal 0.55)

[redacted] **20[redacted] HCV TEST:** 0.038 COI (Normal 0-0.9)

[redacted] **20[redacted] HEART RATE:** 81 /min

[redacted] **20[redacted] HEMATOCRIT:** 0.36 L/L (Normal 0.40-0.50)

[redacted] **20[redacted] HEMATOCRIT:** 0.38 L/L (Normal 0.40-0.50)

[redacted] **20[redacted] HEMOGLOBIN:** 120 G/L (normal 130 to 175)

[redacted] **20[redacted] HEPATITIS B E ANTIGEN SEMI-QUANTITATIVE:** 0.106 COI (Normal 0-1.0)

[redacted] **20[redacted] HEPATITIS B CORE ANTIBODY SEMI-QUANTITATIVE:** 2.280 COI (Normal 1.0)

[redacted] **20[redacted] HEPATITIS B SURFACE ANTIGEN SEMI-QUANTITATIVE:** 0.464 COI (Normal 0-0.9)

[redacted] **20[redacted] HYDROXYBUTYRIC ACID:** 0.72 MMOL/L (normal 0.02 to 0.27)

[redacted] **20[redacted] INFLUENZA A ANTIGEN:** Pharyngeal swab: Negative

[redacted] **20[redacted] INFLUENZA B ANTIGEN:** Throat swab: Negative

[redacted] **20[redacted] LYMPHOCYTES %:** 10.5 % (normal 20 to 50)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.85 X10**9/L (normal 1.1 to 3.2)

[redacted] **20[redacted] MYCOBACTERIA SPUTUM TEST:** Negative: Smear acid-fast staining: no acid-fast bacilli were detected

[redacted] **20[redacted] NEUTROPHILS %:** 80.7 % (normal 40 to 75)

[redacted] **20[redacted] NEUTROPHILS ABS:** 6.51 X10**9/L (normal 1.8 to 6.3)

[redacted] **20[redacted] PHYSICAL EXAMINATION:** Bilateral lung percussion showed left lung breath sounds a bit low; No smell and obvious dry and wet then; bilateral breathing exercises uniform symmetry, no increase or decrease; Bilateral tactile language fibrillation symmetric without exception, untouched pleural friction feeling, thoracic no exception; bilateral breast symmetry, no exception, Heart is normal, rhythm of the heart, each valve did not hear a murmur.

[redacted] **20[redacted] PULSE:** 81 /min

[redacted] **20[redacted] RED BLOOD CELLS:** 3.98 X10**12/L (normal 4.3 to 5.8)

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

[redacted] **20[redacted] RHINOVIRUS TEST:** Positive

[redacted] **20[redacted] SPUTUM CULTURE OF PHARYNGEAL BACTERIA:** Negative: Normal mixed flora, no haemophilus isolated

[redacted] **20[redacted] SPUTUM TEST:** Positive (Smear for fungi and bacteria): Smear gram staining: no fungus detected microscopically, squamous epithelial cells < 10/LP leucocyte > 25/LP were qualified more G+ Streptococcus (+++), Low G- bacillus (+), Oligg + cocci (+), Oligg + Streptococcus (+)

[redacted] **20[redacted] SPUTUM TEST:** Smear for bacteria and fungi: Positive - Smear gram staining: no fungus detected microscopically, squamous epithelial cells < 25/LP and white blood cells 10-25/LP were basically qualified Low G- bacillus (+)

[redacted] **20[redacted] SPUTUM TEST:** Smear mycobacterium: Negative - Smear acid-fast staining: No acid-fast bacilli were detected; Culture for sputum fungi: Negative - Non fungal growth.

[redacted] **20[redacted] TB ANTIBODY TEST:** Negative

[redacted] **20[redacted] TEMPERATURE:** 37.1 Degrees C

[redacted] **20[redacted] TREPONEMA PALLIDUM ANTIBODY:** 0.10 No units (normal 0 to 1)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.07 X10**9/L (normal 3.5 to 9.5)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	4[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: TINNITUS	20[redacted]
OTHER: LITHANGIURIA	20[redacted]
OTHER: ANAL FISSURE	20[redacted]
PEPTIC ULCER DISEASE: GASTRIC ULCER	20[redacted]
DEGENERATIVE DISC DISEASE: PROTRASION OF THE LUMBAR INTERVERTEBRAL DISCI	20[redacted]
OTHER: CERVICAL SPONDYLOSIS	20[redacted]
OTHER: CONSTIPATION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: ACTIVE PLAQUE PSORIASIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	20[redacted]
SURGERY: EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY(URINARY CALCULI)	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.2 PACK	24	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 251	82

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CALCIPOTRIOL	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -119
CELECOXIB	200 mg	BID	Y-M: 20[redacted] / -119
EPIPEVISONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -119
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -119
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -119
TARS	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -119

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
CELECOXIB	200 mg	BID	Y-M: 20[redacted] / -119	ONGOING
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -119	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / 113	ONGOING
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	4 OTHER: PILL	TID	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 220
CEFTIZOXIME	2 g	BID	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 219
LEVOFLOXACIN;SODIUM CHLORIDE	0.3 g	BID	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 219
PYRIDOXINE	0.1 g	QD	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 219
FLUCONAZOLE	50 mg	QD	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 231
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 231
DOXYCYCLINE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 272
FUSIDIC ACID	APPROPRIATE OTHER: APPROPRIATE	BID	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 299

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

Event Description	URINARY TRACT INFECTION
Preferred term	尿路感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 206
Age at AE Onset	4[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 206): Bilirubin: 36 [2 - 21] UMOL/L; Cholesterol: 5.26 [0 - 5.2] MMOL/L; Creatinine: 60 [62 - 115] UMOL/L; Erythrocytes: 4.5 [4 - 5.5] 10^12/L; HDL Cholesterol: 1.86 [1.07 - 1.73] MMOL/L; Leukocytes: 3 [4 - 10] 10^9/L; NPTST012-ABNORMAL LYMPHOCYTE RATIO: 2.4 [0 - 2] %; NPTST038-ALT: 125 [5 - 40] U/L; NPTST076-AST: 75 [8 - 45] U/L; NPTST235-DIRECT BILIRUBIN: 12.55 [0 - 6.8] UMOL/L; NPTST357-HYPERSENSITIVE C-REACTIVE PROTE: 1.1 [1 - 1] MG/L; NPTST380-INDIRECT BILIRUBIN: 23.17 [4 - 18] UMOL/L; NPTST436-MEAN ERYTHROCYTE HEMOGLOBIN CON: 314 [320 - 360] G/L; NPTST614-STANDARD DEVIATION OF RED BLOOD: 56.9 [35 - 56] FL; Neutrophils: 1.83 [2 - 7] 10^9/L; Platelets: 131 [100 - 300] 10^9/L; [redacted]20[redacted] (RX DAY 260): Alanine Aminotransferase: 44 [5 - 40] U/L; Albumin: 50 [35 - 55] G/L; Alkaline Phosphatase: 57 [40 - 150] U/L; Aspartate Aminotransferase: 32 [0 - 40] U/L; Basophils: 0.03 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.6 [0 - 1] %; Bilirubin: 18 [5 - 28] UMOL/L; Creatinine: 81 [44 - 97] UMOL/L; Eosinophils: 0.25 [0.05 - 0.5] 10^9/L; Eosinophils/Leukocytes: 5.3 [0.5 - 5] %; Erythrocytes: 4.7 [3.5 - 5.5] 10^12/L; Glucose: 4.9 [3.9 - 6.1] MMOL/L; Hematocrit: 0.43 [0.34 - 0.45] FRACTION OF 1; Hemoglobin: 144 [110 - 160] G/L; Leukocytes: 4.7 [4 - 10] 10^9/L; Lymphocytes: 0.74 [1.26 - 3.35] 10^9/L; Lymphocytes/Leukocytes: 15.6 [17 - 48] %; Monocytes: 0.44 [0.12 - 0.8] 10^9/L; Monocytes/Leukocytes: 9.3 [2.7 - 11.7] %; NPTST298-GGT: 23 [11 - 50] U/L; NPTST299-GLB: 27.8 [20 - 35] G/L; NPTST315-HCV: 92.7 [85 - 98] FL; NPTST350-HIV: 0.16 [0 - 1] 099,S/CO; NPTST358-IBIL: 11 [5.1 - 18] UMOL/L; NPTST427-MCH: 30.9 [26 - 31] PG; NPTST428-MCHC: 333 [310 - 370] G/L; NPTST634-TOTAL CHOLESTEROL: 4.56 [2.8 - 5.17] MMOL/L; NPTST662-UREA: 5.97 [1.7 - 8.3] MMOL/L; Neutrophils: 3.28 [2 - 7.7] 10^9/L; Neutrophils/Leukocytes: 69.2 [43 - 76] %; Platelets: 150 [100 - 300] 10^9/L; Protein: 78 [60 - 88] G/L

Microbiology

[redacted]20[redacted] (RX DAY 206): BLOOD NPTST640-TREPONEMA PALLIDUM ANTIBODIES: Negative-NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 199): ULTRASONOGRAPHY OF KIDNEY, URETER, BLADDER AND PROSTATE: LEFT KIDNEY STONES. RIGHT URETERAL BLADDER WALL STONES. PROSTATE CALCIFICATION?; [redacted]20[redacted] (RX DAY 206): ULTRASONOGRAPHY OF KIDNEY, URETER, BLADDER AND PROSTATE: THERE WERE NO ABNORMALITIES EXCEPT FOR CALCIFICATION IN THE PROSTATE

AE Stopped Rx Day	359 (108 DAYS AFTER LAST TREATMENT)
Duration of AE	154 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は中国の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，尿路感染の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，体外衝撃波砕石（8 回）（尿路結石），尿路結石，乾癬性関節炎，局面型乾癬，現喫煙者（1 日 0.2 箱を 24 年間）及び元飲酒者（1 日 2～4 杯）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は尿路感染を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，尿路感染は消失した。

本事象発現前，20[redacted]年[redacted]月[redacted]日，被験者は排尿時に疼痛の発現を来した。20[redacted]年[redacted]月[redacted]日，被験者は左側尿路結石及び右側腎結石と診断された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左側尿路結石及び右側腎結石の治療のため入院した。また，この時点で被験者は尿路感染（UTI）と診断された。治験責任医師はこれを結石によるものと考えた。UTI に対して抗生物質による治療が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

退院後，被験者から尿道口の発赤や腫脹，並びに膿性分泌物や不快感の報告はなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，有効性欠如のため，治験薬の投与が完全に中止された。

20[redacted] 年 [redacted] 月，進行中の尿路感染に対しドキシサイクリン及びフシジン酸クリームが開始された。

投与された薬剤は，アベロックス，doxycycline hyclate，フシジン酸ナトリウム，レボフロキサシン塩酸塩，塩化ナトリウム注射剤，jie shi tong pian 及び ceftriaxone sodium であった。

The patient's past medications include:

CALCIPOTRIOL for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

PINE TAR AND ZINC OXIDE OINTMENT for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

TRIAMCINOLONE ACETONIDE ACETATE AND ECONAZOLE NITRATE CREAM for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Urinary tract infection (10046571) (Urinary tract infection (10046571)) [v.23.0] [10046571]

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 URINARY TRACT INFECTION

- Investigator: Not applicable

- AbbVie: Event more likely related to concurrent urinary and kidney stones, risk factor for which includes pre-existing history of urinary calculi.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABNORMAL LYMPHOCYTE RATIO:** 2.4 % (normal 0.0 to 2.0)

[redacted] **20[redacted] ALT:** 125 U/L (normal 5 to 40)

[redacted] **20[redacted] AST:** 75 U/L (normal 8 to 45)

[redacted] **20[redacted] CHOLESTEROL:** 5.26 MMOL/L (normal 0 to 5.2)

[redacted] **20[redacted] CREATININE:** 59.85 umol/L (normal 62 to 115)

[redacted] **20[redacted] CREATININE:** 81 MCMOL/L (normal 44 to 97)

[redacted] **20[redacted] CRP:** 1.1 MG/L (normal <1.0)

[redacted] **20[redacted] DIRECT BILIRUBIN:** 12.55 umol/L (normal 0 to 6.8)

[redacted] **20[redacted] HDL:** 1.86 MMOL/L (normal 1.07 to 1.73)

[redacted] **20[redacted] INDIRECT BILIRUBIN:** 23.17 umol/L (normal 4.0 to 18.0)

[redacted] **20[redacted] LYMPHOCYTES:** 15.6 % (normal 17 to 48)

[redacted] **20[redacted] MEAN ERYTHROCYTE HEMOGLOBIN CONCENTRATION:** 314 G/L (normal 320 to 360)

[redacted] **20[redacted] NEUTROPHILS:** 69.2 % (normal 43 to 76)

[redacted] **20[redacted] NEUTROPHILS ABSOLUTE:** 1.83 X10**9/L (normal 2.00 to 7.00)

[redacted] **20[redacted] NEUTROPHILS ABSOLUTE:** 3.28 X10**9/L (normal 2.00 to 7.00)

[redacted] **20[redacted] PLATELET COUNT:** 131 X10**9/L (normal 100 to 300)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.49 X10**12/L (normal 4.00 to 5.50)

[redacted] **20[redacted] STANDARD DEVIATION OF RED BLOOD CELL DISTRIBUTION WIDTH:** 56.9 FL (normal 35.0 to 56.0)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 35.72 umol/L (normal 1.7 to 21)

[redacted] **20[redacted] TREPONEMA PALLIDUM ANTIBODIES:** Negative

[redacted] **20[redacted] ULTRASONOGRAPHY OF KIDNEY, URETER, BLADDER AND PROSTATE:** Left kidney stones. Right ureteral bladder wall stones. Prostate calcification?

[redacted] **20[redacted] ULTRASONOGRAPHY OF KIDNEY, URETER, BLADDER AND PROSTATE:** There were no abnormalities except for calcification in the prostate.

[redacted] **20[redacted] WBC:** 3.02 X10**9/L (normal 4.0 to 10.0)

[redacted] **20[redacted] WBC:** 4.74 X10**9/L (normal 4.0 to 10.0)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	4[redacted]	MALE	ASIAN

Medical History	Onset Year
PSORIATIC ARTHRITIS	20[redacted]
HYPERLIPIDEMIA	20[redacted]
OTHER: CALCIFICATION OF INFERIOR LOBE OF RIGHT LUNG	20[redacted]
OTHER: DEGENERATED BILATERAL SACROILIAC JOINTS	20[redacted]
OTHER: SEDIMENT OF STEROL IN GALL BLADDER WALL	20[redacted]
OTHER: ACTIVE PLAQUE PSORIASIS	20[redacted]
TUBERCULOSIS: LATENT TB	20[redacted]

Prior Procedures	Procedure Year
SURGERY: ANAL FISTULA SURGERY	19[redacted]
SURGERY: POLYPECTOMY OF PYLORUS	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACECLOFENAC	100 mg	BID	Y-M: 20[redacted] / -113
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -113
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -113
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -102
MELOXICAM	15 mg	OTHER: EVERY NIGHT	Y-M: 20[redacted] / -102
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -102
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -95
MELOXICAM	7.5 mg	BID	Y-M: 20[redacted] / -63
UNSPECIFIED HERBAL	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / -63
ISONIAZID	300 mg	QD	Y-M: 20[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
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -102	Y-M: 20[redacted] / 64
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -95	Y-M: 20[redacted] / 66
MELOXICAM	7.5 mg	BID	Y-M: 20[redacted] / -63	ONGOING
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -14	ONGOING
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 66
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	0.4 g	TID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 66
CEFMETAZOLE	0.5 g	QD	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
ACETYLSALICYLIC ACID	1.8 g	TID	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 68
ASCORBIC ACID	2 g	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 71
CEFMETAZOLE	2 g	OTHER: EVERY 12H	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 75

DIGNOWELL	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: (APPLY THE AFFECTED AREA IF NECESSARY)	Y-M: 20[redacted] / 67 - Y-M: 20[redacted] / 67
GLYCYRRHIZA GLABRA	2 OTHER: TABLET	QD	Y-M: 20[redacted] / 67 - Y-M: 20[redacted] / 67
HALOMETASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: APPLY THE AFFECTED AREA IF NECESSARY	Y-M: 20[redacted] / 67 - Y-M: 20[redacted] / 67
ACETYLSALICYLIC ACID	1.8 g	QD	Y-M: 20[redacted] / 68 - Y-M: 20[redacted] / 68
CAFFEIC ACID	0.3 g	TID	Y-M: 20[redacted] / 68 - Y-M: 20[redacted] / 68
HYDROCORTISONE	0.1 g	QD	Y-M: 20[redacted] / 68 - Y-M: 20[redacted] / 68
LEUCOGEN	20 mg	TID	Y-M: 20[redacted] / 68 - Y-M: 20[redacted] / 68
VERAMID	2 mL	QD	Y-M: 20[redacted] / 68 - Y-M: 20[redacted] / 68
CALCIUM GLUCONATE	1 g	QD	Y-M: 20[redacted] / 68 - Y-M: 20[redacted] / 75
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / 68 - Y-M: 20[redacted] / 75
POTASSIUM	10 mL	QD	Y-M: 20[redacted] / 68 - Y-M: 20[redacted] / 75
NAPROXEN	100 mg	QD	Y-M: 20[redacted] / 71 - Y-M: 20[redacted] / 71
TUBERCULIN	50 IU	QD	Y-M: 20[redacted] / 71 - Y-M: 20[redacted] / 71
ZHI CHUANG NING	1 OTHER: ONE	PRN	Y-M: 20[redacted] / 71 - Y-M: 20[redacted] / 71
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / 71 - Y-M: 20[redacted] / 72
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 mL	QD	Y-M: 20[redacted] / 71 - Y-M: 20[redacted] / 72
VERAMID	2 mL	QD	Y-M: 20[redacted] / 71 - Y-M: 20[redacted] / 72
GADOPENTETIC ACID	1 OTHER: ONE	QD	Y-M: 20[redacted] / 72 - Y-M: 20[redacted] / 72
LIDOCAINE	20 mL	QD	Y-M: 20[redacted] / 72 - Y-M: 20[redacted] / 72
MANNITOL	125 mL	OTHER: ONCE	Y-M: 20[redacted] / 72 - Y-M: 20[redacted] / 72
MEROPENEM	500 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 72 - Y-M: 20[redacted] / 73
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / 72 - Y-M: 20[redacted] / 74
GANCICLOVIR	250 mg	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 72 - Y-M: 20[redacted] / 86

VORICONAZOLE	400 mg	OTHER: EVERY 12 HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 73 / 74
MANNITOL	125 mL	OTHER: EVERY 12 HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 73 / 82
MEROPENEM	1000 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 73 / 82
SULFAMETHOXAZOLE	0.8 g	BID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 74 / 75
GLUCOSE	500 mL	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 74 / 82
VITAMIN C	3 g	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 74 / 82
SODIUM CHLORIDE	4 mL	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 75 / 75
SULFAMETHOXAZOLE	0.8 g	TID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 75 / 80
VORICONAZOLE	200 mg	OTHER: Q12H	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 75 / 87
ALBUMIN HUMAN	10 g	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 76 / 76
POLYENE PHOSPHATIDYLCHOLINE	15 mL	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 76 / 87
IMMUNOGLOBULIN HUMAN NORMAL	10 g	QD	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 77 / 85
CHLORHEXIDINE;TRICLOSAN	200 mL	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 79 Y-M: 20[redacted]- [redacted] / 79
SODIUM BICARBONATE	10 OTHER: TABLET	TID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 79 / 105
SULFAMETHOXAZOLE	4 OTHER: TABLETS	TID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 80 / 83
MEROPENEM	1000 mg	OTHER: ONCE	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 82 / 82
SULPERAZON	3 g	OTHER: EVERY 12 HOURS	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 82 / 87
SULFAMETHOXAZOLE	2 OTHER: TABLET	TID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 83 / 87
AMOXICILLIN W/CLAVULANATE POTASSIUM	1 g	BID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 86 / 105
VORICONAZOLE	200 mg	BID	Y-M: 20[redacted]- Y-M: 20[redacted]- [redacted] / 86 / 105
PHOSPHATIDYL CHOLINE	456 mg	TID	Y-M: 20[redacted]- [redacted] / 87 ONGOING

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

Event Description	PULMONARY INFECTION
Preferred term	肺感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 66 (8 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 67): Alanine Aminotransferase: 15 [0 - 50] U/L; Albumin: 42 [35 - 55] G/L; Alkaline Phosphatase: 52 [30 - 120] U/L; Aspartate Aminotransferase: 55 [0 - 50] U/L; Basophils: 0 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.1 [0 - 1] %; Bilirubin: NEGATIVE [NOT REPORTED - NOT REPORTED] 099,NA; Bilirubin: 19 [2 - 28] UMOL/L; Blood: NEGATIVE [NOT REPORTED - NOT REPORTED] 099,NEGATIVE; Calcium: 2.15 [2.09 - 2.54] MMOL/L; Chloride: 105 [98 - 108] MMOL/L; Cholesterol: 3.93 [4.09 - 7.15] MMOL/L; Creatine Kinase: 2872 [NOT REPORTED - NOT REPORTED] U/L; Creatinine: 97 [59 - 114] UMOL/L; Eosinophils: 0.01 [0.05 - 0.5] 10^9/L; Eosinophils/Leukocytes: 0.1 [1 - 5] %; Erythrocyte Sedimentation Rate: 14 [0 - 21] MM/H; Erythrocytes: 3.1 [4.3 - 5.8] 10^12/L; Glucose: NEGATIVE [NOT REPORTED - NOT REPORTED] 099,NA; Glucose: 5.5 [3.9 - 6.1] MMOL/L; HDL Cholesterol: 0.59 [0.9 - 1.55] MMOL/L; Hematocrit: 0.29 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 97 [130 - 175] G/L; Ketones: 0.5WEAK POSITIVE [NOT REPORTED - NOT REPORTED] NA; LDL Cholesterol: 2.69 [2 - 4.5] MMOL/L; Leukocytes: 4.3 [3.5 - 9.5] 10^9/L; Leukocytes: NEGATIVE [NOT REPORTED - NOT REPORTED] NEGATIVE; Lymphocytes: 0.27 [0.7 - 3.8] 10^9/L; Lymphocytes/Leukocytes: 6.2 [20 - 40] %; Monocytes: 0.24 [0.11 - 0.76] 10^9/L; Monocytes/Leukocytes: 5.5 [3 - 8] %; NPTST029-AFP? ALPHA FETOPROTEIN?: ?0.24 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST071-APTT: 33.8 [20 - 40] SEC; NPTST073-ASO?ANTI-STREPTOLYSIN "O ?: 142 [0 - 200] IU/ML; NPTST083-BACT?BACTERIA?: 1 [0 - 7] /UL; NPTST116-BNP: 40 [NOT REPORTED - NOT REPORTED] 099,PG/ML; NPTST126-BYST: 0 [0 - 1] /UL; NPTST135-CA-125: 12.96 [NOT REPORTED - NOT REPORTED] U/mL; NPTST136-CA- 153: 5.69 [NOT REPORTED - NOT REPORTED] U/mL; NPTST137-CA-199: 8.25 [NOT REPORTED - NOT REPORTED] U/mL; NPTST138-CA-242: 3.08 [NOT REPORTED - NOT REPORTED] U/mL; NPTST161-CEA?CARCINOEMBRYONIC ANTIGEN?: 0.98 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST168-CK-MB: 23 [NOT REPORTED - NOT REPORTED] U/L; NPTST176-CO2: 25.1 [22 - 29] MMOL/L; NPTST183-COLOR, CHARACTER, LARVAE EGGS,: NOT DETECTED [NOT REPORTED - NOT REPORTED] NA; NPTST209-CRP: 100.9 [0 - 10] MG/L; NPTST227-DBIL: 3.8 [0 - 8] UMOL/L; NPTST228-DD? D-DIMER?: 1.1 [0 - 1.5] UG/ML; NPTST259-FBG?FIBRINOGEN?: 3.62 [2 - 4] G/L; NPTST260-FBIL: 15.4 [1.7 - 17] UMOL/L; NPTST262-FDP?FIBRINOGEN DEGRADATION PROD: 3.8 [0 - 5] UG/ML; NPTST274-FPSA?FREE PROSTATE SPECIFIC ANT: 0.07 [0 - 1.04] NG/ML; NPTST298-GGT: 107 [5 - 54] U/L; NPTST300-GLOBULIN: 28.1 [20 - 35] G/L; NPTST312-HBDH?AHYDROXYBUTYRATE DEHYDROG: 177 [90 - 180] U/L; NPTST342-HGH?HUMAN GROWTH HORMONE?: ?0.01 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST355- HYAL?HYALINE CAST?: 0 [0 - 1] /HPF; NPTST405-LDH: 323 [109 - 250] U/L; NPTST423-MALB(MICROALBUMIN): NEGATIVE [NOT REPORTED - NOT REPORTED] 099,NEGATIVE; NPTST427-MCH: 31 [27 - 34] PG; NPTST434-MEAN CORPUSCULAR HEMOGLOBIN CON: 337 [316 - 354] G/L; NPTST435-MEAN CORPUSCULAR VOLUME: 92 [82 - 100] FL; NPTST444-MG?MAGNESIUM?: 0.78 [0.65 - 1.1] MMOL/L; NPTST458-MUCS?VISCOSE RAYON?: 14 [0 - 28] /UL; NPTST477-NSE?NEURONE SPECIFIC ENOLASE?: 2.91 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST478-NSE?NON-SQUAMOUS EPITHELIAL CEL: 0 [0 - 6] /UL; NPTST486-OSM: 275.34 [275 - 295] 099,MOSM/KG; NPTST524-PROCALCITONIN: 0.63 [0 - 0.5] NG/ML; NPTST540-PSA: 0.13 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST541-PT: 13.2 [9 - 14] SEC; NPTST568-RED BLOOD CELL DISTRIBUTION WID: 50.8 [35 - 56] FL; NPTST577-RF?RHEUMATOID FACTOR?: 9.9 [0 - 20] IU/ML; NPTST594- SF?FERRITIN?: ?600.00 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST610- SQEP?SQUAMOUS EPITHELIAL CELL?: 1 [0 - 28] /UL; NPTST657-TT?THROMBIN TIME?: 16.7 [14 - 21] SEC; NPTST660-UNCX?UNCLASSIFIED CRYSTALLIZATI: 0 [0 - 28] /UL; NPTST662-UREA: 4 [2.1 - 7.2] MMOL/L; NPTST685-VARIATION COEFFICIENT OF ERYTHR: 15.7 [11.5 - 14.5] %; NPTST687-VC: ?=5.7 [NOT REPORTED - NOT REPORTED] 099,NA; NPTST695-WHITE BLOOD CELL GROUP: 0 [0 - 2] /UL; Neutrophils: 3.77 [1.75 - 6.75] 10^9/L; Neutrophils/Leukocytes: 88.1 [50 - 70] %; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] 099,NEGATIVE; Phosphate: 0.76 [0.8 - 1.5] MMOL/L; Platelets: 48 [100 - 300] 10^9/L; Potassium: 3.3 [3.5 - 5.3] MMOL/L; Protein: NEGATIVE [NOT REPORTED - NOT REPORTED] 099,NEGATIVE; Protein: 70 [60 - 83] G/L; Sodium: 138 [135 - 145] MMOL/L; Triglycerides: 2.73 [0.65 - 3.7] MMOL/L; Urate: 329 [90 - 420] UMOL/L; Urobilinogen: NEGATIVE [NOT REPORTED - NOT REPORTED] 099,NEGATIVE; [redacted]20[redacted] (RX DAY 72): Albumin: 50 [56 - 66] G/L; Albumin: 38 [40 - 55] G/L; Erythrocyte Sedimentation Rate: 43 [0 - 15] MM/H; Erythrocytes: 2.9 [4.3 - 5.8] 10^12/L; Erythrocytes: 290 [4.2 - 5.6] 10^12/L; Glucose: 4.5 [2.5 - 4.4] MMOL/L; Hemoglobin: 89 [130 - 175] G/L; Leukocytes: 9.2 [3.5 - 9.5] 10^9/L; NPTST033-ALPHA 1: 7.1 [2.9 - 4.9] %; NPTST074-ASPERGILLUS GALACTOMANNAN: 0.04 [NOT REPORTED - NOT REPORTED] 099,GMI; NPTST080-B B E ANTIBODY SEMI - QUANTITAT: 0.820 [NOT REPORTED - NOT REPORTED] 099,POSITIVE; NPTST129-C-REACTIVE PROTEIN: 157 [NOT REPORTED - NOT REPORTED] mg/L; NPTST153-CD3 COUNT: 3333 [941 - 2226] /MM3; NPTST155-CD4 COUNT: 1375 [471 - 1220] /MM3; NPTST157-CD8 COUNT: 1905 [303 - 1003] /MM3; NPTST165-CHLORINE: 122.5 [120 - 130] MMOL/L; NPTST184-COMBINED DETECTION OF HIV ANTIG: 0.19 [0 - 0.9] 099,COI; NPTST281-FUNGI 1, 3-B-D GLUCAN: 40.66 [NOT REPORTED - NOT REPORTED] pg/mL; NPTST286-GAMMA: 22.5 [11.1 - 18.8] %; NPTST304-GLUTAMYL TRANSPEPTIDASE: 80 [NOT REPORTED - NOT REPORTED] IU/L; NPTST316-HCV-AB: 0.04 [0 - 0.9] 099,COI? NEGATIVE; NPTST326-HEPATITIS B CORE ANTIBODY SEMI: 0.008 [NOT REPORTED - NOT REPORTED] 099,POSITIVE; NPTST327- HEPATITIS B E ANTIBODY: POSITIVE [NOT REPORTED - NOT REPORTED] 099,COI; NPTST332-HEPATITIS B SURFACE

ANTIBODY QU: ?2.000 [0 - 10] 099,NEGATIVE; NPTST335-HEPATITIS B SURFACE ANTIGEN SEM: 0.46 [0 - 0.9] 099,COI ?NEGATIVE; NPTST356-HYDROXYBUTYRATE DEHYDROGENASE: 248 [72 - 182] IU/L; NPTST375-IMMUNOGLOBULIN G: 16 [8 - 15.5] G/L; NPTST376- IMMUNOGLOBULIN M: 3170 [700 - 2200] MG/L; NPTST392-INTERLEUKIN 6: 148.2 [0 - 7] 099,PG/ML; NPTST396-KARYOCYTE: 0 [0 - 16] 10^6/L; NPTST403- LACTIC DEHYDROGENASE: 331 [110 - 220] IU/L; NPTST448-MICROPROTEIN: 0.5 [0.15 - 0.45] G/L; NPTST453-MONOVESICULAR VIRUS ANTIBODY I/: 2.65 [NOT REPORTED - NOT REPORTED] 099,INDEX; NPTST471-NON-WRINKLED ERYTHROCYTES: 100 [NOT REPORTED - NOT REPORTED] %; NPTST524-PROCALCITONIN: 0.19 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST567-REAL-TIME FLUORESCENCE DETECTIO: 1.43*10^4 [NOT REPORTED - NOT REPORTED] 099,COPIES/ML/; NPTST630-TORCH?MONOVESICULAR VIRUS ANTIB: 2.65 [NOT REPORTED - NOT REPORTED] 099,INDEX; Platelets: 114 [100 - 300] 10^9/L; Potassium: 3.3 [3.5 - 5.3] MMOL/L; Triglycerides: 3.46 [0.29 - 1.83] MMOL/L; [redacted]20[redacted] (RX DAY 75): NPTST209-CRP: 329 [NOT REPORTED - NOT REPORTED] mg/L; [redacted]20[redacted] (RX DAY 79): NPTST174-CMV-DNA: 2.28?10? [NOT REPORTED - NOT REPORTED] 099,COPIES/ML; [redacted]20[redacted] (RX DAY 85): NPTST209-CRP: 13.90 [NOT REPORTED - NOT REPORTED] mg/L; NPTST524-PROCALCITONIN: 0.19 [NOT REPORTED - NOT REPORTED] ng/mL; [redacted]20[redacted] (RX DAY 103): NPTST329- HEPATITIS B E ANTIGEN SEMI - QU: 0.09 [0 - 1] 099,NEGATIVE

Microbiology

[redacted]20[redacted] (RX DAY 67): SPUTUM NPTST004- SPUTUM SMEAR: Negative-NO ACIDRESISTANT BACTERIA, NO FUNGUS, A SMALL AMOUNT OF G+ COCCI, WHITE BLOOD CELLS > 25/LP, EPITHELIAL CELLS > 10/LP WERE DETECTED; SPUTUM NPTST607- SPUTUM CULTURE: Negative-NORMAL MIXED FLORA; [redacted]20[redacted] (RX DAY 72): BLOOD NPTST042-ANAEROBIC BLOOD CULTURE: Negative-NO ANAEROBIC GROWTH; BLOOD NPTST104-BLOOD AND BONE MARROW CULTURE: Negative-NO BACTERIA AND FUNGUS GROWTH AFTER 5 DAYS CULTURE; CEREBROSPINAL FLUID NPTST280-FUNGAL CULTURE: Negative-NO FUNGUS GROWTH AT 2 WEEKS?CULTURE WAS EXTENDED TO 21 DAYS; CEREBROSPINAL FLUID NPTST379-INDIA INK STAIN: Negative-SMEAR INK STAINING: NO CRYPTOCOCCUS WAS FOUND; CEREBROSPINAL FLUID NPTST598-SMEAR FOR BACTERIA + FUNGUS: Negative-SMEAR GRAM STAINING: NO FUNGUS AND BACTERIA WERE DETECTED; CEREBROSPINAL FLUID NPTST600-SMEAR FOR DISMITOBACTERIUM: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE FOUND; CEREBROSPINAL FLUID NPTST602-SMEAR MYCOBACTERIUM: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE DETECTED; [redacted]20[redacted] (RX DAY 73): SPUTUM NPTST213-CULTURE OF SPUTUM AND PHARYNGEA: Negative-NORMAL MIXED BACTERIUM IS OVERGROWN LONG, DID NOT ISOLATE HAEMOPHILUS BACTERIUM; CEREBROSPINAL FLUID NPTST231-DETECTION OF CRYPTOCOCCAL ANTIG: Negative; SPUTUM NPTST597-SMEAR CHECK BACTERIA + FUNGUS: Negative-SMEAR GRAM STAINING: NO FUNGUS DETECTED MIXED UPPER RESPIRATORY TRACT FLORA: SQUAMOUS EPITHELIAL CELLS > 25/LP WHITE BLOOD CELLS < 10/LP, NOT DEEP; [redacted]20[redacted] (RX DAY 76): SPUTUM NPTST602-SMEAR MYCOBACTERIUM: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE DETECTED; [redacted]20[redacted] (RX DAY 78): OTHER ALVEOLAR LAVAGE NPTST517- PNEUMOCYSTIS NUCLEIC ACID CHARA: Positive-BE POSITIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 72): BILATERAL KNEE JOINT COLOR DOPPLER ULTRASOUND REPORT: THE KNEE JOINT: STRONG ECHOGENICS WERE DETECTED ON THE CORTICAL SURFACE OF BILATERAL QUADRICEPS TENDON ATTACHMENT BONE, AND NO OBVIOUS BLOOD FLOW SIGNAL WAS OBSERVED.NO OBVIOUS ECHO AREA WAS FOUND INEACH SPACE OF BILATERAL KNEE JOINT, AND NO ABNORMAL MORPHOLOGY OF BONE AND CARTILAGE WAS OBSERVED IN OTHER JOINTS.NO OBVIOUS ABNORMALITIES WERE OBSERVED IN THE TENDONS OF THE REST KNEE JOINTS.NO ABNORMAL ECHO WAS OBSERVED IN THE SOFT TISSUE AROUND THE JOINT.CDFI: NO ABNORMAL BLOOD FLOW SIGNAL WAS OBSERVED. DIAGNOSTIC HINT OSTEOPHYTES AT BILATERAL QUADRICEPS TENDON ATTACHMENTS.; BOTH HANDS DIGITAL X - RAY AMBIDEXTROUS PHOTOGRAPHY: SUMMARY COMMENTS: THE HANDS AND DOUBLE OSTEOPOROSIS, PART ON THE LEFT SIDE OF THE RADIOCARPAL JOINT, WRIST JOINTS, JOINT FROM 1 AND NARROW CLEARANCE, HANDS OF INTERPHALANGEAL JOINT SURFACE COARSE, HARDENING, SURROUNDING SOFT TISSUE IS A BIT SWOLLEN, RIGHT HAND IS BUCKLING, THE DISTAL INTERPHALANGEAL (PIP) 4 LOCAL DISPLAY OWE, THE PROMPT ARTICULAR INFLAMMATORY LESIONS, COMBINED WITH CLINICAL AND OTHER CHECKS, PLEASE.; COLOR DOPPLER ULTRASOUND REPORT: LIVER, PANCREAS, SPLEEN, KIDNEY, BLADDER, URETER NO ABNORMALITIES, NO SPACE OCCUPATION. NO ABNORMALITY WAS FOUND IN THE VISCERA, WHICH SUGGESTED CHOLESTEROL DEPOSITION IN THE GALLBLADDER WALL AND PROSTATE CALCIFICATION; CT CHEST PLAIN SCAN + THIN LAYER RESOLUTION SCAN: 1. MULTIPLE FROSTED GLASS NODULES AND SMALL PATCHES IN BOTH LUNGS, DISTRIBUTED ALONG THE BRONCHI, AND MULTIPLE INFECTION FOCI, PLEASE REVIEW IN COMBINATION WITH CLINICAL PRACTICE AND TREATMENT. 2. NOENLARGEMENT OF THE

HEART. 3. INCREASED MEDIASTINAL LYMPH NODES.; LUMBAR PUNCTURE: THE INITIAL PRESSURE WAS FLUSHED INTO THE TUBE AND 20ML CEREBROSPINAL FLUID WAS TAKEN FOR EXAMINATION. THE FINAL PRESSURE WAS 170MMH2O; THE HEAD SCAN: NO ABNORMAL DENSITY SHADOW WAS FOUND IN THE INTRACRANIAL, NO ABNORMAL SHAPE OR SIZE OF VENTRICLE AND CISTERN, AND NO DEVIATION OF MIDLINE STRUCTURE.CEREBELLUM AND BRAINSTEM WERE LESS CLEAR DUE TO SKULL ARTIFACTS, AND NO ABNORMALITIES WERE OBSERVED IN THE SKULL; [redacted]20[redacted] (RX DAY 73): ECHOCARDIOGRAPHY: DIAGNOSTIC COMMENTS: CARDIAC STRUCTURE AND BLOOD FLOW WERE NOT ABNORMAL LEFT VENTRICULAR SYSTOLIC FUNCTION WAS NORMAL; MRI HEAD AXIAL CORONAL SAGITTAL SCAN + ENHANCEMENT: SMALL NODULAR T2 HYPERINTENSITY SHADOWS SCATTERED IN BOTH HEMISPHERES, FLAIR SHOWED HYPERINTENSITY, WITH NO ENHANCEMENT.THE SULCUS AND FISSURE OF BRAIN WERE NOT ENLARGED, AND THE MIDLINE STRUCTURE WASIN THE MIDDLE.NO DEFINITE ABNORMALITY WAS FOUND IN SKULL SIGNAL. SUMMARY COMMENTS: 1. THE BRAIN PARENCHYMA IS SCATTERED IN SMALL ISCHEMIC FOCI, PLEASE FOLLOW UP AND REVIEW. 2. PARANASAL SINUSITIS.

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, LIFE THREATENING

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は中国の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺感染の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，乾癬性関節炎，右肺下葉の石灰化，高脂血症，潜伏結核，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺感染を発現した。

20[redacted]年[redacted]月の事象発現前，被験者は上気道の感染（非重篤）を発現した。20[redacted]年[redacted]月[redacted]日，被験者は肝機能障害（非重篤）と診断された。20[redacted]年[redacted]月[redacted]日，被験者は白血球減少症（非重篤）及び好中球顆粒球減少症（非重篤）と診断された。20[redacted]年[redacted]月[redacted]日，治験 8 週目にベースラインから 3 g/dL 以上のヘモグロビン減少が認められた。

20[redacted]年[redacted]月[redacted]日，被験者は発熱及び浮動性めまいの発現を来した。発熱は悪化した。喉の渇き及び暗黄色尿が見られたが，いずれも適切な水分補給後に消失した。20[redacted]年[redacted]月[redacted]日，被験者は 39°C（自宅で測定）の発熱を来した。20[redacted]年[redacted]月[redacted]日，被験者は治療のため入院した。20[redacted]年[redacted]月[redacted]日，被験者は治療と確定診断のため他院に転院となった。20[redacted]年[redacted]月[redacted]日，診察と回診が行われた。対症療法として冷却療法が行われ，抗ウイルス薬及び利尿薬が追加された。この時点では，発熱の原因は肺感染及び頭蓋内感染であると考えられた。20[redacted]年[redacted]月[redacted]日，被験者はサイトメガロウイルス感染（非重篤）を来していることが判明した。20[redacted]年[redacted]月[redacted]日，被験者の状態は改善していた。発熱，咳嗽，頭痛，悪心，嘔吐，腹痛及び労作時の胸部絞扼感は見られなかった。診察時において，両肺に乾性ラ音及び湿性ラ音は聴取されず，両下肢の腫れも認められなかった。被験者はその後，この日に退院した。

この事象により治験薬の投与が完全に中止された。

投与された薬剤は，セフメタゾール，モキシフロキサシン，グルコン酸カルシウム，塩化カリウム，aminophenazone・barbital 合剤，ヒドロコルチゾンコハク酸エステルナトリウム，ビタミン C 注射剤，leucogen，ガンシクロビル，マンニットール，ナプロキセン，メロペネム，ボリコナゾール，スルファメトキサゾール，アモキシシリン・クラブラン酸カリウム，lysine acetylsalicylate，スルペラゾン，ポリエンホスファチジルコリン注射剤及び柴胡注射剤であった。

The patient's past medications include:

XUESHANJINLUOHAN ZHITONGTUMOJI for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Lung infection (10061229) (Pneumonia (10035664)) [v.23.0] [10061229]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of PULMONARY INFECTION

- Investigator: Not applicable.

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALVEOLAR LAVAGE:** Positive

[redacted] **20[redacted] ANTI-HEP B SURFACE AG2 QUAL:** Positive

[redacted] **20[redacted] BLOOD ANTI HIV:** NEGATIVE

[redacted] **20[redacted] BLOOD ANTI-TP:** NEGATIVE

[redacted] **20[redacted] BODY TEMPERATURE:** 39 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 36.2 Degrees C

[redacted] **20[redacted] CD3 COUNT:** 3333 cell/uL (normal 941 to 2226)

[redacted] **20[redacted] CD4 COUNT:** 1375 cell/uL (normal 471 to 1220)

[redacted] **20[redacted] CD8 COUNT:** 1905 cell/uL (normal 303 to 1003)

[redacted] **20[redacted] CEREBROSPINAL FLUID:** RBC’s of 290, microprotein of 0.5 (0.15-0.45), glucose of 4.47 (2.5-4.4)

[redacted] **20[redacted] CEREBROSPINAL FLUID:** Smear mycobacterium - negative Smear acid-fast staining: no acid-fast bacilli were detected

[redacted] **20[redacted] CHEST X-RAY:** screening chest x-ray: There are nodules in the lower field of the left lung, which may be inflammatory nodules or vascular sections.

[redacted] **20[redacted] CMV-DNA:** 2.28 x10**3 copies/ML (lower range normal 1.0 x10**2, upper normal 5.0 x10**7)

[redacted] **20[redacted] CSF INDIA INK STAIN:** SMEAR INK STAINING: NO CRYPTOCOCCUS WAS FOUND

[redacted] 20[redacted] **CSF SMEAR FOR BACTERIA AND FUNGUS:** SMEAR GRAM STAINING: NO FUNGUS AND BACTERIA WERE DETECTED

[redacted] 20[redacted] **CSF SMEAR FOR DISMITOBACTERIUM:** SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE FOUND

[redacted] 20[redacted] **CT CHEST:** 1. MULTIPLE FROSTED GLASS NODULES AND SMALL PATCHES IN BOTH LUNGS, DISTRIBUTED ALONG THE BRONCHI, AND MULTIPLE INFECTION FOCI, PLEASE REVIEW IN COMBINATION WITH CLINICAL PRACTICE AND TREATMENT. 2. NO ENLARGEMENT OF THE HEART. 3. INCREASED MEDIASTINAL LYMPH NODES.

[redacted] 20[redacted] **CT HEAD:** NO ABNORMAL DENSITY SHADOW WAS FOUND IN THE INTRACRANIAL, NO ABNORMAL SHAPE OR SIZE OF VENTRICLE AND CISTERN, AND NO DEVIATION OF MIDLINE STRUCTURE.CEREBELLUM AND BRAINSTEM WERE LESS CLEAR DUE TO SKULL ARTIFACTS, AND NO ABNORMALITIES WERE OBSERVED IN THE SKULL.

[redacted] 20[redacted] **DIGITAL X-RAY AMBIDEXTROUS PHOTOGRAPHY:** SUMMARY COMMENTS: THE HANDS AND DOUBLE OSTEOPOROSIS, PART ON THE LEFT SIDE OF THE RADIOCARPAL JOINT, WRIST JOINTS, JOINT FROM 1 AND NARROW CLEARANCE, HANDS OF INTERPHALANGEAL JOINT SURFACE COARSE, HARDENING, SURROUNDING SOFT TISSUE IS A BIT SWOLLEN, RIGHT HAND IS BUCKLING, THE DISTAL INTERPHALANGEAL (PIP) 4 LOCAL DISPLAY OWE, THE PROMPT ARTICULAR INFLAMMATORY LESIONS.

[redacted] 20[redacted] **DOPPLER ULTRASOUND:** Liver, pancreas, spleen, kidney, bladder, ureter no abnormalities, no space occupation. NO ABNORMALITY WAS FOUND IN THE VISCERA, WHICH SUGGESTED CHOLESTEROL DEPOSITION IN THE GALLBLADDER WALL AND PROSTATE CALCIFICATION

[redacted] 20[redacted] **DOPPLER ULTRASOUND:** THE KNEE JOINT: STRONG ECHOGENICS WERE DETECTED ON THE CORTICAL SURFACE OF BILATERAL QUADRICEPS TENDON ATTACHMENT BONE, AND NO OBVIOUS BLOOD FLOW SIGNAL WAS OBSERVED.NO OBVIOUS ECHO AREA WAS FOUND IN EACH SPACE OF BILATERAL KNEE JOINT, AND NO ABNORMAL MORPHOLOGY OF BONE AND CARTILAGE WAS OBSERVED IN OTHER JOINTS.NO OBVIOUS ABNORMALITIES WERE OBSERVED IN THE TENDONS OF THE REST KNEE JOINTS.NO ABNORMAL ECHO WAS OBSERVED IN THE SOFT TISSUE AROUND THE JOINT.CDFI: NO ABNORMAL BLOOD FLOW SIGNAL WAS OBSERVED. DIAGNOSTIC HINT OSTEOPHYTES AT BILATERAL QUADRICEPS TENDON ATTACHMENTS.

[redacted] 20[redacted] **ECHO:** DIAGNOSTIC COMMENTS: CARDIAC STRUCTURE AND BLOOD FLOW WERE NOT ABNORMAL LEFT VENTRICULAR SYSTOLIC FUNCTION WAS NORMAL

[redacted] 20[redacted] **FLUORESCENCE DETECTION OF HUMAN CYTOMEGALOVIRUS:** 1.43 x10**4 copies/ml

[redacted] 20[redacted] **FUNGAL CULTURE (CSF):** Negative. No fungus growth at 2 weeks, culture was extended to 21 days.

[redacted] 20[redacted] **FUNGI 1 3-B-D GLUCAN:** 40.66 pg/ml (Negative < 70 - Positive > 95)

[redacted] 20[redacted] **HEP B SURFACE ANTIGEN:** Negative

[redacted] 20[redacted] **HEPATITIS B CORE TOTAL:** Negative

[redacted] **20[redacted] HEPATITIS B E ANTIBODY:** POSITIVE

[redacted] **20[redacted] IMMUNOGLOBULIN G:** 16 MG/L (normal 8 to 15.5)

[redacted] **20[redacted] IMMUNOGLOBULIN M:** 3170 MG/L (normal 700 to 2200)

Unknown date LUMBAR PUNCTURE: The initial pressure was flushed into the tube and 20ml cerebrospinal fluid was taken for examination. The final pressure was 170mmH2O

[redacted] **20[redacted] MONOVESICULAR VIRUS ANTIBODY TYPE I/II IGM:** 2.65 Index (normal <1.1)

[redacted] **20[redacted] MRI HEAD:** SMALL NODULAR T2 HYPERINTENSITY SHADOWS SCATTERED IN BOTH HEMISPHERES, FLAIR SHOWED HYPERINTENSITY, WITH NO ENHANCEMENT.THE SULCUS AND FISSURE OF BRAIN WERE NOT ENLARGED, AND THE MIDLINE STRUCTURE WAS IN THE MIDDLE.NO DEFINITE ABNORMALITY WAS FOUND IN SKULL SIGNAL. SUMMARY COMMENTS: 1. THE BRAIN PARENCHYMA IS SCATTERED IN SMALL ISCHEMIC FOCI. 2. PARANASAL SINUSITIS.

[redacted] **20[redacted] NEUTROPHILS:** 1.55 X10**3/MCL (normal 1.96 to 7.23)

[redacted] **20[redacted] SPUTUM CULTURE:** NEGATIVE

[redacted] **20[redacted] SPUTUM SMEAR:** NO ACID-RESISTANT BACTERIA, NO FUNGUS, A SMALL AMOUNT OF G positive COCCI, WHITE BLOOD CELLS > 25/LP, EPITHELIAL CELLS > 10/LP WERE DETECTED

[redacted] **20[redacted] STOOL CULTURE:** larvae eggs, whipworm eggs, hook eggs, red blood cells, white blood cells, pus, phagocytes, occult blood - not detected

[redacted] **20[redacted] URINE BILIRUBIN:** negative

[redacted] **20[redacted] URINE GLUCOSE:** negative

[redacted] **20[redacted] URINE KETONES:** 0.5 (weak positive)

[redacted] **20[redacted] WBC:** 2.29 X10**3/MCL (normal 3.8 to 10.7)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肝臓血管腫	X			X

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 30 mg QD	4[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: ACUTE PHARYNGITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: IMPLANTATION OF INTRAUTERINE DEVICE	1995
SURGERY: REMOVAL OF INTRAUTERINE DEVICE	20[redacted]
SURGERY: FIBROMA OF BREAST	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)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 391	223
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 392		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
MELOXICAM	7.5 mg	BID	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
PAEONIA OFFICINALIS	0.6 g	TID	Y-M: 20[redacted]
THALIDOMIDE	50 mg	OTHER: QN	Y-M: 20[redacted]
DICLOFENAC	50 mg	BID	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
PAEONIA OFFICINALIS	0.6 g	TID	Y-M: 20[redacted]
THALIDOMIDE	50 mg	OTHER: QN	Y-M: 20[redacted]
MELOXICAM	7.5 mg	BID	Y-M: 20[redacted] / -153
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -153
SULFASALAZINE	0.5 g	TID	Y-M: 20[redacted] / -153
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1.0 g	TID	Y-M: 20[redacted] / -153
ERGOCALCIFEROL	300 mg	BID	Y-M: 20[redacted] / -117
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -117
LEVONORGESTREL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -50
CEFDINIR	0.1 g	BID	Y-M: 20[redacted] / -33
CEFDINIR	0.1 g	BID	Y-M: 20[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
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -153	NOT REPORTED
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -117	NOT REPORTED
LEKOVIT CA	0.3 g	QD	Y-M: 20[redacted] / 396	NOT REPORTED
DYDROGESTERONE	10 mg	BID	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 499
IBUPROFEN	0.6 g	OTHER: ST	Y-M: 20[redacted] / 573	Y-M: 20[redacted] / 573

Event #1: Serious Adverse Event, Event of Interest - Hepatic Disorder

Event Description	HEPATIC CAVERNOUS HEMANGIOMA
Preferred term	肝臓血管腫
AE Onset Date / Rx Day	[redacted]20[redacted] / 520
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 527): Alkaline Phosphatase: 28 [35 - 100] U/L; Erythrocytes: 3.6 [3.8 - 5.1] 10^12/L; Hematocrit: 0.35 [0.35 - 0.45] FRACTION OF 1; Leukocytes: 5.3 [3.5 - 9.5] 10^9/L; Lymphocytes: 1.05 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 19.9 [20 - 50] %; Monocytes: 0 [0.1 - 0.6] 10^9/L; Monocytes/Leukocytes: 0 [3 - 10] %; NPTST413-LIPOPROTEIN A: 687 [0 - 300] MG/L; NPTST523-PREALBUMIN: 413 [150 - 400] MG/L; NPTST535-PROTHROMBIN ACTIVITY: 141.7 [70 - 130] %; NPTST537-PROTHROMBIN TIME: 9.2 [9.8 - 12.1] 099,S; Neutrophils/Leukocytes: 79 [40 - 75] %; Phosphate: 0.7 [0.85 - 1.51] MMOL/L; Protein: 63 [65 - 85] G/L

Microbiology

[redacted]20[redacted] (RX DAY 520): OTHER THROAT SWAB NPTST472-NOVEL CORONAVIRUS NUCLEIC ACID: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 520): CT SCAN-CHEST: TWO LOW-DENSITY FOCI IN THE LIVER;INFLAMMATION OF BOTH LUNGS; [redacted]20[redacted] (RX DAY 521): COLOR DOPPLER ULTRASOUND OF LIVER: HEPATIC PARENCHYMAL SPACE OCCUPYING; [redacted]20[redacted] (RX DAY 528): ECG: NORMAL; LIVER BIOPSY: CAVERNOUS HEMANGIOMA

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	MAY BE RELATED TO ESTROGEN LEVELS IN THE BODY
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: M15-572

治験責任医師からの報告。本被験者は中国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肝海綿状血管腫の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乳房線維腫，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された

皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肝海綿状血管腫を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，病院の新型コロナウイルス予防・管理要件に従い，被験者は胸部 CT 検査と核酸検査を受けた。CT スキャン検査で肝臓に低吸収病巣が 2 ヵ所認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はさらに治療を受けるため腫瘍内科クリニックを受診し，肝臓と腫瘍の精査を受けた（CEA，AFP，CA125，CA15-3，CA19-9 など）。肝臓のカラードップラー検査で，肝実質が相当に占拠されており，腫瘍医から精査のための入院が提案された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，関連する検査を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，免疫学的スクリーニング，ルーチンの血液検査，凝固機能，ルーチンの生化学検査，核酸検査が行われ，明らかな異常は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，心電図検査が行われ，結果は正常であった。同日，局所麻酔下で肝生検が行われた。手術終了後，術後出血を止めるためヘモコアグラーゼが使用された。病理報告から「海綿状血管腫」が示唆された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，定期的に経過観察を受けた。

The patient's past medications include:

MELOXICAM for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

TOTAL GLUCOSIDE OF RADIX PAEONIAE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

THALIDOMIDE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

DICLOFENAC SODIUM for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SULFASALAZINE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

XIANLING GUBAO for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Hemangioma of liver (10019396) (Haemangioma of liver (10018821)) [v.23.0] [10019396]

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 HEPATIC CAVERNOUS HEMANGIOMA

- Investigator: May be related to estrogen levels in the body.

- AbbVie: Hepatic hemangioma is the most common benign liver tumor. Literature places its incidence at 0.4% to 20% of the total population, most often being discovered incidentally during imaging investigations for various unrelated pathologies.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 28 U/L (normal 35 to 100)

[redacted] **20[redacted] CA125:** Not reported

[redacted] **20[redacted] CA15-3:** Not reported

[redacted] **20[redacted] CA19-9:** Not reported

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

[redacted] **20[redacted] CHEST CT:** Showed two low-density foci in the liver; Inflammation of both lungs.

[redacted] **20[redacted] COLOR DOPPLER ULTRASOUND OF LIVER:** Hepatic parenchymal space occupying.

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

[redacted] **20[redacted] HEMATOCRIT:** 0.349 L/L (normal 0.35 to 0.45)

[redacted] **20[redacted] INORGANIC PHOSPHORUS:** 0.70 MMOL/L (normal 0.85 to 1.51)

[redacted] **20[redacted] LIPOPROTEIN A:** 687 MG/L (normal 0 to 300)

[redacted] **20[redacted] LIVER BIOPSY:** Cavernous hemangioma.

[redacted] **20[redacted] LYMPHOCYTES %:** 19.9 % (normal 20 to 50)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 1.05 X10**9/L (normal 1.1 to 3.2)

[redacted] **20[redacted] MONOCYTES %:** 0 % (normal 3 to 10)

[redacted] **20[redacted] MONOCYTES ABS:** 0 X10**9/L (normal 0.1 to 0.6)

[redacted] **20[redacted] NASOPHARYNGEAL SWAB:** Negative.

[redacted] **20[redacted] NEUTROPHILS %:** 79 % (normal 40 to 75)

[redacted] **20[redacted] NUCLEIC ACID TEST:** Not reported.

[redacted] **20[redacted] NUCLEIC ACID TEST:** Not reported.

[redacted] **20[redacted] PREALBUMIN:** 413 MG/L (normal 150 to 400)

[redacted] **20[redacted] PROTHROMBIN ACTIVITY:** 141.7 % (normal 70 to 130)

[redacted] **20[redacted] PROTHROMBIN TIME:** 9.2 SEC (normal 9.8 to 12.1)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.57 X10**12/L (normal 3.8 to 5.1)

[redacted] **20[redacted] TOTAL PROTEIN:** 63.3 G/L (normal 65 to 85)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.28 X10**9/L (normal 3.5 to 9.5)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: ANEMIA	NOT REPORTED
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: LYMPH NODE ENLARGEMENT	20[redacted]

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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
UNSPECIFIED HERBAL	20 mg	TID	Y-M: 20[redacted]
ACITRETIN	10 mg	BID	Y-M: 20[redacted]
HALCINONIDE	NOT REPORTED	TID	Y-M: 20[redacted]

DICLOFENAC	25 mg	TID	Y-M: 20[redacted]
LEFLUNOMIDE	10 mg	QD	Y-M: 20[redacted]
HYDROCORTISONE	NOT REPORTED	BID	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
UNSPECIFIED HERBAL	0.7 g	BID	Y-M: 20[redacted]
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	0.6 g	TID	Y-M: 20[redacted]
UNSPECIFIED HERBAL	20 mg	TID	Y-M: 20[redacted]
UNSPECIFIED HERBAL	20 mg	TID	Y-M: 20[redacted]
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	0.6 g	BID	Y-M: 20[redacted]
UNSPECIFIED HERBAL	0.7 g	TID	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
UNSPECIFIED HERBAL	20 mg	TID	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
HALCINONIDE	UNK OTHER: UNK	TID	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
GLYCYRRHIZA GLABRA	2 OTHER: PILLS	TID	Y-M: 20[redacted]
HALOMETASONE	UNK OTHER: UNK	QD	Y-M: 20[redacted]
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted]
UNSPECIFIED HERBAL	20 mg	TID	Y-M: 20[redacted]
HALCINONIDE	UNK OTHER: UNK	BID	Y-M: 20[redacted]
HALOMETASONE	UNK OTHER: UNK	BID	Y-M: 20[redacted] / -258
UNSPECIFIED HERBAL	20 mg	TID	Y-M: 20[redacted] / -229
PANCURONIUM	0.6 mg	QD	Y-M: 20[redacted] / -201
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -159
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / -150
TRAMADOL	100 mg	OTHER: Q12H	Y-M: 20[redacted] / -149
SULFASALAZINE	0.75 g	BID	Y-M: 20[redacted] / -140
TRAMADOL	100 mg	OTHER: Q12H	Y-M: 20[redacted] / -42
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -31
TRAMADOL	100 mg	QD	Y-M: 20[redacted] / -31
TRAMADOL	100 mg	OTHER: Q12H	Y-M: 20[redacted] / -27
OMEPRAZOLE	20 mg	QD	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
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / -150	Y-M: 20[redacted] / 420
SULFASALAZINE	0.75 g	BID	Y-M: 20[redacted] / -140	NOT REPORTED
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / 7	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / 144	ONGOING

LOXOPROFEN	60 mg	BID	Y-M: 20[redacted] / 421	Y-M: 20[redacted] / 422
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / 422	NOT REPORTED
DRACAENA COCHINCHINENSIS	1 OTHER: PILL	QD	Y-M: 20[redacted] / 422	Y-M: 20[redacted] / 425
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / 435	Y-M: 20[redacted] / 437
BENZYLPENICILLIN	16000 OTHER: U	OTHER: ONCE	Y-M: 20[redacted] / 437	Y-M: 20[redacted] / 437
BENZYLPENICILLIN	1600000 OTHER: U	TID	Y-M: 20[redacted] / 437	Y-M: 20[redacted] / 437
BENZYLPENICILLIN	4800000 IU	TID	Y-M: 20[redacted] / 437	Y-M: 20[redacted] / 446
PANTOPRAZOLE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 439	Y-M: 20[redacted] / 439
ESOMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 440	NOT REPORTED
TEPRENONE	50 mg	TID	Y-M: 20[redacted] / 440	NOT REPORTED
BENZYLPENICILLIN	16000 OTHER: U	OTHER: ONCE	Y-M: 20[redacted] / 443	Y-M: 20[redacted] / 443
ERYTHROMYCIN	10 g	BID	Y-M: 20[redacted] / 443	Y-M: 20[redacted] / 443
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 446	NOT REPORTED
ESOMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 457
CEFIXIME	0.2 g	BID	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 459
TEPRENONE	50 mg	TID	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 460

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

Event Description	LEFT DORSAL CELLULITIS
Preferred term	蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 437
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 437): Hemoglobin: 126 [130 - 175] G/L; NPTST346-HIGHSENSITIVITY C-REACTIVE PRO: 38.55 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 438): Albumin: 36 [40 - 55] G/L; Calcium: 2.06 [2.11 - 2.52] MMOL/L; Erythrocyte Sedimentation Rate: 61 [NOT REPORTED - 43] mm/h; HDL Cholesterol: 1.74 [1.03 - 1.55] MMOL/L; NPTST002- ACTIVATED PARTIAL THROMBOPLAST: 37.3 [25.1 - 36.5] SEC; NPTST268-FIBRINOGEN: 5.7 [2 - 4] G/L; NPTST483-OCCULT BLOOD IN STOOL: ++ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 60 [65 - 85] G/L; [redacted]20[redacted] (RX DAY 439): NPTST483-OCCULT BLOOD IN STOOL: + [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 443): Erythrocyte Sedimentation Rate: 55 [NOT REPORTED - 43] mm/h; Erythrocytes: 4 [4.3 - 5.8] 10^12/L; Hematocrit: 0.39 [0.4 - 0.5] FRACTION OF 1; NPTST357-HYPERSENSITIVE CREACTIVE PROTE: 9.25 [0 - 5] MG/L; NPTST483-OCCULT BLOOD IN STOOL: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 38 [40 - 55] G/L; [redacted]20[redacted] (RX DAY 445): NPTST483-OCCULT BLOOD IN STOOL: +++ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 452): Erythrocytes: 4 [4.3 - 5.8] 10^12/L; Hematocrit: 0.38 [0.4 - 0.5] FRACTION OF 1; Leukocytes: ?.?? [3.5 - 9.5] 10^9/L; Lymphocytes: ??? [1.1 - 3.2] 10^9/L; NPTST437-MEAN PLATELET VOLUME: 12.2 [9.1 - 12] FL; NPTST514-PLATELET VOLUME DISTRIBUTION WI: 17.4 [9.8 - 15.2] FL; NPTST568-RED BLOOD CELL DISTRIBUTION WID: 11.8 [12.2 - 14.6] %; Protein: 65 [65 - 85] G/L; [redacted]20[redacted] (RX DAY 463): Hematocrit: 0.4 [0.4 - 0.5] FRACTION OF 1; NPTST437-MEAN PLATELET VOLUME: 12.4 [9.1 - 12] FL; NPTST438-MEAN RBC HEMOGLOBIN CONCENTRATI: 356 [316 - 354] G/L; NPTST697- WIDTH OF PLATELET VOLUME DISTRI: 15.7 [9.8 - 15.2] FL

Microbiology
[redacted]20[redacted] (RX DAY 437): BLOOD NPTST107-BLOOD CULTURE AND DRUG SENSITIV: Not applicable-NO BACTERIAL GROWTH WAS OBSERVED AFTER 120 HOURS OF CULTURE; [redacted]20[redacted] (RX DAY 446): BLOOD NPTST107-BLOOD CULTURE AND DRUG SENSITIV: Not applicable-NO BACTERIAL GROWTH WAS OBSERVED AFTER 120 HOURS OF CULTURE

SAE Supplemental Procedure
NOT REPORTED

AE Stopped Rx Day	455
Duration of AE	19 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は中国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左背部の蜂巣炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左背部の蜂巣炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左背部の蜂巣炎は消失した。

本事象発現前，20[redacted] 年 [redacted] 月，被験者は尺骨側左前腕遠位部の熱傷の事象（非重篤）を発現した。治験責任医師によると，この熱傷に対する治療法は適切でなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は「left-handed luktomyis」と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，左手首及び左手背部の発赤を伴う腫れと痛みのため入院した。発熱は伴っていなかった。尺骨側左前腕遠位部の熱傷が本事象と関連のある危険因子であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，テプレノン，モキシフロキサシン，ペニシリン，エリスロマイシン，セフトリアキソン，セフィキシム及び esomeprazole magnesium enteric であった。

The patient's past medications include:

TRIPTERYGIUM GLYCOSIDES for PSORIATIC ARTHRITIS ([redacted])

LEFLUNOMIDE for PSORIATIC ARTHRITIS ([redacted])

VOLTAREN for PSORIATIC ARTHRITIS ([redacted])

PAVLIN for PSORIATIC ARTHRITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Cellulitis (10007882) (Cellulitis (10007882)) [v.23.0] [10007882]

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 LEFT DORSAL CELLULITIS

- Investigator: Not applicable

- AbbVie: risk factor includes recent burns on distal ulnar left side of the arm.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 35.9 G/L (normal 40 to 55)

[redacted] **20[redacted] BLOOD CULTURE AND DRUG SENSITIVITY:** No bacterial growth observed after 120 hours of culture.

[redacted] **20[redacted] BLOOD CULTURE AND DRUG SENSITIVITY:** No bacterial growth observed after 120 hours of culture.

[redacted] **20[redacted] FIBRINOGEN:** 5.7 G/L (normal 2 to 4)

[redacted] **20[redacted] HEMATOCRIT:** 38.6 % (normal 40 to 50)

[redacted] **20[redacted] HEMOGLOBIN:** 126 G/L (normal 130 to 175)

[redacted] **20[redacted] HS-CRP:** 38.55 MG/L (normal 0 to 5)

[redacted] **20[redacted] HS-CRP:** 9.25 MG/L (normal 0 to 5)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 1.0 X10**9/L (normal 1.1 to 3.2)

[redacted] **20[redacted] PLATELET VOLUME DISTRIBUTION WIDTH:** 17.4 FL (normal 9.8 to 15.2)

[redacted] **2019RED BLOOD CELL DISTRIBUTION WIDTH:** 11.8 % (normal 12.2 to 14.6)

[redacted] **20[redacted] TOTAL PROTEIN:** 60.1 G/L (normal 65 to 85)

[redacted] **20[redacted] TOTAL PROTEIN:** 64.9 G/L (normal 65 to 85)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3.30 X10**9/L (normal 3.5 to 9.5)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	6[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: PAUSIMENIA	20[redacted]
OTHER: UTERINE FIBROIDS	20
OTHER: PLAQUE PSORIASIS	20
HYPERTENSION	20
PSORIATIC ARTHRITIS	20
OTHER: RABIES VACCINE INJECTION	20
LIVER DISEASE (EXCLUDING HEPATITIS): ABNORMAL LIVER FUNCTION	20
OTHER: ABNORMAL GLUCOSE TOLERANCE	20

Prior Procedures	Procedure Year
SURGERY: UTERINE FIBROIDS	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)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1 OTHER: DOSE	BID	Y-M: 20[redacted]
LOSARTAN	150 mg	QD	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
UNSPECIFIED HERBAL	20 mg	BID	Y-M: 20[redacted]
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]
UNSPECIFIED HERBAL	20 mg	BID	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -307
UNSPECIFIED HERBAL	20 mg	BID	Y-M: 20[redacted] / -307
UNSPECIFIED HERBAL	20 mg	BID	Y-M: 20[redacted] / -272
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -202
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -202
RABIES VACCINE	0.5 mL	OTHER: ON THE DAY OF BEING BITTEN BY A DOG, ON THE 7TH DAY, ON THE 28TH DAY, A SEPARATE INJECTION	Y-M: 20[redacted] / -180

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LOSARTAN	150 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -202	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -202	NOT REPORTED
IBUPROFEN	10 mL	QD	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 479
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 479
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 479	Y-M: 20[redacted] / 486
ASCORBIC ACID	2 g	QD	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 481
POTASSIUM	10 mL	QD	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 481
VITAMIN B COMPLEX	0.2 g	QD	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 481

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

Event Description	INFECTIOUS FEVER
Preferred term	熱性感染症
AE Onset Date / Rx Day	[redacted]20[redacted] / 479
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 480): Eosinophils: 0 [0.02 - 0.52] 10^9/L; Eosinophils/Leukocytes: 0 [0.4 - 0.8] %; Erythrocytes: 3.6 [3.8 - 5.1] 10^12/L; Hematocrit: 0.33 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 111 [115 - 150] G/L; Leukocytes: 11.2 [3.5 - 9.5] 10^9/L; Lymphocytes: 0.6 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 5 [20 - 50] %; Monocytes/Leukocytes: 2.9 [3 - 10] %; NPTST152-CD19: 31.15 [6 - 25] %; NPTST154-CD3+HLA-DR+CELLS: 1.98 [4.1 - 17.7] %; NPTST156-CD4+CD25+CELLS: 3.63 [6.1 - 13.5] %; NPTST156-CD4+CD25+CELLS: 2.66 [3.3 - 10.6] %; NPTST158-CD8+CD38+CELLS: 1.79 [2.3 - 15] %; NPTST159-CD8+HLA-DR+CELLS: 0.56 [1.3 - 13.4] %; NPTST255-ERYTHROCYTE DISTRIBUTION WIDTH: 15.1 [12.2 - 15] %; NPTST352-HS-CRP: 65.52 [0 - 5] MG/L; NPTST375-IMMUNOGLOBULIN G: 1630 [751 - 1560] MG/DL; NPTST470-NK: 8.78 [14 - 40] %; NPTST626-THROMBOCYTOCRIT: 0.18 [0.19 - 0.4] %; Neutrophils: 10.3 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 92 [40 - 75] %

Microbiology

[redacted]20[redacted] (RX DAY 480): BLOOD NPTST059-ANTIBODIES TO MYCOPLASMA PNEUMO: Negative; BLOOD NPTST106-BLOOD CULTURE + DRUG SENSITIVIT: Negative; BLOOD NPTST106-BLOOD CULTURE + DRUG SENSITIVIT: Negative; BLOOD NPTST175-CMVDNA: Negative; BLOOD NPTST240-EBV -DNA: Positive-7.53*10?; SPUTUM NPTST348-HINI AND HIB SCREENING TEST: Negative; BLOOD NPTST465-NCOV-IGGNOVEL CORONAVIRUS ANTIB: Negative; SPUTUM NPTST472-NOVEL CORONAVIRUS NUCLEIC ACID: Negative; BLOOD NPTST696-WIDAL REACTION: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 479): CHEST CT PLAIN SCAN: 1. INFLAMMATION OF THE UPPER LOBE OF THE RIGHT LUNG AND THE LOWER LOBE OF THE LEFT LUNG IS CONSIDERED, AND REEXAMINATION AFTER TREATMENT IS RECOMMENDED 2. RIGHT MIDDLE LOBE FUNICULAR FOCI 3. LOCAL PLEURAL THICKENING AND CALCIFICATION ON THE RIGHT SIDE ADJUNCT: GALLBLADDER ENLARGEMENT

AE Stopped Rx Day	481 (1 DAY AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 479
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 480): Eosinophils: 0 [0.02 - 0.52] 10^9/L; Eosinophils/Leukocytes: 0 [0.4 - 0.8] %; Erythrocytes: 3.6 [3.8 - 5.1] 10^12/L; Hematocrit: 0.33 [0.35 - 0.45] FRACTION OF 1; Hemoglobin: 111 [115 - 150] G/L; Leukocytes: 11.2 [3.5 - 9.5] 10^9/L; Lymphocytes: 0.6 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 5 [20 - 50] %; Monocytes/Leukocytes: 2.9 [3 - 10] %; NPTST152-CD19: 31.15 [6 - 25] %; NPTST154-CD3+HLA-DR+CELLS: 1.98 [4.1 - 17.7] %; NPTST156-CD4+CD25+CELLS: 3.63 [6.1 - 13.5] %; NPTST156-CD4+CD25+CELLS: 2.66 [3.3 - 10.6] %; NPTST158-CD8+CD38+CELLS: 1.79 [2.3 - 15] %; NPTST159-CD8+HLA-DR+CELLS: 0.56 [1.3 - 13.4] %; NPTST255-ERYTHROCYTE DISTRIBUTION WIDTH: 15.1 [12.2 - 15] %; NPTST352-HS-CRP: 65.52 [0 - 5] MG/L; NPTST375-IMMUNOGLOBULIN G: 1630 [751 - 1560] MG/DL; NPTST470-NK: 8.78 [14 - 40] %; NPTST626-THROMBOCYTOCRIT: 0.18 [0.19 - 0.4] %; Neutrophils: 10.3 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 92 [40 - 75] %

Microbiology

[redacted]20[redacted] (RX DAY 480): BLOOD NPTST059-ANTIBODIES TO MYCOPLASMA PNEUMO: Negative; BLOOD NPTST106-BLOOD CULTURE + DRUG SENSITIVIT: Negative; BLOOD NPTST106-BLOOD CULTURE + DRUG SENSITIVIT: Negative; BLOOD NPTST175-CMVDNA: Negative; BLOOD NPTST240-EBV -DNA: Positive-7.53*10?; SPUTUM NPTST348-HINI AND HIB SCREENING TEST: Negative; BLOOD NPTST465-NCOV-IGGNOVEL CORONAVIRUS ANTIB: Negative; SPUTUM NPTST472-NOVEL CORONAVIRUS NUCLEIC ACID: Negative; BLOOD NPTST696-WIDAL REACTION: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 479): CHEST CT PLAIN SCAN: 1. INFLAMMATION OF THE UPPER LOBE OF THE RIGHT LUNG AND THE LOWER LOBE OF THE LEFT LUNG IS CONSIDERED, AND REEXAMINATION AFTER TREATMENT IS RECOMMENDED 2. RIGHT MIDDLE LOBE FUNICULAR FOCI 3. LOCAL PLEURAL THICKENING AND CALCIFICATION ON THE RIGHT SIDE ADJUNCT: GALLBLADDER ENLARGEMENT

AE Stopped Rx Day	490 (10 DAYS AFTER LAST TREATMENT)
Duration of AE	12 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は中国の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，感染性発熱及び肺炎の事象を発現した。

Event 3 及び 4 の臨床経過：

関連する病歴は，局面型乾癬，高血圧，乾癬性関節炎，耐糖能異常，肝機能異常，非飲酒者及び非喫煙者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は感染性発熱及び肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，感染性発熱は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は空調の効いた部屋で冷たい食べ物を摂取した。発熱が始まり，体温は 39℃ であった。被験者は自身でイブプロフェンを内服した。黄色の下痢が見られ，1 回嘔

吐した。被験者は救急治療室に運ばれ，体温は 40°C であった。ルーチンの臨床検査と画像検査が行われた。被験者は発汗しており，抗感染症薬を 1 回投与された。その結果，体温は 38°C に下がった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は地域病院の免疫科に移り，肺炎及び感染性発熱のため入院した。症状として，悪寒を伴う発熱，下痢，嘔吐及び肺の炎症が見られた。被験者によると，出血や胸痛，膿，出血，腹痛，咳嗽はなかった。粘膜黄染はなく，発疹，頻尿は見られなかったが，排尿時痛が見られた。リンパ節の腫脹は見られなかった。被験者は輸液と抗感染症薬による治療を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，セフメタゾール，イブプロフェン及びモキシフロキサシン塩酸塩であった。

The patient's past medications include:

LEIGONGTENGDUOGAN PIAN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] Jun 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Febrile infection (10051998) (Febrile infection (10051998)) [v.23.0] [10051998]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2) 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 INFECTIOUS FEVER

- Investigator: Not applicable

- AbbVie: Not applicable

Event of PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Liver is slightly dense. Cholesterol crystals on gallbladder wall

[redacted] **20[redacted] ANTIBODIES TO MYCOPLASMA PNEUMONIAE:** Negative

[redacted] **20[redacted] BLOOD CULTURE + DRUG SENSITIVITY:** Negative

[redacted] **20[redacted] BODY TEMPERATURE:** 39 Degrees C

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

[redacted] **20[redacted] BODY TEMPERATURE:** 38 Degrees C

[redacted] **20[redacted] CALCITONIN:** 0.05 NG/ML

[redacted] **20[redacted] CD19:** 31.15 % (normal 6 to 25)

[redacted] **20[redacted] CD3+HLA DR CELLS:** 1.98 % (normal 4.1 to 17.7)

[redacted] **20[redacted] CD4+CD25 CELLS:** 3.63 % (normal 6.1 to 13.5)

[redacted] **20[redacted] CD4+CD25 CELLS:** 2.66 % (normal 6.1 to 13.5)

[redacted] **20[redacted] CD8+CD38 CELLS:** 1.79 % (normal 2.3 to 15)

[redacted] **20[redacted] CD8+HLA-DR CELLS:** 0.56 % (normal 1.3 to 13.4)

[redacted] **20[redacted] CHEST CT:** 1. Inflammation of the upper lobe of the right lung and the lower lobe of the left lung is considered, and reexamination after treatment is recommended 2. Sclerenchymal lesion in the middle lobe of

the right lung 3. Local pleural thickening and calcification on the right side adjunct: Gallbladder enlargment

[redacted] **20[redacted] CMV DNA:** Negative

[redacted] **20[redacted] COLOR DOPPLER SONOGRAPHY (ROUTINE HEART EXAMINATION):** Left ventricular diastolic function is poor

[redacted] **20[redacted] COLOR DOPPLER ULTRASONOGRAPHY (DOUBLE KIDNEYS/DOUBLE URETERS/BLADDER):** No obvious abnormalities were found in both kidneys, ureters and bladder

[redacted] **20[redacted] COLOR DOPPLER ULTRASONOGRAPHY (LEFT/RIGHT THYROID/CERVICAL LYMPH NODES):** Bilateral thyroid lobe nodules, ti-rads type 2

[redacted] **20[redacted] COVID-19 TEST (BLOOD):** Negative

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

[redacted] **20[redacted] EBV DNA:** Positive

[redacted] **20[redacted] H1N1/HIB SCREENING:** Negative

[redacted] **20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN:** 65.52 MG/L (normal 0 to 5)

[redacted] **20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN:** 20.18 MG/L (normal 0 to 5)

[redacted] **20[redacted] HIGH SENSITIVITY C REACTIVE PROTEIN:** 11.11 MG/L (normal 1.8 to 6.3)

[redacted] **20[redacted] LYMPHOCYTES:** 5 % (normal 20 to 50)

[redacted] **20[redacted] NCOV-IGG NOVEL CORONAVIRUS ANTIBODY IGG:** Negative

[redacted] **20[redacted] NEUTROPHILS:** 92 % (normal 40 to 75)

[redacted] **20[redacted] NEUTROPHILS ABS:** 10.3 X10**9/L (normal 1.8 to 6.3)

[redacted] **20[redacted] NEW CROWN ANTIBODY TEST:** Negative

[redacted] **20[redacted] NEW CROWN NEUCLEIC ACID RNA:** Negative

[redacted] **20[redacted] NOVEL CORONAVIRUS NUCLEIC ACID TEST (SPUTUM):** Negative

[redacted] **20[redacted] THROMBOCYTE:** 0.18 % (normal 0.19 to 0.4)

[redacted] **20[redacted] THROMBOCYTE:** 0.16 % (normal 0.19 to 0.4)

[redacted] **20[redacted] THROMBOCYTE:** 0.15 % (normal 0.19 to 0.4)

[redacted] **20[redacted] WBC:** 9.2 X10**9/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.2 X10**9/L (normal 3.5 to 9.5)

[redacted] **20[redacted] WIDAL REACTION:** Negative

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
大腸ポリープ	X			

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: POLIOMYELITIS	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: APPENDICITIS	19[redacted]
OTHER: CONSTIPATION	20[redacted]
OTHER: HERNIA OF INTERVERTEBRAL DISCS	20[redacted]
OTHER: GASTRITIS	20[redacted]
HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: LATENT TB	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: TUBAL LIGATION	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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 399	231
ADA	40MG	SC	EOW	[redacted]20[redacted] / 400		

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]
GLYCEROL	1 OTHER: BOTTLE	OTHER: IN NECESSITY	Y-M: 20[redacted]
LOSARTAN	75 mg	QD	Y-M: 20[redacted]
DICLOFENAC	75 mg	QD	Y-M: 20[redacted]
DICLOFENAC	75 mg	QD	Y-M: 20[redacted]
GLUCOSAMINE	0.25 g	TID	Y-M: 20[redacted]
LEFLUNOMIDE	10 mg	QD	Y-M: 20[redacted] / -344
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / -344
CELECOXIB	0.2 g	BID	Y-M: 20[redacted] / -330
GLUCOSAMINE	2 OTHER: PILL	TID	Y-M: 20[redacted] / -330
UNSPECIFIED HERBAL	6 OTHER: PILL	TID	Y-M: 20[redacted] / -330
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	UNK g	OTHER: IN NECESSARY	Y-M: 20[redacted] / -330
COLCHICINE	1 mg	BID	Y-M: 20[redacted] / -306
MELOXICAM	7.5 mg	BID	Y-M: 20[redacted] / -306
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	3 OTHER: PILL	TID	Y-M: 20[redacted] / -306
CELECOXIB	0.2 g	BID	Y-M: 20[redacted] / -301
GLUCOSAMINE	2 OTHER: PILL	TID	Y-M: 20[redacted] / -301
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 OTHER: BAG	QD	Y-M: 20[redacted] / -301
CELECOXIB	0.2 g	BID	Y-M: 20[redacted] / -294
CELECOXIB	0.2 g	QD	Y-M: 20[redacted] / -287
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -287
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -287
UNSPECIFIED HERBAL	20 mg	BID	Y-M: 20[redacted] / -287
CELECOXIB	0.2 g	QD	Y-M: 20[redacted] / -211
CELECOXIB	0.2 g	QD	Y-M: 20[redacted] / -155
CELECOXIB	0.2 g	QD	Y-M: 20[redacted] / -139

METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -139
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted] / -132
CELECOXIB	0.2 g	QD	Y-M: 20[redacted] / -111
CELECOXIB	0.2 g	QD	Y-M: 20[redacted] / -69
CELECOXIB	0.2 g	QD	Y-M: 20[redacted] / -52
ISONIAZID	0.3 g	QD	Y-M: 20[redacted] / -27

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
GLYCEROL	1 OTHER: BOTTLE	OTHER: IN NECESSITY	Y-M: 20[redacted]	NOT REPORTED
LOSARTAN	75 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -287	NOT REPORTED
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted] / -132	NOT REPORTED
CELECOXIB	0.2 g	QD	Y-M: 20[redacted] / -52	NOT REPORTED
COLOPEG	208.68 g	QD	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
DEXTROSE AND SODIUM CHLORIDE INJECTION	500 mL	QD	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
DIMETICONE	12 mL	QD	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
ETAMSILATE	2 g	QD	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
GLUCOSE INJECTION	500 mL	QD	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
PHYTOMENADIONE	10 mg	QD	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
BACILLUS LICHENFORMIS	0.5 g	TID	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 366
BIFIDOBACTERIUM BIFIDUM W/LACTOBACI	0.63 g	BID	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 368

Event #1: Serious Adverse Event

Event Description COLON POLYPS
Preferred term 大腸ポリープ
AE Onset Date / Rx Day [redacted]20[redacted] / 350
Age at AE Onset 6[redacted]
Laboratory Testing
[redacted]20[redacted] (RX DAY 350): NPTST078-AVERAGE HEMOGLOBIN CONTENT: 34.5 [27 - 34] PG
Microbiology
NOT REPORTED
SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 350): ENDOSCOPIC INTESTINAL POLYP RESECTION WAS PERFORMED: THE POSTOPERATIVE CONDITION WAS GOOD AND THERE WAS NO SEQUELA; BIOPSY: (ASCENDING COLON) SUPERIOR TUBULOVILLOUS ADENOMA.

AE Stopped Rx Day	350
Duration of AE	1 DAY
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	IT IS ASSOCIATED WITH CHRONIC INTESTINAL INFLAMMATION, LIFESTYLE AND AGE FACTORS
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: M15-572

治験責任医師からの報告。本被験者は中国の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，結腸ポリープの事象を発現した。

Event 1 の臨床経過：

関連する病歴は，灰白髄炎，局面型乾癬，便秘，胃炎，高血圧，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。記録によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は結腸ポリープを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，結腸ポリープは消失した。

本事象発現前の 20[redacted] 年 [redacted] 月，被験者はしばらく便秘であった。被験者は結腸内視鏡検査を受け，腸管ポリープと診断された。これは非重篤とみなされた。内視鏡的介入治療を勧められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は内視鏡的腸管ポリープ切除及び acid-stopping hemihydrate 治療のため入院した。腹痛，下痢，腹部膨満，悪心，吐血，メレナ，食欲不振，るいそう及び発熱は認められなかった。被験者には意識があり，ほかに異常は認められなかった。被験者は術後回復

し，腹痛も血便も見られなかった。被験者に不快感や低体温は見られず，半流動食で同日退院した。胃腸薬が指示された。生検で上行結腸の管状絨毛腺腫が認められた。

投与された薬剤は，bacillus lichenformis live，live combined bifidobacterium，lactobacillus and enterococcus，ブドウ糖，ブドウ糖加生理食塩液，ビタミン K1 及び etamsylate であった。

The patient's past medications include:

LEFLUNOMIDE for PSORIATIC ARTHRITIS ([redacted])

LOXOPROFEN SODIUM for PSORIATIC ARTHRITIS ([redacted])

LEIGONGTENGDUOGAN PIAN for PSORIATIC ARTHRITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Colonic polyp (10010003) (Large intestine polyp (10051589)) [v.23.0] [10010003]

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 COLON POLYPS

- Investigator: It is associated with chronic intestinal inflammation, lifestyle and age factors.

- AbbVie: Colon polyps are common in the general population and in women between age 65-69, there was a 24% prevalence on routine colonoscopy.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **AVERAGE HEMOGLOBIN CONTENT:** 34.5 PG (normal 27 to 34)

[redacted] **BIOPSY:** (ascending colon) superior tubulovillous adenoma

[redacted] **ENDOSCOPY:** intestinal polyp resection was performed

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
椎間板突出	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	5[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: LUMBAR DISC HERNIATION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: SINUS BRADYCARDIA	20[redacted]
OTHER: ST-T CHANGED(EARLY REACTIVATION IS POSSIBLE)	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	1995

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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 385	216
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 386		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LOXOPROFEN	60 mg	BID	Y-M: 20[redacted] / -163
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -163
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -28

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -163	NOT REPORTED
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -28	NOT REPORTED
MANNITOL	150 mL	OTHER: Q12H	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 213
COBAMAMIDE	1.5 mg	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 219
ESCIN	10 mg	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 219
GASTRODIN	0.5 g	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 219
KETOROLAC	30 mg	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 219
LIGUSTRAZINE	80 mg	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 219
VITAMIN D NOS	15 mg	OTHER: ST	Y-M: 20[redacted] / 216	Y-M: 20[redacted] / 216

Event #1: Serious Adverse Event

Event Description	LUMBAR DISC HERNIATION AGGRAVATES
Preferred term	椎間板突出
AE Onset Date / Rx Day	[redacted]20[redacted] / 211
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 211): Alanine Aminotransferase: 15 [0 - 41] U/L; Albumin: 42 [40 - 55] G/L; Alkaline Phosphatase: 66 [53 - 128] U/L; Aspartate Aminotransferase: 19 [0 - 37] U/L; Calcium: 2.06 [2.1 - 3] MMOL/L; Chloride: 105 [96 - 106] MMOL/L; Creatine Kinase: 51.9 [24 - 190] U/L; Creatinine: 54 [70 - 115] UMOL/L; Erythrocyte Sedimentation Rate: 34 [0 - 15] MM/H; Glucose: 5.8 [3.3 - 6.1] MMOL/L; Leukocytes: NEGATIVE [NOT REPORTED - NOT REPORTED] CELLS/U; NPTST005-?-AMYLASE: 88 [0 - 100] U/L; NPTST006-?-HYDROXYBUTYRATE DEHYDROGENASE: 193 [72 - 182] U/L; NPTST007-?2-MICROGLOBULIN: 1.81 [1 - 3] MG/L; NPTST021-ADENOSINE DEHYDROGENASE: 16.8 [4 - 24] U/L; NPTST060-ANTICYCLIC CITRULLINATED PEPTID: ?1 [0 - 30] IU/mL; NPTST062-ANTIHEMOLYTIC STREPTOCOCCUS O: 67.65 [0 - 170] IU/ML; NPTST067-APOLIPOPROTEINB: 0.51 [0.66 - 1.33] G/L; NPTST085-BACTERIAL: 0 [0 - 60] 099,A/UL; NPTST142-CALCIUM OXALATE CRYSTAL: 0 [0 - 20] 099,A/UL; NPTST146-CARBON DIOXIDE: 28.97 [20 - 29] MMOL/L; NPTST151-CARRIER PROTEINA1: 1.34 [1.1 - 1.7] G/L; NPTST200-CREATINE KINASE MB ISOENZYME: 8.8 [0 - 24] U/L; NPTST232-DETERMINATION OF 25 HYDROXYVITA: 31.64 [19 - 57.6] 099,UG/L; NPTST282-FUNGUS: 0 [0 - 10] 099,A/UL; NPTST325-HEPATITIS B CORE ANTIBODY: 2.81 [1 - NOT REPORTED] UNIT NOT REPORTED; NPTST327-HEPATITIS B E ANTIBODY: 1.77 [1 - NOT REPORTED] 099,NA; NPTST328-HEPATITIS B E ANTIGEN: 0.28 [NOT REPORTED - 1] UNIT NOT REPORTED; NPTST334-HEPATITIS B SURFACE ANTIGEN: <0.05 [NOT REPORTED - 0.08] IU/mL; NPTST344-HIGH DENSITY LIPOPROTEIN: 1.24 [0.9 - NOT REPORTED] mmol/L; NPTST346-HIGH-SENSITIVITY C-REACTIVE PRO: 8.82 [0.5 - 10] MG/L; NPTST400-LACTATE DEHYDROGENASE: 229.1 [135 - 225] U/L; NPTST409-LEUKERGY: 0 [NOT REPORTED - NOT REPORTED] A/UL; NPTST415-LOW-DENSITY LIPOPROTEIN: 1.99 [0 - 4.11] MMOL/L; NPTST459-MUCUS SILK: 0 [NOT REPORTED - NOT REPORTED] A/UL; NPTST511-PHOSPHORUS: 0.92 [0.81 - 1.62] MMOL/L; NPTST547-PYOCYTE: 0 [0 - 0] 099,A/UL; NPTST576-RETINOL BINDING PROTEIN ASSAY: 3.67 [3.6 - 7.2] MG/DL; NPTST578-RHEUMATOID FACTOR: 3 [0 - 20] IU/ML; NPTST590-SERUM CYSTATIN DETERMINATION: 0.76 [0.63 - 1.25] MG/L; NPTST592-SERUM LIPASE DETERMINATION: 83.5 [13 - 60] U/L; NPTST593-SERUM URIC ACID: 247 [202 - 416] UMOL/L; NPTST605-SPERM: 0 [0 - 10] 099,A/UL; NPTST634-TOTAL CHOLESTEROL: 3.58 [0 - 5.6] MMOL/L; NPTST658-TUBE TYPE: 0 [0 - 1] 099,A/UL; NPTST662-UREA: 5.59 [1.7 - 8.3] MMOL/L; NPTST668-URINE BILIRUBIN: NEGATIVE [NOT REPORTED - NOT REPORTED] umol/L; NPTST671-URINE KETONE BODIES: NEGATIVE [NOT REPORTED - NOT REPORTED] mmol/L; NPTST673-URINE NITRITE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST674-URINE OCCULT BLOOD: NEGATIVE [NOT REPORTED - NOT REPORTED] CELLS/UL; NPTST675-URINE PH: 6.5 [5 - 8.5] 099,NA; NPTST677-URINE PROTEIN: NEGATIVE [NOT REPORTED - NOT REPORTED] g/L; NPTST680-URINE SPECIFIC GRAVITY: 1.02 [1.01 - 1.03] 099,NA; NPTST681-URINE SUGAR: NEGATIVE [NOT REPORTED - NOT REPORTED] mmol/L; NPTST686-VASCULAR ENDOTHELIAL GROWTH FAC: 126.25 [0 - 160] 099,PG/ML; Potassium: 4.1 [3.5 - 5.5] MMOL/L; Protein: 77 [65 - 85] G/L; Sodium: 141 [135 - 145] MMOL/L; Triglycerides: 0.97 [0 - 2.1] MMOL/L; Urobilinogen: 3.2 [NOT REPORTED - NOT REPORTED] umol/L;

[redacted]20[redacted] (RX DAY 242): NPTST424-MALIGNANT TUMOR SPECIFIC GROWTH: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 211): COMPUTED TOMOGRAPHY (CT) OF THE HIP: BILATERAL HIP JOINT CT PLAIN SCAN SHOWED NO OBVIOUS ABNORMALITY; ELECTROCARDIOGRAM: NORMAL SINUS RHYTHM VENTRICULAR PREMATURE BEAT (DUPLE RHYTHM) QTC EXTENDED ABNORMAL ECG COUNTERCLOCKWISE ROTATION; THE LUMBAR INTERVERTEBRAL DISCS CT: DEGENERATIVE LUMBAR SPINE DISC BULGING OF L2/3, L4/5, AND L5/S1 PROSTATIC HYPERTROPHY WITH CALCIFICATION; URINARY SYSTEM ULTRASONIC EXAMINATION: ULTRASOUND SUGGESTS ENLARGEMENT OF THE PROSTATE?PI JUDGMENT HAS NO CLINICAL SIGNIFICANCE?; [redacted]20[redacted] (RX DAY 216): 20[redacted].[redacted].[redacted]-20[redacted].[redacted].[redacted] TRADITIONAL CHINESE MEDICINE FOR PACKET THERAPY: TREATMENT OF LUMBAR DISC HERNIATION; FROM [redacted] [redacted] 20[redacted] TO [redacted] [redacted] 20[redacted], [redacted] DISC HERNIATION MASSAGE THERAPY: TO TREAT LUMBAR DISC HERNIATION; [redacted] [redacted] 20[redacted]-[redacted] [redacted] 20[redacted], PARTITION MOXIBUSTION: TO TREAT LUMBAR DISC HERNIATION; [redacted] [redacted] 20[redacted]-[redacted] [redacted] 20[redacted], TRADITIONAL CHINESE MEDICINE DIRECTED PENETRATION: TREATMENT OF LUMBAR DISC HERNIATION

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	THIS A WORSENING OF MEDICAL HISTORY LUMBAR INTERVERTEBRAL DISC
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: M15-572

治験責任医師からの報告。本被験者は中国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，腰椎椎間板ヘルニアの悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，腰椎椎間板ヘルニア，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された

皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腰椎椎間板ヘルニアの悪化を発現した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，左股関節と腰痛及び下肢痛が見られた。疼痛は，伸展で増悪し屈曲で楽になった。

20[redacted] 年 [redacted] 月 [redacted] 日，左股関節と左大腿の疼痛を伴う腰痛が生じた。疼痛と併せて両下肢の腫脹，屈曲制限及び歩行困難が見られた。被験者は左股関節に圧痛があり，左下肢の伸展挙上テスト陰性，下肢の筋力と筋張力は正常であった。20[redacted] 年 [redacted] 月 [redacted] 日，CT スキャン検査が行われ，被験者は椎間板ヘルニアと診断された。被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで，被験者は腰椎椎間板ヘルニアに対しマッサージ療法，漢方薬，医療用灸及び漢方薬による薬物横断療法を受けた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は状態が改善し退院した。被験者の腰痛症及び左臀部痛は顕著に緩和したが，腰痛は持続した。被験者の歩行困難は顕著に軽減した。左下肢の疼痛はわずかに残り，左股関節の疼痛は持続していたが，以前よりは軽減していた。

投与された薬剤は，gastrodin，sodium aescinate，コバマミド，ligustrazine hydrochloride，ketorolac tromethamine 及びマンニットールであった。

The patient's past medications include:

LOXOPROFEN SODIUM for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Lumbar disc herniation (10066256) (Intervertebral disc protrusion (10050296)) [v.23.0] [10066256]

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 LUMBAR DISC HERNIATION AGGRAVATES

- Investigator: This a worsening of medical history lumbar intervertebral disc.

- AbbVie: Risk factors include pre-existing lumbar disc herniation and psoriatic arthritis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] A-HYDROXYBUTYRATE DEHYDROGENASE:** 193 U/L (normal 72 to 182)

[redacted] **20[redacted] ANTICYCLIC CITRULLINATED PEPTIDE ANTIBODY:** <1 IU/mL (normal range 0 - 30)

[redacted] **20[redacted] ANTIHEMOLYTIC STREPTOCOCCUS O:** 67.65 IU/L (normal 0 to 170)

[redacted] **20[redacted] APOLIPOPROTEIN B:** 0.51 G/L (normal 0.66 to 1.33)

[redacted] **20[redacted] BLOOD PRESSURE:** . 142/78 MMHG

[redacted] **20[redacted] BODY TEMPERATURE:** 36.5 Degrees C

[redacted] **20[redacted] CALCIUM:** 2.06 MMOL/L (normal 2.1 to 3.0)

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

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

[redacted] **20[redacted] CT SCAN:** LUMBAR INTERVERTEBRAL DISCS + HIP JOINT: degenerative lumbar spine, Disc bulging of L2/3, L4/5, and L5/S1. Bilateral hip joint CT plain scan showed no obvious abnormality. Prostatic hyperplasia with calcified

[redacted] **20[redacted] DETERMINATION OF 25 HYDROXYVITAMIN D:** 31.64 MCG/L (normal 19 to 57.6)

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Normal sinus rhythm Ventricular premature beat (duple rhythm) QTc extended Abnormal ECG counterclockwise rotation.

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 34 MM/HR (normal 0 to 35)

[redacted] **20[redacted] HEPATITIS B CORE ANTIBODY:** 2.81 no units (normal >1.00)

[redacted] **20[redacted] HEPATITIS B E ANTIBODY:** 1.77 no units (normal >1)

[redacted] **20[redacted] HEPATITIS B E ANTIGEN:** 0.28 no units (normal <1.00)

[redacted] **20[redacted] HEPATITIS B SURFACE ANTIGEN:** <0.05 IU/mL (high normal value 0.08)

[redacted] **20[redacted] HIGH-SENSITIVITY C-REACTIVE PROTEIN:** 8.82 MG/L (normal 0.5 to 10)

[redacted] **20[redacted] LACTATE DEHYDROGENASE:** 229.10 U/L (normal 135 to 225)

[redacted] **20[redacted] MALIGNANT TUMOR SPECIFIC GROWTH FACTOR:** negative

[redacted] **20[redacted] PHOSPHORUS:** 0.92 MMOL/L (normal 0.81 to 1.62)

[redacted] **20[redacted] PULSE:** 48 bpm

[redacted] **20[redacted] RHEUMATOID FACTOR:** <3 (normal 0 <=20)

[redacted] **20[redacted] SERUM LIPASE DETERMINATION:** 83.5 U/L (normal 13 to 60)

[redacted] **20[redacted] URINARY SYSTEM ULTRASONIC EXAMINATION:** Enlargement of the prostate (PI judgment has no clinical significance).

[redacted] **20[redacted] VASCULAR ENDOTHELIAL GROWTH FACTOR:** 126.25 PG/ML (normal 0 to 160)

[redacted] **20[redacted] WEIGHT:** 67.0 KG

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: OBESITAS	20[redacted]
OTHER: PSOROASIS VULGARIS	20[redacted]
HYPERTENSION	20[redacted]
OTHER: REDUCED GLUCOSE INTOLERANCE	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	1973

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	15	20[redacted]
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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 391	223
ADA	40MG	SC	EOW	[redacted]20[redacted] / 392		

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]
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted]

VALSARTAN	160 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
NAPROXEN	550 mg	BID	Y-M: 20[redacted] / -241

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
VALSARTAN	160 mg	QD	Y-M: 20[redacted]	NOT REPORTED
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 114
NAPROXEN	550 mg	BID	Y-M: 20[redacted] / -241	NOT REPORTED
BISOPROLOL	5 mg	QD	Y-M: 20[redacted] / 114	NOT REPORTED
ENOXAPARIN	0.8 mg	BID	Y-M: 20[redacted] / 115	Y-M: 20[redacted] / 121
RIVAROXABAN	15 mg	BID	Y-M: 20[redacted] / 122	NOT REPORTED
ROSUVASTATIN	20 mg	QD	Y-M: 20[redacted] / 122	NOT REPORTED

Event #1: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description	THROMBOSIS IN THE LEFT SUPERFICIAL FEMORAL AND POPLITEAL VEINS
Preferred term	深部静脈血栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 112
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 117): Erythrocyte Sedimentation Rate: 46 [3 - 15] MM/H; NPTST003- C-REACTIVE PROTEIN: 45.2 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 114): ULTRASOUND: LEFT LIMB OF THROMBOSIS VENA FEMORAL SUPERFICIALIS; [redacted]20[redacted] (RX DAY 115): SKULL CT: NEGATIVE; [redacted]20[redacted] (RX DAY 117): ABDOMINAL ULTRASOUND SCAN: NEGATIVE; CHEST X-RAY: NEGATIVE

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	OBESITY LESS MOVEMENT
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: M15-572

治験責任医師からの報告。本被験者はハンガリーの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左浅大腿・膝窩静脈の血栓症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元紙巻タバコ喫煙者（1 日 1 箱を 15 年間），尋常性乾癬，高血圧，耐糖能低下，乾癬性関節炎（両側アキレス腱に発症），非飲酒者及び不整脈であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左浅大腿・膝窩静脈の血栓症を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，超音波検査で確認された左浅大腿・膝窩静脈の血栓症のため入院した。低分子量ヘパリン及び伸縮包帯による治療が行われた。血栓症の原因となる占拠性突起は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

40 歳を超える年齢，肥満及び高血圧が本事象の危険因子に該当した。

医療記録より：

被験者は救急科（ED）より入院した。左下腿に前週の火曜日から圧痛があり，入院の前日にはかなり腫れていた。被験者によると，乾癬はアキレス腱にも及んでいた。アキレス腱に圧痛が見られた。移動困難がしばしば生じた。また，右半身のしびれ感が新たに出現し，2～3 日間続いた。発熱及び悪寒は見られなかった。脚の痛み以外に，胸痛やその他の痛みはなかった。息切れ及び胸部不快感はなかった。咳嗽もなかった。食欲は十分にあり，体重も維持されており，悪心及び嘔吐はなかった。1 日 1 回の規則正しい便通があり，血便や黒色便は見られなかった。排尿関連の症状はなかった。臨床検査及び診断検査が行われた。超音波検査で左下腿の深部静脈血栓症が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，外来泌尿器科を受診した。泌尿器系の異常は見られなかった。

入院中の経過

被験者の既往歴は，高血圧，乾癬及び乾癬性関節炎であった。被験者は，デュプレックス超音波検査で明らかとなった左下腿の大腿部の深部静脈血栓症のため緊急入院した。臨床検査で，

血沈亢進，C-反応性蛋白増加，γGT 増加及び脂質増加が認められた。画像診断及び臨床検査で，炎症マーカー増加の原因となる感染を示唆するような異常は認められなかった。医師は乾癬が原因であると判断した。血栓症により，治験薬の投与は中止され，被験者の担当医は被験者の入院の原因を知らされた。被験者は，低分子量ヘパリン投与下かつ伸縮包帯着用下にて，理学療法士の介助の下に動くことができた。画像検査，泌尿器系検査，内視鏡検査及び腫瘍マーカー検査の結果，深部静脈血栓症の原因となる占拠性突起は認められなかった。上部消化管内視鏡検査では，十二指腸炎及びバレット化生に相当する所見が偶発的に認められた。組織学的検査のため検体が採取された。これ以上の入院治療は不要となり，被験者は退院した。

投与された薬剤は，noacid，algopyrin，イグザレルト，ヘパリン及びクレキサンであった。

The patient's past medications include:

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Deep vein thrombosis leg (10065052) (Deep vein thrombosis (10051055)) [v.22.1] [10065052]

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 THROMBOSIS IN THE LEFT SUPERFICIAL FEMORAL AND POPLITEAL VEINS

- Investigator: Obesity less movement.

- AbbVie: Risk factors include obesity (BMI of 42.4 at time of event) and pre-existing psoriasis. Patients with obesity and psoriasis are at increased risk of developing VTE (OR 2.33 and 1.46 respectively). Additionally, patients older than 40 years are at higher risk for VTE, and that risk doubles with each subsequent decade.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ABDOMINAL (COMPLEX) ULTRASOUND SCAN:** Diffuse liver parenchymal lesions. Cyst in the liver. Pyelectasis of the left kidney, minimal extent. Renal parenchymal lesion in the left kidney.

[redacted] 20[redacted] **ABSOLUTE BASOPHIL:** 0.0 G/L

[redacted] 20[redacted] **ABSOLUTE MONOCYTE:** 1.004 G/L

[redacted] 20[redacted] **ACETONE:** Negative

[redacted] 20[redacted] **AFP:** 4.38 IU/L

[redacted] 20[redacted] **ALANINE AMINOTRANSFERASE:** 40 U/L

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 85 U/L

[redacted] 20[redacted] **ASPARTATE AMINOTRANSFERASE:** 26 U/L

[redacted] 20[redacted] **BASOPHIL GRANULOCYTES:** 0.3 %

[redacted] 20[redacted] **BILIRUBIN:** 10 MCMOL/L

[redacted] 20[redacted] **BLOOD PRESSURE:** 150/80 mmHg

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 6.2 MMOL/L

[redacted] 20[redacted] **BMI:** 42.4 kg/m2

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 45.2 MG/L

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 45.2 MG/L (normal 0 to 5)

[redacted] 20[redacted] **CA19:** 24.10 U/ML

[redacted] 20[redacted] **CEA:** 0.70 NG/ML

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

[redacted] 20[redacted] **CHLORIDE:** 105.0 MMOL/L

[redacted] 20[redacted] **CHOLESTEROL:** 6.0 MMOL/L

[redacted] 20[redacted] **CREATININE:** 84 MCMOL/L

[redacted] 20[redacted] **EOSINOPHIL:** 0.451 G/L

[redacted] 20[redacted] **EOSINOPHIL GRANULOCYTES:** 4.6 %

[redacted] 20[redacted] **ERYTHROCYTE SEDIMENTATION RATE:** 46 MM/HR

[redacted] 20[redacted] **ESOPHAGO-GASTRO-DUODENOSCOPY:** Duodenitis, suspected Barrett’s metaplasia

[redacted] **20[redacted] ESTIMATED GFR:** Greater than 90

[redacted] **20[redacted] GAMMA-GLUTAMYL TRANSPEPTIDASE:** 82 U/L

[redacted] **20[redacted] HEMATOCRIT:** 0.44 L/L

[redacted] **20[redacted] HEMOGLOBIN:** 152.0 G/L

[redacted] **20[redacted] LACTATE DEHYDROGENASE:** 364 U/L

[redacted] **20[redacted] LYMPHOCYTE:** 3.344 G/L

[redacted] **20[redacted] LYMPHOCYTES:** 33.8 %

[redacted] **20[redacted] MEAN CORPUSCULAR HEMOGLOBIN:** 32.4 PG

[redacted] **20[redacted] MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION:** 348.0 G/L

[redacted] **20[redacted] MEAN CORPUSCULAR VOLUME:** 93.3 FL

[redacted] **20[redacted] MEAN PLATELET VOLUME:** 11.3 FL

[redacted] **20[redacted] MONOCYTES:** 10.1 %

[redacted] **20[redacted] NEUTROPHIL:** 5.071 G/L

[redacted] **20[redacted] NEUTROPHIL GRANULOCYTES:** 51.21 %

[redacted] **0[redacted] NON-CONTRAST CT SCAN OF THE HEAD:** Negative intracranial status

[redacted] **20[redacted] PLATELETS:** 163 G/L

[redacted] **20[redacted] POTASSIUM:** 4.06 MMOL/L

[redacted] **20[redacted] PSA:** 0.773 NG/ML

[redacted] **20[redacted] PULSE RATE:** 97 bpm

[redacted] **20[redacted] RECTO-SIGMOIDO-COLONOSCOPY:** Negative report.

[redacted] **20[redacted] RED BLOOD CELLS:** 4.7 T/L

[redacted] **20[redacted] RED CELL DISTRIBUTION WIDTH:** 12.4 %

[redacted] **20[redacted] SODIUM:** 143.1 MMOL/L

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

[redacted] **20[redacted] TRIGLYCERIDES:** 3.2 MMOL/L

[redacted] **20[redacted] ULTRASOUND:** Deep vein thrombosis in the left lower extremity

[redacted] 20[redacted] **URIC ACID:** 452 MCMOL/L

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

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

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

[redacted] 20[redacted] **URINE PH:** 5.5 No units

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

[redacted] 20[redacted] **URINE SPECIFIC GRAVITY:** 1.020 No units

[redacted] 20[redacted] **UROBILINOGEN:** Normal

[redacted] 20[redacted] **WE:** 46 MM/HR (normal 3 to 15)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 9.9 G/DL

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 30 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: LEFT FEMUR FRACTURE	19[redacted]
OTHER: PLAQUE PSORIASIS	19
PSORIATIC ARTHRITIS	19
HYPERTENSION	19
OTHER: HEPATITIS C	19
OTHER: CATARACTS ON BOTH EYES	20
OSTEOPOROSIS	20
CHOLELITHIASIS	20
OTHER: ATHEROSCLEROSIS	20
OTHER: LEFT VENTRICULAR HYPERTROPHY	20
OTHER: ABDOMINAL EXPLORATION DUE TO CAR ACCIDENT	20
OTHER: PAROXYSMAL ATRIAL FLUTTER	20
OTHER: ABDOMINAL HERNIA	20
OTHER: ANGINA PECTORIS	20
OTHER: HYPERCHOLESTERINAEMIA	20
DIABETES MELLITUS	20
OTHER: LATENS TB	20
OTHER: ABDOMINAL HERNIA SURGERY	20

Prior Procedures	Procedure Year
SURGERY: SURGERY DUE TO LEFT FEMUR FRACTURE	19[redacted]
SURGERY: SURGERY DUE TO CATARACTS ON BOTH EYES	20
SURGERY: CHOLECYSTECTOMY	20

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 169	169
ABT-494	30 MG	ORAL	QD	[redacted] / 170	[redacted] / 398	229
ABT-494	30 MG	ORAL	QD	[redacted] / 399		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	UNK mg	OTHER: UNK	Y-M: 19[redacted]
NAPROXEN	550 mg	BID	Y-M: 20[redacted]
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted] / -278
ENALAPRIL	20 mg	BID	Y-M: 20[redacted] / -278
ENALAPRIL	20 mg	QD	Y-M: 20[redacted] / -278
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted] / -278
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted] / -278
LERCANIDIPINE	10 mg	QD	Y-M: 20[redacted] / -278
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / -278
RIVAROXABAN	20 mg	QD	Y-M: 20[redacted] / -278
ROSUVASTATIN	20 mg	QD	Y-M: 20[redacted] / -278
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -240
FOLIC ACID	6 mg	EVERY WEEK	Y-M: 20[redacted] / -230
ISONIAZID	450 mg	OTHER: DAILY DOSE	Y-M: 20[redacted] / -124

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
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted] / -278	NOT REPORTED
ENALAPRIL	20 mg	BID	Y-M: 20[redacted] / -278	NOT REPORTED
ENALAPRIL	20 mg	QD	Y-M: 20[redacted] / -278	NOT REPORTED
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted] / -278	NOT REPORTED
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted] / -278	NOT REPORTED
LERCANIDIPINE	10 mg	QD	Y-M: 20[redacted] / -278	NOT REPORTED
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / -278	NOT REPORTED
ROSUVASTATIN	20 mg	QD	Y-M: 20[redacted] / -278	NOT REPORTED
RIVAROXABAN	20 mg	QD	Y-M: 20[redacted] / -278	Y-M: 20[redacted] / 302
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -240	NOT REPORTED
FOLIC ACID	6 mg	EVERY WEEK	Y-M: 20[redacted] / -230	NOT REPORTED
ISONIAZID	450 mg	QD	Y-M: 20[redacted] / 274	Y-M: 20[redacted] / 548
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 312

Event #1: Serious Adverse Event

Event Description	WORSENING LEFT UPPER ARM FRACTURE
Preferred term	上肢骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 300
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
[redacted]20[redacted] (RX DAY 303): WOUND NPTST446-MICROBIOLOGICAL TEST FOR SURGIC: Negative

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 303): LEFT UPPER LIMB SURGERY: PERCUTANEOUS STAPLING THREADED KIRSCHNER SUPPLY DECOLLEMENT

AE Stopped Rx Day	308
Duration of AE	9 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	UPPER ARM FRACTURE AS A RESULT OF MOTORCYCLE ACCIDENT ON [redacted] 20[redacted].
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: M15-572

治験責任医師からの報告。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が投与され，左上腕骨折の悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，左大腿骨骨折，左大腿骨骨折による手術，局面型乾癬，乾癬性関節炎，高血圧，骨粗鬆症，元紙巻タバコ喫煙者（1 日 1 箱を 40 年間），糖尿病及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，

盲検化された皮下注製剤の最終投与は20[redacted]年[redacted]月[redacted]日であった。

20[redacted]年[redacted]月[redacted]日，被験者は左上腕骨折の悪化を発現した。20[redacted]年[redacted]月[redacted]日，左上腕骨折の悪化は消失した。

20[redacted]年[redacted]月[redacted]日，被験者は，約 20 km/h の速度で運転していた際のオートバイ事故により，左上腕骨折（非重篤）を来した。被験者は当初，入院を拒否していたが，痛みが悪化した。

20[redacted]年[redacted]月[redacted]日，被験者は中等度の左上肢の腫れと痛みで再受診し，同日入院した。20[redacted]年[redacted]月[redacted]日，ネジ付きキルシュナー鋼線を用いた左上腕の経皮的固定手術が行われた。20[redacted]年[redacted]月[redacted]日，被験者は退院した。

The patient's past medications include:

METHYLPREDNISOLONE for PSORIATIC ARTHRITIS (19[redacted] - [redacted] 20[redacted])

NAPROXEN for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Arm fracture (10049127) (Upper limb fracture (10061394)) [v.22.1] [10049127]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING LEFT UPPER ARM FRACTURE

- Investigator: UPPER ARM FRACTURE AS A RESULT OF MOTORCYCLE ACCIDENT ON [redacted] [redacted] 20[redacted].

- AbbVie: Event is more likely related to trauma sustained from a motorcycle accident.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] MICROBIOLOGICAL TEST FOR SURGICAL WOUNDS: Negative

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
HEPATITIS: VIRAL HEPATITIS A	19[redacted]
OTHER: NODULAR GOITER	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: MENOPAUSE	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: VARICOSE VEINS	20[redacted]

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	FORMER	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 83	83

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	0.005 g	OTHER: EVERY DAY EXCEPT DAYS OF MTX INTAKE	Y-M: 20[redacted]
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	0.005 g	OTHER: EVERY DAY EXCEPT DAYS OF MTX INTAKE	Y-M: 20[redacted]	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
IBUPROFEN	200 mg	PRN	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 84
METRONIDAZOLE	0.25 g	TID	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 89
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 92
ZOPICLONE	7,5 mg	OTHER: ONCE	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 89
PIPERACILLIN	4 g	TID	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 93
SULBACTAM	0.5 g	TID	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 93
ATROPINE	0,5 mL	OTHER: ONCE	Y-M: 20[redacted] / 90	Y-M: 20[redacted] / 90

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

Event Description FEVER OF UNKNOWN ORIGIN

Preferred term 発熱

AE Onset Date / Rx Day [redacted]20[redacted] / 64

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 85): Alanine Aminotransferase: 19 [0 - 30] U/L; Alkaline Phosphatase: 62 [0 - 250] U/L; Aspartate Aminotransferase: 27 [0 - 30] U/L; Bilirubin: 44 [5 - 20] UMOL/L; Blood Urea Nitrogen: 7.4 [2.4 - 8.2] MMOL/L; Cholesterol: 6.56 [3.4 - 6.4] MMOL/L; Creatine Kinase: 181 [0 - 180] U/L; Creatinine: 95 [52 - 96] UMOL/L; Erythrocytes: 3.7 [3.7 - 4.7] 10^12/L; Glucose: 6.3 [3.2 - 5.5] MMOL/L; HDL Cholesterol: 1.69 [0 - 1.2] MMOL/L; Hematocrit: 0.35 [0.36 - 0.42] FRACTION OF 1; Hemoglobin: 110 [120 - 140] G/L; LDL Cholesterol: 4.96 [0 - 3] MMOL/L; Leukocytes: 5.8 [4 - 9] 10^9/L; Platelets: 291 [180 - 320] 10^9/L; Protein: 70 [65 - 85] G/L; Prothrombin Intl. Normalized Ratio: 1.06 [0.8 - 1.3] RATIO; Triglycerides: 1.92 [0 - 1.7] MMOL/L; Urate: 286 [240 - 540] UMOL/L; [redacted]20[redacted] (RX DAY 91): Creatine Kinase: 61 [0 - 180] U/L; [redacted]20[redacted] (RX DAY 103): Alanine Aminotransferase: 25 [0 - 30] U/L; Alkaline Phosphatase: 57 [0 - 250] U/L; Aspartate Aminotransferase: 19 [0 - 30] U/L; Bilirubin: 24 [5 - 20] UMOL/L; Blood Urea Nitrogen: 5.9 [2.4 - 8.2] MMOL/L; Cholesterol: 6.33 [3.4 - 6.4] MMOL/L; Creatinine: 71 [52 - 96] UMOL/L; Erythrocytes: 3.7 [3.7 - 4.7] 10^12/L; Glucose: 4.8 [3.2 - 5.5] MMOL/L; HDL Cholesterol: 1.09 [0 - 1.2] MMOL/L; Hematocrit: 0.36 [0.36 - 0.42] FRACTION OF 1; Hemoglobin: 110 [120 - 140] G/L; LDL Cholesterol: 4.73 [0 - 3] MMOL/L; Leukocytes: 6.5 [4 - 9] 10^9/L; Platelets: 249 [180 - 320] 10^9/L; Protein: 69 [65 - 85] G/L; Prothrombin Intl. Normalized Ratio: 0.99 [0.8 - 1.3] RATIO; Urate: 320 [240 - 540] UMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 85): ECG: CHANGES IN THE ANTERIOR LOWER WALL OF THE LEFT VENTRICLE (NCS); [redacted]20[redacted] (RX DAY 86): ESOPHAGOGASTRODUODENOSCOPY WITH BIOPSY: CARDIA FAILURE, REFLUX ESOPHAGITIS, ERYTHEMATOUS GASTROPATHY 1; [redacted]20[redacted] (RX DAY 89): ECHOCARDIOGRAPHY: CHANGES IN MYOCARDIUM AND VALVES, NOT CLINICALLY SIGNIFICANT, LEFT VENTRICULAR EJECTION FRACTION 60%, SYSTOLIC PRESSURE IN THE PULMONARY ARTERY 33 MMHG, MEAN PULMONARY ARTERY PRESSURE 15 MMHG; [redacted]20[redacted] (RX DAY 90): ULTRASOUND EXAMINATION OF

THE ABDOMINAL ORGANS AND KIDNEYS: SUSPICIOUS FOR MALIGNANCY NOT IDENTIFIED. DIFFUSE CHANGES IN THE LIVER AND PANCREAS? NOT CLINICALLY SIGNIFICANT; [redacted]20[redacted] (RX DAY 93): ULTRASOUND OF THE PELVIC ORGANS: NO PATHOLOGICAL CHANGES

AE Stopped Rx Day	90 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	27 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はベラルーシの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，原因不明の発熱の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，局面型乾癬，結節性甲状腺腫，閉経，末梢血管疾患（静脈［静脈瘤］），元飲酒者（1 日 2 杯未満）及び非喫煙者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は原因不明の発熱を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，原因不明の発熱は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日の事象発現前，被験者は白血球減少症（非重篤）及び好中球減少症と診断された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は原因不明の発熱を発現した。被験者は NSAID を併用していた。その他の訴えはなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は診断及び治療のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，metronidasol，piperacillinum，スルバクタム及びイブプロフェンであった。

Causality for UPADACITINIB (Blinded)

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1) Fever of unknown origin (10016563) (Pyrexia (10037660)) [v.22.1] [10016563]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of FEVER OF UNKNOWN ORIGIN

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BLOOD PRESSURE:** 130/70 mmHg

[redacted] **BLOOD PRESSURE:** 134/90 mmHg

[redacted] **BLOOD PRESSURE:** 116/74 mmHg

[redacted] **CHEST X-RAY (SCREENING):** Normal

[redacted] **ECG:** Changes in the anterior lower wall of the left ventricle (NCS).

[redacted] **ECHOCARDIOGRAPHY:** Changes in myocardium and valves, not clinically significant, left ventricular ejection fraction 60%, systolic pressure in the pulmonary artery 33 mmHg, mean pulmonary artery pressure 15 mmHg.

[redacted] **ESOPHAGOGASTRODUODENOSCOPY WITH BIOPSY:** Cardiac failure, reflux esophagitis, erythematous gastropathy 1.

[redacted] 20[redacted] **GLUCOSE:** 6.26 MMOL/L (normal 3.2 to 5.5)

[redacted] 20[redacted] **HEMATOCRIT:** 34.55 % (normal 36 to 42)

[redacted] 20[redacted] **HEMOGLOBIN:** 110 G/L (normal 120 to 140)

[redacted] 20[redacted] **PLATELET COUNT:** 291 X10**9/L (normal 180 to 320)

[redacted] 20[redacted] **PULSE:** 68 bpm

[redacted] 20[redacted] **PULSE:** 74 bpm

[redacted] 20[redacted] **PULSE:** 74 bpm

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.73 X10**12/L (normal 3.7 to 4.7)

[redacted] 20[redacted] **RESPIRATORY RATE:** 16 /min

[redacted] 20[redacted] **RESPIRATORY RATE:** 16 /min

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

[redacted] 20[redacted] **TEMPERATURE:** 36.4 Degrees C

[redacted] 20[redacted] **TEMPERATURE:** 36.8 Degrees C

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

[redacted] 20[redacted] **TOTAL BILIRUBIN:** 43.7 MCMOL/L (normal 5 to 20)

[redacted] 20[redacted] **ULTRASOUND EXAMINATION OF THE ABDOMINAL ORGANS AND KIDNEYS:** Suspicious for malignancy not identified. Diffuse changes in the liver and pancreas not clinically significant.

[redacted] 20[redacted] **ULTRASOUND OF THE PELVIC ORGANS:** No pathological changes.

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 5.82 X10**9/L (normal 4 to 9)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腹膜炎	X			X
卵管炎	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CYSTECTOMY OF LEFT KNEE	NOT REPORTED
SURGERY: LEFT ADENOMAMMECTOMY	20[redacted]
SURGERY: LEFT ADENOMAMMECTOMY	20[redacted]
SURGERY: CAESAREAN SECTION	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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 393		

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-M: 19[redacted]
DIPROSPAN	1.0 mL	OTHER: ONCE IN YEAR	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	10 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
ACECLOFENAC	100 mg	BID	Y-M: 20[redacted] / -164

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
ACECLOFENAC	100 mg	BID	Y-M: 20[redacted] / -164	NOT REPORTED
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 441	Y-M: 20[redacted] / 443

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

Event Description	ACUTE RIGHT-SIDED SALPINGITIS
Preferred term	卵管炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 441
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 442): Alanine Aminotransferase: 20.5 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 63.5 [NOT REPORTED - NOT REPORTED] U/L; Bilirubin: 9 [5 - 21] UMOL/L; Erythrocytes: 3.3 [3.8 - 5.1] 10^12/L; Glucose: 5.1 [4.1 - 5.9] MMOL/L; Hemoglobin: 101 [117 - 155] G/L; Leukocytes: 4.3 [4.5 - 11] 10^9/L; Leukocytes: 10-12 [NOT REPORTED - NOT REPORTED] HPF; NPTST114-BLOOD GROUP: A(II) RH(+) [NOT REPORTED - NOT REPORTED] NA; NPTST585-RW (WASSERMANN REACTION): NEGATIVE [NOT REPORTED - NOT REPORTED] NA; NPTST612-SQUAMOUS EPITHELIUM: 1-2 [NOT REPORTED - NOT REPORTED] HPF; NPTST662-UREA: 2.09 [NOT REPORTED - NOT REPORTED] mmol/L; Platelets: 146 [150 - 400] 10^9/L; Protein: 60 [64 - 83] G/L; pH: ALKALINE [4.5 - 8] NA; [redacted]20[redacted] (RX DAY 443): NPTST011- ABHCV: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; NPTST313-HBSAG: NEGATIVE [NOT REPORTED - NOT REPORTED] NA

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 441): ELECTROCARDIOGRAM: SINUS RHYTHM, SIGNS OF INCOMPLETE AV BLOCKADE OF THE I DEGREE, VIOLATIONS OF INTRAVENTRICULAR CONDUCTION, CHANGES IN MYOCARDIAL METABOLISM; SURGERY: HYPOGASTRIC REGION. DIAGNOSTIC LAPAROSCOPY PROCEDURE FOR DIAGNOSIS: ACUTE RIGHT-SIDED SALPINGITIS.

AE Stopped Rx Day	443
Duration of AE	3 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	PELVIC PURULENT PERITONITIS

Preferred term	腹膜炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 881
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ACUTE PURULENT SALPINGITIS
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: M15-572

治験責任医師からの報告。本被験者はロシア連邦の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性右側卵管炎の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，左子宮腺筋症摘出術，帝王切開，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性右側卵管炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性右側卵管炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は重度の腹痛が 2 日間続いたため入院し，骨盤部超音波検査及び子宮頚部培養が行われ，被験者は婦人科医の診察を受けた。同日，診断のための腹腔鏡下手術が

行われ，急性右側卵管炎と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤はセフトリアキソンであった。

The patient's past medications include:

MOVALIS for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute salpingitis (10001061) (Salpingitis (10039453)) [v.22.1] [10001061]

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 ACUTE RIGHT-SIDED SALPINGITIS

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABHCV:** Negative

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 20.5 U/L

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 63.5 U/L

[redacted] **20[redacted] BLOOD GROUP:** A(II) Rh(+)

[redacted] **20[redacted] BLOOD TOTAL BILIRUBIN:** 9.1 MCMOL/L

[redacted] **20[redacted] BLOOD TOTAL PROTEIN:** 59.9 G/L

[redacted] **20[redacted] BLOOD UREA:** 2.09 MMOL/L

[redacted] **20[redacted] CERVICAL CULTURE:** not reported

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Sinus rhythm, signs of incomplete AV blockade of the I degree, violations of intraventricular conduction, changes in myocardial metabolism.

[redacted] **20[redacted] GLUCOSE:** 5.11 MMOL/L

[redacted] **20[redacted] HBSAG:** Negative

[redacted] **20[redacted] HEMOGLOBIN:** 101 G/L

[redacted] **20[redacted] PLATELET COUNT:** 146 X10**9/L

[redacted] **20[redacted] RED BLOOD CELLS:** 3.3 X10**12/L

[redacted] **20[redacted] ULTRASOUND:** PELVIC: not reported

[redacted] **20[redacted] URINE PH:** alkaline

[redacted] **20[redacted] URINE SQUAMOUS EPITHELIUM:** 1-2 HPF

[redacted] **20[redacted] URINE WBC:** 10-12 HPF

[redacted] **20[redacted] WASSERMANN REACTION:** Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.33 X10**9/L
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はロシア連邦の 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，骨盤の化膿性腹膜炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，手術（左子宮腺筋症摘出術），手術（帝王切開），局面型乾癬，乾癬性関節炎，非喫煙者及び禁酒であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は骨盤の化膿性腹膜炎を発現した。

入院前の 20[redacted] 年 [redacted] 月から，被験者は月経周期後に腹痛があった。20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで，膣からわずかに出血が見られた。被験者は医師の診察を受けず，未診断であった。

20[redacted] 年 [redacted] 月 [redacted] 日，体温が 37.5°C に上昇し，左腹部に重度の腹痛が出現した。被験者は急性化膿性卵管炎（非重篤）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は救急車を呼び，入院した。腹腔内ドレナージのため腹腔鏡手術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

DIPROSPAN for SYNOVITIS (20[redacted] - 20[redacted])

MOVALIS for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pelvic peritonitis (10049608) (Peritonitis (10034674)) [v.23.0] [10049608]

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 PELVIC PURULENT PERITONITIS

- Investigator: Acute purulent salpingitis.

- AbbVie: Event is more likely related to concurrent non-serious acute purulent salpingitis, most common reason for salpingitis is sexually transmitted disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] **20[redacted] BODY TEMPERATURE:** 37.5 Degrees C

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

[redacted] **20**[redacted] **ECG:** Violation of repolarization processes of the anterior-septum wall of left ventricle.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
四肢膿瘍	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 455	287
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 456		

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]
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -226
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -226

METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted] / -226
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -212
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -202
DIPYRIDAMOLE	25 mg	TID	Y-M: 20[redacted] / -95
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -95
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted] / -95
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -95
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -95

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
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -95	NOT REPORTED
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted] / -95	NOT REPORTED
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -95	NOT REPORTED
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -95	NOT REPORTED
DEXAMETHASONE	16 mg	OTHER: ONCE	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 393
HAEMOFILTRATIONSLOESUNG HF 24	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 393
OMEPRAZOLE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 393
CEFTRIAXONE	2 mg	QD	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 402
ENOXAPARIN	0.4 mL	QD	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 402
ERTAPENEM	1 mg	QD	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 402
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 402
METOCLOPRAMIDE	2 mg	TID	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 402
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 393	Y-M: 20[redacted] / 402

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

Event Description LEFT BUTTOCK ABSCESS

Preferred term 四肢膿瘍

AE Onset Date / Rx Day [redacted]20[redacted] / 392

Age at AE Onset 4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 396): Alanine Aminotransferase: 40.2 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 20.3 [NOT REPORTED - NOT REPORTED] U/L; Bilirubin: 6 [5 - 21] UMOL/L; Creatinine: 67.6 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Erythrocytes: 3.6 [3.8 - 5.3] 10^12/L; Glucose: 5.8 [4.1 - 5.9] MMOL/L; Hematocrit: 0.34 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 108 [117 - 160] G/L; Leukocytes: 5.2 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 38 [20 - 44] %; NPTST041-AMYLASE: 74.1 [NOT REPORTED - NOT REPORTED] U/L; NPTST526-PROSEPSIN: 127 [NOT REPORTED - NOT REPORTED] PG/ML; Platelets: 334 [150 - 400] 10^9/L; Potassium: 4.5 [3.4 - 4.4] MMOL/L; Protein: 62 [64 - 83] G/L; Sodium: 139 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 393): FIBROGASTRODUODENOSCOPY: CONCLUSION OF FIBROGASTRODUODENOSCOPY IS ABSENT IN THE PATIENT'S DISCHARGE; OPERATION: OPENING AND DRAINAGE OF THE ABSCESS OF THE LEFT GLUTEAL REGION: THE DYNAMICS OF THE EARLY PROCESS IS POSITIVE, THE INFLAMMATORY REACTION IS STOPPED, THE WOUND IS 3.0*0.5 CM WITH MODERATE SEROUS DISCHARGE, CLEAN, GRANULATES.; [redacted]20[redacted] (RX DAY 394): EXAMINATION BY THE RHEUMATOLOGIST: RECOMMENDED TO STOP TAKING IMMUNOSUPPRESSIVE DRUGS, CONTINUE TO USE METIPRED; [redacted]20[redacted] (RX DAY 396): ECG: NORMAL, WITHOUT PATHOLOGY; [redacted]20[redacted] (RX DAY 414): ADDITIONAL FIBROGASTRODUODENOSCOPY: CATARRHAL ESOPHAGITIS. SUPERFICIAL GASTRITIS.

AE Stopped Rx Day	402
Duration of AE	11 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はロシア連邦の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左臀部膿瘍の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左臀部膿瘍を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左臀部膿瘍は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，左臀部痛，皮膚の充血，39°C の発熱及び脱力が出現した。被験者より，発熱に対し，アセトアミノフェン 500 mg を服用したと報告された。同日，被験者は入院した。

20[redacted] 年 [redacted] 月 [redacted] 日，左臀部の切開と膿瘍ドレナージが行われた。この手術で，創傷は 3.0×5.0 cm の大きさであることが確認された。中等度の漿液性分泌物及び透明顆粒を伴って，初期過程の動態が認められ，炎症反応は消失した。同日，胃十二指腸内視鏡検査が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はリウマチ専門医を受診した。この医師から，免疫抑制剤の服用を中止し，Metipred の使用を継続するよう勧められた。20[redacted] 年 [redacted] 月 [redacted] 日，WBC が 5.2×10^9/L であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，アセトアミノフェン，invanz，デキサメタゾン，methylprednisolon，エノキサパリン及びセフトリアキソンであった。

The patient's past medications include:

FOLIC ACID for MTX TOXICITY THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

MELOXICAM for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Abscess on buttock (10000309) (Abscess limb (10050473)) [v.22.1] [10000309]

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 LEFT BUTTOCK ABSCESS

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY TEMPERATURE:** 39 Degrees C

[redacted] **20[redacted] ECG:** NORMAL, WITHOUT PATHOLOGY

[redacted] **20[redacted] FIBROGASTRODUODENOSCOPY:** CONCLUSION OF FIBROGASTRODUODENOSCOPY IS ABSENT IN THE PATIENT'S DISCHARGE

[redacted] **20[redacted] FIBROGASTRODUODENOSCOPY:** CATARRHAL ESOPHAGITIS. SUPERFICIAL GASTRITIS

[redacted] **20[redacted] LYMPHOCYTES %:** 38 %

[redacted] **20[redacted] PLATELET COUNT:** 334 X10**9/L

[redacted] **20[redacted] RED BLOOD CELLS:** 3.6 X10**12/L

[redacted] **20[redacted] TOTAL PROTEIN:** 61.8 G/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.2 X10**9/L

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
HYPERTENSION	20[redacted]
OTHER: SPHENOIDITIS	20[redacted]
ANEMIA: MILD	20[redacted]
OTHER: BRONCHIAL ASTHMA,EASY CURRENT	20[redacted]
OTHER: PSORIASIS	20[redacted]
OTHER: MENOPAUSA	20[redacted]
CHOLECYSTITIS: IDENTIFIED BY ULTRASOUND	20[redacted]
CHOLELITHIASIS: IDENTIFIED BY ULTRASOUND	20[redacted]
OTHER: CHRONIC GASTRITIS	20[redacted]
OTHER: POLYP OF THE STOMACH	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: REMOVAL OF CYSTS OF THE SPHENOID SINUS	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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted]
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted]
MOXONIDINE	0.4 mg	QD	Y-M: 20[redacted]
FAMOTIDINE	40 mg	QD	Y-M: 20[redacted]
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]
NIMESULIDE	100 mg	BID	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
MOXONIDINE	0.4 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FAMOTIDINE	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
NIMESULIDE	100 mg	BID	Y-M: 20[redacted]	NOT REPORTED
ACICLOVIR	200 mg	OTHER: 5 A DAY	Y-M: 20[redacted] / 210	Y-M: 20[redacted] / 216
AMBROXOL	30 mg	TID	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 490
DUOVENT	1 mL	TID	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 490

Event #2: Serious Adverse Event

Event Description	EXACERBATION OF CALCULOUS CHOLECYSTITIS
Preferred term	胆嚢炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 490
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 490): Erythrocyte Sedimentation Rate: 10 [2 - 15] MM/H; Erythrocytes: 4 [3.5 - 5.4] 10^12/L; Glucose: 5.2 [3.9 - 6.4] MMOL/L; Hemoglobin: 131 [120 - 156] G/L; Leukocytes: 7.2 [4.5 - 10] 10^9/L; Platelets: 248 [160 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 491): Erythrocytes: 0 [0 - 1] IU/mL; Leukocytes: 15-20 [0 - 1] IU/mL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 491): ULTRASONOGRAPHY OF ABDOMINAL ORGANS: SIGNS OF CHOLELITHIASIS, CHRONIC PANCREATITIS

AE Stopped Rx Day	499
Duration of AE	10 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	EXACERBATION OF A CHRONIC DISEASE
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: M15-572

治験責任医師からの報告。本被験者はロシア連邦の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，結石性胆嚢炎の増悪の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，高血圧，乾癬，閉経，胆嚢炎，胆石症，慢性胃炎，乾癬性関節炎，非喫煙者及び禁酒であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は結石性胆嚢炎の増悪を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，結石性胆嚢炎の増悪は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は食事療法を違反したことで腹痛と悪心が出現した翌日に入院した。被験者は輸液，鎮痙薬，分泌抑制薬及び鎮痛薬による治療を受けた。疼痛症候群の軽減という形で positive dynamics が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は問題ない状態で退院した。

Causality for UPADACITINIB (Blinded)

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1) Calculous cholecystitis (10062750) (Cholecystitis (10008612)) [v.23.0] [10062750]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of EXACERBATION OF CALCULOUS CHOLECYSTITIS

- Investigator: Exacerbation of a chronic disease

- AbbVie: Event more likely related to pre-existing cholelithiasis and cholecystitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 10 mm/h (normal 2 to 15)

[redacted] **20[redacted] GLUCOSE:** 5.2 MMOL/L (normal 3.9 to 6.4)

[redacted] **20[redacted] HEMOGLOBIN:** 131 G/L (normal 120 to 156)

[redacted] **20[redacted] PLATELET COUNT:** 248 X10**9/L (normal 160 to 400)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.0 X10**12/L (normal 3.5 to 5.4)

[redacted] **20[redacted] RED BLOOD CELLS:** 0 IU/mL (normal 0 to 1)

[redacted] **20[redacted] ULTRASONOGRAPHY OF ABDOMINAL ORGANS:** Signs of cholelithiasis, chronic pancreatitis.

[redacted] **20[redacted] WBC:** 7.2 X10**9/L (normal 4.5 to 10.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 15-20 IU/mL (normal 0 to 1)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: POST-MENOPAUSAL	20[redacted]
HYPERTENSION	20[redacted]
OTHER: HYSTEROMYOMA	20[redacted]

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)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 170	170
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 171	[redacted]20[redacted] / 394	224
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 395		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DICLOFENAC	50 mg	TID	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
DICLOFENAC	100 mg	QD	Y-M: 20[redacted]
VALSARTAN	40 mg	TID	Y-M: 20[redacted]
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -124

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
VALSARTAN	40 mg	TID	Y-M: 20[redacted]	NOT REPORTED
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -124	NOT REPORTED
CEFTRIAXONE	1,0 mL	QD	Y-M: 20[redacted] / 777	Y-M: 20[redacted] / 783

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

Event Description	BILATERAL POLYSEGMENTAL PNEUMONIA, MODERATE
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 777
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 778): Erythrocyte Sedimentation Rate: 20 [0 - 30] MM/H; Erythrocytes: 4.1 [3.8 - 5.3] 10^12/L; Hemoglobin: 124 [117 - 160] G/L; Leukocytes: 4.6 [4.5 - 11] 10^9/L; Platelets: 213 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 780): Alanine Aminotransferase: 20 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 21 [NOT REPORTED - NOT REPORTED] U/L; Bilirubin: 4600 [5 - 21] UMOL/L; Creatinine: 69 [53 - 97] UMOL/L; Glucose: 4 [4.1 - 5.9] MMOL/L; NPTST129-C-REACTIVE PROTEIN: 35.6 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 778): OTHER SMEAR FROM THE MUCOUS MEMBRANE OF THE NOSE AND MOUTH NPTST581-RNA SARS-COV-2: Negative; [redacted]20[redacted] (RX DAY 787): OTHER SMEAR FROM THE MUCOUS MEMBRANE OF THE NOSE AND MOUTH NPTST581-RNA SARS-COV-2: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 778): CHEST RADIOGRAPHY: BILATERAL INTERSTITIAL PNEUMONIA

AE Stopped Rx Day	798
Duration of AE	22 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ACUTE RESPIRATORY DISEASE, ETIOLOGICAL AGENT NOT DETERMINED
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: M15-572

治験責任医師からの報告。本被験者はロシア連邦の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，両側の多区域肺炎（中等症）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両側の多区域肺炎（中等症）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，両側の多区域肺炎（中等症）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は中等度の全身脱力を感じ，乾性咳嗽が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は往診医を呼んだ。診察では肺炎が疑われ，被験者は精査及び治療のため入院すべく搬送された。入院時の重症度は中等度，意識清明で小さな湿性咳嗽が認められた。被験者の体温は 36.6℃ であった。診察の結果，局所リンパ節の腫大はなく，主に左肺で下部に行くほど減弱する肺胞呼吸音が聴取された。被験者の呼吸数は 19 回／分，SpO2 は 97%であった。診断のための画像検査と臨床検査が行われた。胸部 X 線検査で両側の間質性肺炎が認められた。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日と 20[redacted] 年 [redacted] 月 [redacted] 日の 2 回，新型コロナウイルスの検査を受け，結果は陰性であった。被験者は抗菌療法による治療を受け，効果は良好であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は問題ない状態で退院した。体温は 36.6℃ であった。肺の診察で正常な呼吸音が認められ，呼吸数は 17 回／分であった。

投与された薬剤は，セフトリアキソンであった。

The patient's past medications include:

VOLTAREN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Bilateral pneumonia (10058686) (Pneumonia (10035664)) [v.23.0] [10058686]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of BILATERAL POLYSEGMENTAL PNEUMONIA, MODERATE

- Investigator: ACUTE RESPIRATORY DISEASE, ETIOLOGICAL AGENT NOT DETERMINED

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

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

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

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 35.6 MG/L (normal 0 to 5)

[redacted] **20[redacted] CHEST XRAY:** Bilateral interstitial pneumonia

[redacted] **20[redacted] CREATININE:** 69 MCMOL/L

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 20 MM/HR

[redacted] **20[redacted] GLUCOSE:** 4 MMOL/L

[redacted] **20[redacted] PLATELET:** 213 X10**9/L

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

[redacted] **20[redacted] RESPIRATORY RATE:** 17 /min

[redacted] **20[redacted] RNA SARS-COV-2:** SMEAR FROM THE MUCOUS MEMBRANE OF THE NOSE AND MOUTH: Negative

[redacted] **20[redacted] RNA SARS-COV-2:** SMEAR FROM THE MUCOUS MEMBRANE OF THE NOSE AND MOUTH: Negative

[redacted] **20[redacted] SPO2:** 97 %

[redacted] **20[redacted] WBC:** 4.62 X10**9/L

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
コロナウイルス感染	X			X
肺炎	X			X

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

Medical History	Onset Year
ASTHMA	19[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 170	170
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 171	[redacted]20[redacted] / 389	219
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 390		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	2 g	QD	Y-M: 20[redacted]
LEFLUNOMIDE	100 mg	QD	Y-M: 20[redacted]
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted]
DICLOFENAC	100 mg	QD	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]

METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
NIMESULIDE	100 mg	BID	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
NIMESULIDE	100 mg	BID	Y-M: 20[redacted]	NOT REPORTED
ENOXAPARIN	0.4 mL	BID	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 806
ASCORBIC ACID	6.0 mL	QD	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 811
CEFTRIAXONE	2.0 mL	QD	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 811
DUOVENT	2 OTHER: INHALE	BID	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 811
SERETIDE	1 OTHER: INHALE	BID	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 811
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 816
AMINOPHYLLINE	5.0 mL	BID	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 819
DEXAMETHASONE	4 mg	BID	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 819
TROPHICARD	5.0 mL	BID	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 819
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] / 816	Y-M: 20[redacted] / 836

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] / 797

Age at AE Onset 5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 805): Alanine Aminotransferase: 27 [NOT REPORTED - NOT REPORTED] U/L; Albumin: 47 [34 - 49] G/L; Aspartate Aminotransferase: 46 [NOT REPORTED - NOT REPORTED] U/L; Bilirubin: 2 [5 - 21] UMOL/L; Bilirubin: 8 [5 - 21] UMOL/L; Eosinophils: 0.01 [0 - 0.43] 10^9/L; Erythrocyte Sedimentation Rate: 40 [0 - 20] MM/H; Erythrocytes: 4 [4.2 - 5.6] 10^12/L; Hematocrit: 0.35 [0.39 - 0.5] FRACTION OF 1; Hemoglobin: 121 [131 - 172] G/L; Leukocytes: 3.5 [4.5 - 11] 10^9/L; Lymphocytes: 0.46 [0.96 - 4.75] 10^9/L; NPTST129-C-REACTIVE PROTEIN: 39.52 [NOT REPORTED - NOT REPORTED] mg/L; Neutrophils: 2.57 [2.4 - 7.56] 10^9/L; Platelets: 251 [150 - 400] 10^9/L; Protein: 72 [64 - 83] G/L; [redacted]20[redacted] (RX DAY 813): Alanine Aminotransferase: 63 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 36 [NOT REPORTED - NOT REPORTED] U/L; Erythrocyte Sedimentation Rate: 24 [0 - 20] MM/H; Leukocytes: 21.6 [4.5 - 11] 10^9/L; NPTST003- C-REACTIVE PROTEIN: 5.26 [NOT REPORTED - NOT REPORTED] mg/L; Neutrophils: 17.93 [2.4 - 7.56] 10^9/L; [redacted]20[redacted] (RX DAY 820): Albumin: 40 [34 - 49] G/L; Erythrocytes: 4.3 [4.2 - 5.6] 10^12/L; Hemoglobin: 132 [131 - 172] G/L; Leukocytes: 18.8 [4.5 - 11] 10^9/L; NPTST003- C-REACTIVE PROTEIN: 0.91 [NOT REPORTED - NOT REPORTED] mg/L; Neutrophils: 16.36 [2.4 - 7.56] 10^9/L; Platelets: 314 [150 - 400] 10^9/L; Protein: 63 [64 - 83] G/L

Microbiology

[redacted]20[redacted] (RX DAY 802): OTHER SMEAR FROM THE MUCOUS MEMBRANE OF THE MOUTH AND NOSE NPTST586-SARS-COV-2: Positive-CORRESPOND TO THE ESTABLISHED DIAGNOSIS - A NEW CORONAVIRUS INFECTION; [redacted]20[redacted] (RX DAY 804): OTHER SMEAR FROM THE MUCOUS MEMBRANE OF THE MOUTH AND NOSE NPTST586-SARS-COV-2: Negative-CORRESPOND TO THE ESTABLISHED DIAGNOSIS - A NEW CORONAVIRUS INFECTION; [redacted]20[redacted] (RX DAY 814): OTHER SMEAR FROM THE MUCOUS MEMBRANE OF THE MOUTH AND NOSE NPTST586-SARS-COV-2: Negative-CORRESPOND TO THE ESTABLISHED DIAGNOSIS - A NEW CORONAVIRUS INFECTION

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 808): CHEST COMPUTED TOMOGRAPHY: SIGNS OF BILATERAL POLYSEGMENTAL PNEUMONIA. THE PERCENTAGE OF LESIONS OF EACH LUNG 25-50%; [redacted]20[redacted] (RX DAY 813): CHEST COMPUTED TOMOGRAPHY: COMPARED WITH THE DATA FROM [redacted]/[redacted]/20[redacted]-COMPACTION OF PREVIOUSLY IDENTIFIED AREAS OF THE PARENCHYMA WITHOUT INCREASING THE VOLUME OF DAMAGE.; [redacted]20[redacted] (RX DAY 819): COMPUTED TOMOGRAPHY OF THE CHEST: COMPARED WITH THE DATA FROM [redacted]20[redacted], THE PICTURE CORRESPONDS TO THE REVERSE PROCESS.

AE Stopped Rx Day	821
Duration of AE	25 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ACUTE RESPIRATORY DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	BILATERAL POLYSEGMENTAL PNEUMONIA OF MODERATE SEVERE COURSE
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 797
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 805): Alanine Aminotransferase: 27 [NOT REPORTED - NOT REPORTED] U/L; Albumin: 47 [34 - 49] G/L; Aspartate Aminotransferase: 46 [NOT REPORTED - NOT REPORTED] U/L; Bilirubin: 2 [5 - 21] UMOL/L; Bilirubin: 8 [5 - 21] UMOL/L; Eosinophils: 0.01 [0 - 0.43] 10^9/L; Erythrocyte Sedimentation Rate: 40 [0 - 20] MM/H; Erythrocytes: 4 [4.2 - 5.6] 10^12/L; Hematocrit: 0.35 [0.39 - 0.5] FRACTION OF 1; Hemoglobin: 121 [131 - 172] G/L; Leukocytes: 3.5 [4.5 - 11] 10^9/L; Lymphocytes: 0.46 [0.96 - 4.75] 10^9/L; NPTST129-C-REACTIVE PROTEIN: 39.52 [NOT REPORTED - NOT REPORTED] mg/L; Neutrophils: 2.57 [2.4 - 7.56] 10^9/L; Platelets: 251 [150 - 400] 10^9/L; Protein: 72 [64 - 83] G/L; [redacted]20[redacted] (RX DAY 813): Alanine Aminotransferase: 63 [NOT REPORTED - NOT REPORTED] U/L; Aspartate Aminotransferase: 36 [NOT REPORTED - NOT REPORTED] U/L; Erythrocyte Sedimentation Rate: 24 [0 - 20] MM/H; Leukocytes: 21.6 [4.5 - 11] 10^9/L; NPTST003- C-REACTIVE PROTEIN: 5.26 [NOT REPORTED - NOT REPORTED] mg/L; Neutrophils: 17.93 [2.4 - 7.56] 10^9/L; [redacted]20[redacted] (RX DAY 820): Albumin: 40 [34 - 49] G/L; Erythrocytes: 4.3 [4.2 - 5.6] 10^12/L; Hemoglobin: 132 [131 - 172] G/L; Leukocytes: 18.8 [4.5 - 11] 10^9/L; NPTST003- C-REACTIVE PROTEIN: 0.91 [NOT REPORTED - NOT REPORTED] mg/L; Neutrophils: 16.36 [2.4 - 7.56] 10^9/L; Platelets: 314 [150 - 400] 10^9/L; Protein: 63 [64 - 83] G/L

Microbiology

[redacted]20[redacted] (RX DAY 802): OTHER SMEAR FROM THE MUCOUS MEMBRANE OF THE MOUTH AND NOSE NPTST586-SARS-COV-2: Positive-CORRESPOND TO THE ESTABLISHED DIAGNOSIS - A NEW CORONAVIRUS INFECTION; [redacted]20[redacted] (RX DAY 804): OTHER SMEAR FROM THE MUCOUS MEMBRANE OF THE MOUTH AND NOSE NPTST586-SARS-COV-2: Negative-CORRESPOND TO THE ESTABLISHED DIAGNOSIS - A NEW CORONAVIRUS INFECTION; [redacted]20[redacted] (RX DAY 814): OTHER SMEAR FROM THE MUCOUS MEMBRANE OF THE MOUTH AND NOSE NPTST586-SARS-COV-2: Negative-CORRESPOND TO THE ESTABLISHED DIAGNOSIS - A NEW CORONAVIRUS INFECTION

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 808): CHEST COMPUTED TOMOGRAPHY: SIGNS OF BILATERAL POLYSEGMENTAL PNEUMONIA. THE PERCENTAGE OF LESIONS OF EACH LUNG 25-50%; [redacted]20[redacted] (RX DAY 813): CHEST COMPUTED TOMOGRAPHY: COMPARED WITH THE DATA FROM [redacted]/[redacted]/20[redacted]-COMPACTION OF PREVIOUSLY IDENTIFIED AREAS OF THE PARENCHYMA WITHOUT INCREASING THE VOLUME OF DAMAGE.; [redacted]20[redacted] (RX DAY 819): COMPUTED TOMOGRAPHY OF THE CHEST: COMPARED WITH THE DATA FROM [redacted].20[redacted], THE PICTURE CORRESPONDS TO THE REVERSE PROCESS.

AE Stopped Rx Day	821
Duration of AE	25 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility

Investigator Alternative Etiology	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: M15-572

治験責任医師からの報告。本被験者はロシア連邦の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，新型コロナウイルス感染症及び両側の多区域肺炎（中等度から重度の経過）の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，喘息，局面型乾癬，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は新型コロナウイルス感染症及び両側の多区域肺炎（中等度から重度の経過）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，新型コロナウイルス感染症及び両側の多区域肺炎（中等度から重度の経過）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者に発熱，安静時の息切れ，喀痰を伴わない咳嗽，筋肉痛，全身脱力が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は検査に送られ，胸部 CT 検査で両側の多区域肺炎の徴候が認められた。被験者は SARS-COV-2 の検査を受け，陽性であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は最高 39°C の発熱，安静時の息切れ，喀痰を伴わない咳嗽，筋肉痛，全身脱力の状態が悪化したため入院した。入院時，被験者の体温は 37.2°C，呼吸数は 22 回／分，SPO2 は 93%であった。被験者は病院で基礎疾患に対する治療を受け，問題ない状態であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脱力が顕著に軽減し，体温が正常に戻り，呼吸不全の徴候は認められず，退院した。

投与された薬剤は，デキサメタゾン，euphyllin，asparkam，アベロックス，セフトリアキソン，ビタミン C，クレキサン，rebagit，seretid 及び inspirax であった。

The patient's past medications include:

METHIPRED for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SULFASALAZIN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ARAVA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

DICLOFENAC for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) COVID-19 (10084268) (COVID-19 (10084268)) [v.23.0] [10084268]

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) Bilateral pneumonia (10058686) (Pneumonia (10035664)) [v.23.0] [10058686]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 INFECTION

- Investigator: Acute respiratory disease.

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

Event of BILATERAL POLYSEGMENTAL PNEUMONIA OF MODERATE SEVERE COURSE

- Investigator: COVID-19

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 27 U/L

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 63 U/L

[redacted] **20[redacted] ALBUMIN:** 46.7 G/L

[redacted] **20[redacted] ALBUMIN:** 39.5 G/L

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 46 U/L

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 36 U/L

[redacted] **20[redacted] BILIRUBIN:** 2.1 umol/L

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 39.52 MG/L

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 5.26 MG/L

[redacted] **20[redacted] CHEST CT:** Signs of bilateral polysegmental pneumonia. The percentage of lesions of each lung 25-50%

[redacted] **20[redacted] CHEST CT:** Compared with the data from [redacted] 20[redacted]-compaction of previously identified areas of parenchyma without increasing the volume of damage.

[redacted] **20[redacted] CHEST CT:** Compared with the data from [redacted] 20[redacted], the picture corresponds to the reverse process.

[redacted] **20[redacted] CRP:** 0.91 MG/L

[redacted] **20[redacted] EOSINOPHILS ABS:** 0.01 X10**9/L

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 40 MM/HR

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 24 MM/HR

[redacted] **20[redacted] HEMATOCRIT:** 35.1 %

[redacted] **20[redacted] HEMOGLOBIN:** 121 G/L

[redacted] **20[redacted] HEMOGLOBIN:** 132 G/L

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 0.46 X10**9/L

[redacted] 20[redacted] **NEUTROPHILS ABS:** 2.57 X10**9/L

[redacted] 20[redacted] **NEUTROPHILS ABS:** 17.93 X10**9/L

[redacted] 20[redacted] **NEUTROPHILS ABS:** 16.36 X10**9/L

[redacted] 20[redacted] **PLATELET COUNT:** 251 X10**9/L

[redacted] 20[redacted] **PLATELET COUNT:** 314 X10**9/L

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.96 X10**12/L

[redacted] 20[redacted] **SARS-COV-2:** nasopharyngeal swab: Positive, correspond to the established diagnosis-a new coronavirus infection

[redacted] 20[redacted] **SARS-COV-2:** Smear from mouth and nose: Negative; Correspond to the established diagnosis - a new coronavirus infection

[redacted] 20[redacted] **SARS-COV-2:** Smear from mouth and nose: Negative; Correspond to the established diagnosis - a new coronavirus infection

[redacted] 20[redacted] **SARS-COV2:** Positive

[redacted] 20[redacted] **TOTAL BILIRUBIN:** 7.7 umol/L

[redacted] 20[redacted] **TOTAL PROTEIN:** 71.9 G/L

[redacted] 20[redacted] **TOTAL PROTEIN:** 63.1 G/L

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.48 X10**9/L

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 21.61 X10**9/L

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 18.77 X10**9/L

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 15 mg QD	4[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
PSORIATIC ARTHRITIS	20[redacted]

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] / 168	168
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 394	226
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 395		

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]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted]

PREDNISOLONE	5 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -228
NAPROXEN	550 mg	QD	Y-M: 20[redacted] / -83

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PREDNISOLONE	5 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -228	NOT REPORTED
NAPROXEN	550 mg	QD	Y-M: 20[redacted] / -83	NOT REPORTED
ENOXAPARIN	2000 IU	QD	Y-M: 20[redacted] / 176	Y-M: 20[redacted] / 209
HEPARIN	1000 IU	PRN	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 225

Event #1: Serious Adverse Event

Event Description	FRACTURE TIBIA-LEFT
Preferred term	脛骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 175
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 175): X-RAY: X-RAY SHOWS FRACTURE OF TIBIA; [redacted]20[redacted] (RX DAY 176): CT IMAGING OF KNEE: SHOWS MULTIFRAGMENT FRACTURE OF LATERAL PLATO OF TIBIA, FRACTURE LINE OF ANTERIOR EDGE TIBIA SHAFT AND MEDIAL SIDE OF TIBIA WITH MINIMAL DISLOCATION, FRACTURE LINE POSTERIOR SIDE OF FIBULA HEAD WITHOUT DISLOCATION.

AE Stopped Rx Day	274
Duration of AE	100 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DURING PLAYING VOLLEYBALL SUBJECT FELL AND BROKE HIS LEG.
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: M15-572

治験責任医師からの報告。本被験者はボスニア・ヘルツェゴビナの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左脛骨骨折の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左脛骨骨折を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左脛骨骨折は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はバレーボールをしていて転倒し，脚を骨折して入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for UPADACITINIB (Blinded)

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1) Tibia fracture (10043827) (Tibia fracture (10043827)) [v.22.1] [10043827]

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 FRACTURE TIBIA LEFT

- Investigator: DURING PLAYING VOLLEYBALL SUBJECT FELL AND BROKE HIS LEG.

- AbbVie: Event more likely related to fall while playing volleyball.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT IMAGING OF KNEE:** Shows multifragment fracture of lateral plato of tibia, fracture line of anterior edge tibia shaft and medial side of tibia with minimal dislocation, fracture line posterior side of fibula head without dislocation.

[redacted] **20[redacted] XRAY:** X-RAY shows fracture of tibia

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: POST-MENOPAUSAL	19[redacted]
HYPERTENSION	19[redacted]
TRANSIENT ISCHEMIC ATTACK	19[redacted]
ANGINA	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OSTEOPOROSIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: LATENT TB	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	30	
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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 141	141

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]
ISOSORBIDE MONONITRATE	20 mg	BID	Y-M: 20[redacted]

FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
NEBIVOLOL	5 mg	QD	Y-M: 20[redacted]
VITAMINS, OTHER COMBINATIONS	2 OTHER: TABLETS	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
ALFACALCIDOL	0.25 OTHER: MCG	BID	Y-M: 20[redacted] / -32
IBANDRONIC ACID	150 mg	OTHER: MONTHLY	Y-M: 20[redacted] / -32
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -19
PYRIDOXINE	25 mg	QD	Y-M: 20[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
ISOSORBIDE MONONITRATE	20 mg	BID	Y-M: 20[redacted]	ONGOING
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
NEBIVOLOL	5 mg	QD	Y-M: 20[redacted]	ONGOING
VITAMINS, OTHER COMBINATIONS	2 OTHER: TABLETS	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
ALFACALCIDOL	0.25 OTHER: MCG	BID	Y-M: 20[redacted] / -32	ONGOING
IBANDRONIC ACID	150 mg	OTHER: MONTHLY	Y-M: 20[redacted] / -32	ONGOING
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -19	ONGOING
PYRIDOXINE	25 mg	QD	Y-M: 20[redacted] / -19	ONGOING
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 140	Y-M: 20[redacted] / 147

Event #2: 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 OVARIAN CANCER

Preferred term 卵巣癌

AE Onset Date / Rx Day [redacted]20[redacted] / 145 (18 DAYS AFTER LAST TREATMENT)

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 148): NPTST135-CA-125: 239.8 [0 - 35] U/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 145): CT IMAGING OF ABDOMEN: MESENTERIAL CARCINOMATOSIS WITH LYMPHADENOPATHY AND PERITONEAL FREE-LIQUID-SUSPECTED NEOPLASTIC OVARIAN PROCESS;DILATED LEFT OVARIAN VEIN; [redacted]20[redacted] (RX DAY 149): ULTRASOUND: THE UTERUS 6X4 CM SWIMS IN THE ASCITES, ADNEXALLY SEEN TUMOR MASSES IMPOSE AS DISEMIN'S OVARIAN TUMOR.

AE Stopped Rx Day ONGOING

Duration of AE ONGOING

Severity Severe

Relation to Study Drug by Investigator No Reasonable Possibility

Investigator Alternative Etiology THERE ARE NO MEDICAL CONDITION IN MEDICAL HISTORY THAT ARE IN RELATIONSHIP WITH AE. SUBJECT DONE UNSCHEDULED CT SCAN WERE

SUSPECTED OVARIAN CANCER WAS FOUND AFTER IT WAS CONFIRMED BY GYNECOLOGIST.

Discontinued Study Drug Due to the Event YES

SAE Criteria OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はボスニア・ヘルツェゴビナの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，グレード 3 の卵巣癌の事象を発現した。

Event 2 の臨床経過：

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は卵巣癌を発現した。

被験者は肋骨下に痛みを感じ，体重減少を自覚した（日付不明）。CT スキャン検査と超音波検査で卵巣に腫瘍と腫瘍形成過程が認められた。被験者に癌の家族歴はなかった。

Causality for UPADACITINIB (Blinded)

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1) Ovarian cancer (10033128) (Ovarian cancer (10033128)) [v.22.1] [10033128]

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 OVARIAN CANCER

- Investigator: Other cause of the event are not known. The more likely cause of the event can not be provided because there are not any medical conditions in medical history that are in relationship with AE

- AbbVie: weak temporal association with only 5 months of study drug exposure. Additional risk factors include advanced age and subject's smoking status.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CA-125:** 239.8 U/ML (normal 0 to 35.0)

[redacted] **20[redacted] CT IMAGING OF ABDOMEN:** MESENTERIAL CARCINOMATOSIS WITH LYMPHADENOPATHY AND PERITONEAL FREE-LIQUID-suspected neoplastic ovarian process; DILATED LEFT Ovarian vein

[redacted] **20[redacted] ULTRASOUND:** The uterus 6x4 cm swims in the ascites, adnexally seen tumor masses impose as disemins ovarian tumor.

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)	20[redacted]
TUBERCULOSIS: LATENT TB	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	28	
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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 181	181
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 182	[redacted]20[redacted] / 392	211
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	5 mg	BID	Y-M: 20[redacted]
METHOTREXATE	2.5 mg	EVERY WEEK	Y-M: 20[redacted]

ISONIAZID	100 mg	BID	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
FOLIC ACID	5 mg	BID	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	2.5 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
NAPROXEN	550 mg	BID	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 156
DICLOFENAC	75 MG 3 ML OTHER: MG ML	QD	Y-M: 20[redacted] / 146	Y-M: 20[redacted] / 146
THIOCOLCHICOSIDE	4MG/2ML OTHER: MG/ML	QD	Y-M: 20[redacted] / 146	Y-M: 20[redacted] / 146
DICLOFENAC	50 g	QD	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149

Event #1: Serious Adverse Event

Event Description	JOINT PAIN
Preferred term	関節痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 143
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 143): Alanine Aminotransferase: 16 [0 - 35] U/L; Albumin: 40 [35 - 52] G/L; Alkaline Phosphatase: 71 [30 - 120] U/L; Aspartate Aminotransferase: 22 [0 - 35] U/L; Basophils: 0.106 [0 - 0.2] 10^9/L; Basophils/Leukocytes: 0.79 [0 - 2.5] %; Bilirubin: 4 [5 - 21] UMOL/L; Bilirubin: 3 [5 - 21] UMOL/L; Calcium: 2.2 [2.2 - 2.64] MMOL/L; Chloride: 105 [101 - 109] MMOL/L; Creatine Kinase: 97 [0 - 145] U/L; Creatinine: 52 [45 - 84] UMOL/L; Eosinophils: 0.181 [0 - 0.7] 10^9/L; Eosinophils/Leukocytes: 1.34 [0 - 7] %; Erythrocytes: 4.8 [4 - 6.1] 10^12/L; Hematocrit: 0.43 [0.38 - 0.54] FRACTION OF 1; Hemoglobin: 148 [122 - 181] G/L; Leukocytes: 13.5 [4.6 - 10.2] 10^9/L; Lymphocytes: 1.8 [0.6 - 3.4] 10^9/L; Lymphocytes/Leukocytes: 13.4 [10 - 50] %; Monocytes: 0.755 [0 - 0.99] 10^9/L; Monocytes/Leukocytes: 5.6 [0 - 12] %; NPTST587-SEDIMENTATION: 6 [NOT REPORTED - NOT REPORTED] HOURS; NPTST693-VITAMIN B12: 279 [187 - 883] G/DL; Neutrophils: 10.6 [2 - 6.9] 10^9/L; Neutrophils/Leukocytes: 78.9 [37 - 80] %; Platelets: 236 [142 - 424] 10^9/L; Potassium: 4.6 [3.5 - 5.1] MMOL/L; Protein: 62 [66 - 83] G/L; Sodium: 137 [136 - 146] MMOL/L; Urate: 214.14 [154.66 - 356.91] UMOL/L; pH: 6.5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	157
Duration of AE	15 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PATIENT HAS GENERAL JOINT PAIN DUE TO WORK-RELATED FATIGUE
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: M15-572

治験責任医師からの報告。本被験者はトルコの 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，関節痛の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，現喫煙者（1 日 1 箱を 28 年間）及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は関節痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，関節痛は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は関節痛（膝関節及び両側足関節）のため入院した。また被験者より，1 日 1 時間の朝のこわばり感も報告された。両側足関節に体温上昇が見られた。被験者は，これは被験者の職業によるものであると告げられた。関節痛に対する理学療法が開始され，痛みは軽減された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，keyrelaks，dikloron，diklojik 及び aprol であった。

Causality for UPADACITINIB (Blinded)

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1) Joint pain (10023222) (Arthralgia (10003239)) [v.22.1] [10023222]

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 JOINT PAIN

- Investigator: Patient has general joint pain due to work related fatigue

- AbbVie: Event is more likely related to nature of her job as noted by PI. Additional risk factor includes pre-existing psoriatic arthritis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **RBC:** 4.82 M/uL (normal 4.04 to 6.13)

[redacted] **SED RATE:** 6 /hr

[redacted] **WBC:** 13.5 K/uL (normal 4.60 to 10.20)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肛門膿瘍	X			X
痔瘻	X			

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

Medical History	Onset Year
OTHER: PSORIASIS VULGARIS	20[redacted]
OTHER: PSORIASIC UNGUIM	20[redacted]
OTHER: PSORIASIS VULGARIS GENITAL AREA	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 401	233
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 402		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -96

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
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted] / -96	Y-M: 20[redacted] / 413
IMIQUIMOD	1 OTHER: CENTIMETER	PRN	Y-M: 20[redacted] / 99	Y-M: 20[redacted] / 143
DEXPANTHENOL	1 OTHER: CENTIMETER	PRN	Y-M: 20[redacted] / 128	NOT REPORTED
VERRUMAL	1 APPLICATION OTHER: APPLICATION	TID	Y-M: 20[redacted] / 197	NOT REPORTED
DICLOFENAC	50 mg	TID	Y-M: 20[redacted] / 309	NOT REPORTED
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 309	NOT REPORTED
CEFUROXIME	1500 mg	QD	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 310
METRONIDAZOLE	500 mg	QD	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 310
PARACETAMOL	1 g	QD	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 310
PLANTAGO OVATA	1 OTHER: SPOON	QD	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 351

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

Event Description	PERIANAL ABSCESS
Preferred term	肛門膿瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 124
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 127): OTHER SKIN AND SUBCUTISEXCISAT NPTST349-HISTOPATHOLOGY: Negative-NO MALIGNANCY,CHRONIC ACTIVE AND ABSCESS FORMING INFLAMMATION

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 127): SURGICAL EVACUATION OF PERIANALABSCESS: RESOLVED

AE Stopped Rx Day	127
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ANAL FISSURA
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	ANAL FISTULA

Preferred term	痔瘻
AE Onset Date / Rx Day	[redacted]20[redacted] / 255
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 309): ELECTIVE ANALFISTULAECTOMIA: FISTULOTOMY	
AE Stopped Rx Day	309
Duration of AE	55 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ANAL FISTULA WAS REASON FOR ANAL FISTULECTOMIA (PI'S DECISION)
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Subject Number: 14241006

Protocol Number: M15-572

治験責任医師からの報告。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が投与され，肛門周囲膿瘍の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，尋常性乾癬，性器の尋常性乾癬，乾癬性関節炎，爪白癬，非喫煙者及び禁酒であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肛門周囲膿瘍を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肛門周囲膿瘍は消失した。

本事象発現前，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肛門周囲湿疹（非重篤）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 2 日間に及ぶ肛門周囲の痛み及び腫れのため入院した。同日，被験者は肛門周囲膿瘍と診断され，20[redacted] 年 [redacted] 月 [redacted] 日に外科的に切除された。治験責任医師によると，被験者には既存の性器の尋常性乾癬があった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。

投与された薬剤は，dafalgan，metamucil，ボルタレン，bepanthen クリーム及び novalgin であった。

Causality for UPADACITINIB (Blinded)

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1) Perianal abscess (10034447) (Anal abscess (10048946)) [v.22.1] [10034447]

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 PERIANAL ABSCESS

- Investigator: Anal fissure

- AbbVie: Risk factors includes recent perianal eczema and pre-existing psoriasis vulgaris on the genital area.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] 20[redacted] **HISTOPATHOLOGY:** Negative. No malignancy, chronic active and abscess forming inflammation
Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。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が投与され，痔瘻の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，尋常性乾癬，爪白癬，性器の尋常性乾癬，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は痔瘻を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，痔瘻は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は裂肛（非重篤）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者には肛門周囲膿瘍の括約筋貫通痔瘻のためシートン法によりひもが挿入された。その間，被験者はコンジローマ（非重篤）の治療を受け続けていた。数ヵ月間コンジローマのない状態の場合，瘻孔修復の施行が指示された。

また，被験者は以前に肛門周囲膿瘍を発現しており，20[redacted] 年 [redacted] 月 [redacted] 日，AER 19P-151-2824501-00 で報告されている。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は表在性の痔瘻に対しシートン法によりひもを留置するための待機的手術のため入院した。徴候及び症状として痔瘻及び既治療のコンジローマがあった。被験者の全身状態は良好で，肛門周囲出血の傾向は認められなかった。難なく排便可能であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，cefuroxim，アセトアミノフェン，metamucil，ボルタレン及び metronidazol であった。

The patient's past medications include:

PARACETAMOL for MIGRAINE HEADACHE ([redacted] 20[redacted] - [redacted] 20[redacted])

DAFALGAN for PERIANAL ABSCESS ([redacted] 20[redacted] - [redacted] 20[redacted])

LAXOBERON for PROPHYLAXIS CONSTIPATION ([redacted] 20[redacted] - [redacted] 20[redacted])

METAMUCIL for PERIANAL ABSCESS ([redacted] 20[redacted] - [redacted] 20[redacted])

NOVALGIN for PERIANAL ABSCESS ([redacted] 20[redacted] - [redacted] 20[redacted])

PANTOZOL for PROPHYLAXIS GASTRIC ULCER ([redacted] 20[redacted] - [redacted] 20[redacted])

VOLTAREN for PERIANAL ABSCESS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Anal fistula (10002156) (Anal fistula (10002156)) [v.23.0] [10002156]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of ANAL FISTULA

- Investigator: anal Fistula was reason for anal fistulectomia (PIs decision)

- AbbVie: event is not consistent with study drug's mechanism of action. Additional risk factor includes pre-existing anal fistula from [redacted] 20[redacted] .

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
半月板損傷	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: PENICILLIN ALLERGY	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: POSTMENOPAUSE	19[redacted]
HYPOTHYROIDISM	20[redacted]
OTHER: VARICOSE VEINS OF THE LOWER LIMBS	20[redacted]
OTHER: DEGENERATIVE CHANGES OF THE SPINE L-S	20[redacted]
HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: SPURS OF BOTH CALCANEUS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: NEUROSURGICAL INTERPROVINCIAL STABILIZATION	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	22	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VALSARTAN	80 mg	QD	Y-M: 20[redacted]
LEVOTHYROXINE	100 mg	QD	Y-M: 20[redacted]
PHLEBODRIL	1 OTHER: TABLET	TID	Y-M: 20[redacted]
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -282
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -282
CHONDROITIN	400 mg	QD	Y-M: 20[redacted] / -56
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -56
PHOSPHOLIPIDS	300 mg	TID	Y-M: 20[redacted] / -56

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
VALSARTAN	80 mg	QD	Y-M: 20[redacted]	NOT REPORTED
LEVOTHYROXINE	100 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PHLEBODRIL	1 OTHER: TABLET	TID	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -282	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -282	NOT REPORTED
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -56	NOT REPORTED
PHOSPHOLIPIDS	300 mg	TID	Y-M: 20[redacted] / -56	NOT REPORTED
DALTEPARIN	5000 OTHER: UNITS	QD	Y-M: 20[redacted] / 456	Y-M: 20[redacted] / 486

Event #1: Serious Adverse Event

Event Description	RIGHT MENISCUS KNEE JOINT DAMAGE
Preferred term	半月板損傷
AE Onset Date / Rx Day	[redacted]20[redacted] / 455
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 455): KNEE ARTHROSCOPY: ARTHROSCOPY WAS DONE WITHOUT COMPLICATIONS

AE Stopped Rx Day	456
Duration of AE	2 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	OLD INJURY OF RIGHT MENISCUS KNEE JOINT
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: M15-572

治験責任医師からの報告。本被験者はポーランドの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右膝関節半月板損傷の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，ペニシリンアレルギー，局面型乾癬，元喫煙者（1 日 1 箱を 22 年間），下肢静脈瘤，脊椎 L-S の退行性変化，高血圧，乾癬性関節炎，両踵骨の距状突起及び飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右膝関節半月板損傷を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右膝関節半月板損傷は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は外科的治療のため入院した。被験者は右膝の外側半月板に水平方向の損傷を受けており，外側腓骨コンパートメント（LTC）軟骨組織に 4 度の限局性病変が見られた。同日，被験者は右膝の関節鏡手術（半月板の修復及び Hyalofast 膜の留置）を受け，術後合併症は見られなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。右膝に固定装具を装着，松葉杖を使用し 2 週間は歩行が制限された。

投与された薬剤は，フラグミンであった。

The patient's past medications include:

PENICILLIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Meniscus tear of knee (10027291) (Meniscus injury (10072970)) [v.23.0] [10027291]

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 RIGHT MENISCUS KNEE JOINT DAMAGE

- Investigator: Old injury of right meniscus knee joint.

- AbbVie: Risk factors include old injury of right meniscus knee joint as noted by PI and advanced age.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20**[redacted] **WEIGHT:** 78 KG

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: POSTMENOPAUSE	20[redacted]
OTHER: SINUS TACHYCARDIA	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 167	167
ADA	40MG	SC	EOW	[redacted]20[redacted] / 168	[redacted]20[redacted] / 392	225
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted]

METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted]
NEBIVOLOL	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
PHOSPHOLIPIDS	300 mg	TID	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED
NEBIVOLOL	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
PHOSPHOLIPIDS	300 mg	TID	Y-M: 20[redacted]	NOT REPORTED
IBANDRONIC ACID	150 mg	OTHER: ONCE A MONTH	Y-M: 20[redacted] / 146	Y-M: 20[redacted] / 400
ATROPINE	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 303
MIDAZOLAM	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 303
MORPHINE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 303
PARACETAMOL	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 303
AMOXICILLIN	1 g	BID	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 306
NIMESULIDE	100 mg	BID	Y-M: 20[redacted] / 304	Y-M: 20[redacted] / 307

Event #1: Serious Adverse Event

Event Description	HYPERTROPHY OF TONSILS
Preferred term	扁桃肥大
AE Onset Date / Rx Day	[redacted]20[redacted] / 303
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 303): Eosinophils: 0.51 [0.05 - 0.5] 10^9/L; Leukocytes: 11.4 [4 - 10.5] 10^9/L; Lymphocytes: 3.4 [0.9 - 2.9] 10^9/L; Monocytes: 1.1 [0.3 - 0.9] 10^9/L; NPTST072-APTT(ACTIVATED PARTIAL THROMBO: 36.1 [24 - 35] SEC

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 304): BILATERAL TONSILLECTOMY: HYPERTROPHY OF TONSILLS RESOLVED

AE Stopped Rx Day	304
Duration of AE	2 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INFLAMMATION OF TONSILS

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: M15-572

治験責任医師からの報告。本被験者はポーランドの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，扁桃肥大の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は扁桃肥大を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，扁桃肥大は消失した。

本事象発現前，20[redacted] 年 [redacted] 月，被験者は扁桃肥大（非重篤）の発現を来たした。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両側扁桃摘出術を受けた。術後経過において合併症は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な全身状態で退院した。

投与された薬剤は，モルヒネ，nimesil，midanium，klacid，アトロピン，アセトアミノフェン及び amotaks であった。

Causality for UPADACITINIB (Blinded)

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1) Tonsillar hypertrophy (10044003) (Tonsillar hypertrophy (10044003)) [v.23.0] [10044003]

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 HYPERTROPHY OF TONSILS

- Investigator: Inflammation of tonsils

- AbbVie: Event not consistent with study drug's mechanism of action.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ACTIVATED PARTIAL THROMBOPLASTIN TIME:** 36.1 SEC (normal 24 to 35)

[redacted] **EOSINOPHILS:** 0.51 X10**3/MCL (normal 0.05 to 0.5)

[redacted] **LYMPHOCYTES:** 3.4 X10**3/MCL (normal 0.9 to 2.9)

[redacted] **MONOCYTES:** 1.1 X10**3/MCL (normal 0.3 to 0.9)

[redacted] **WBC:** 11.4 X10**3/MCL (normal 4 to 10.5)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: HEPATITIS A	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: DEGENERATIVE DISCOPATHIC DISEASE OF THE SPINE	20[redacted]
OTHER: FIBROIDS	20[redacted]
OTHER: POSTMENOPAUSAL	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
HYPERTENSION	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CHEILEKTOMIA THE FIRST FINGER OF THE RIGHT FOOT	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	10 PACK	38	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ADA	40MG	SC	EOW	[redacted]20[redacted] / 170	[redacted]20[redacted] / 393	224
ADA	40MG	SC	EOW	[redacted]20[redacted] / 394		

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]
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted]
TRAMADOL	50 mg	OTHER: QD-BID	Y-M: 20[redacted]
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
COLECALCIFEROL	300 IU	QD	Y-M: 20[redacted]
TELMISARTAN	40 mg	QD	Y-M: 20[redacted] / -60

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 182
TRAMADOL	50 mg	OTHER: QD-BID	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	300 IU	QD	Y-M: 20[redacted]	NOT REPORTED
TELMISARTAN	40 mg	QD	Y-M: 20[redacted] / -60	NOT REPORTED
BACLOFEN	25 mg	QD	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 178

Event #1: Serious Adverse Event

Event Description DUODENAL MUCOSITIS

Preferred term 小腸炎

AE Onset Date / Rx Day [redacted]20[redacted] / 179

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 149): NPTST071-APTT: 35.7 [28.4 - 42.8] SEC; [redacted]20[redacted] (RX DAY 179): Basophils/Leukocytes: 0.3 [0.1 - 1.2] %; Chloride: 110 [98 - 107] MMOL/L; Creatinine: 73 [49 - 90] UMOL/L; Eosinophils/Leukocytes: 0.9 [0.7 - 5.8] %; Hematocrit: 0.36 [0.34 - 0.45] FRACTION OF 1; Hemoglobin: 119 [112 - 157] G/L; Lymphocytes/Leukocytes: 41.6 [19.3 - 51.7] %; Monocytes/Leukocytes: 8.9 [4.7 - 12.5] %; NPTST093-BASOPHILIS: 0.02 [0.01 - 0.08] 10^3/UL; NPTST209-CRP: 0.80 [NOT REPORTED - 5] mg/L; NPTST242-EGFR: >60 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST247-EOSINOPHILIS: 0.06 [0.04 - 0.36] 10^3/UL; NPTST253-ERYTHROCYTE: 3.78 [3.93 - 5.22] 10^6/UL; NPTST410-LEUKOCYTES: 6.37 [3.98 - 10.04] 10^3/UL; NPTST419-LYMPHOCYTES: 2.65 [1.18 - 3.74] 10^3/UL; NPTST427-MCH: 31.5 [25.6 - 32.2] PG; NPTST428-MCHC: 32.8 [32.2 - 35.5] G/DL; NPTST429-MCV: 96 [79.4 - 94.8] FL; NPTST454-MPV: 11.7 [9.4 - 12.6] FL; NPTST469-NEUTROCYTY: 3.07 [1.56 - 6.13] 10^3/UL; NPTST491-P-LCR: 39.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST506-PCT: 0.2 [0.16 - 0.38] %; NPTST507-PDW: 14.1 [9.8 - 16.2] FL; NPTST536-PROTHROMBIN INDEX: 105 [80 - 120] %; NPTST563-RDW-CV: 13.5 [11.6 - 14.4] %; NPTST662-UREA: 30 [10 - 45] MG/DL; Neutrophils/Leukocytes: 48.3 [34 - 71.1] %; Platelets: 174 [182 - 369] 10^9/L; Potassium: 4 [3.5 - 4.1] MMOL/L; Prothrombin Intl. Normalized Ratio: 0.95 [0.8 - 1.3] UNIT NOT REPORTED; Sodium: 148 [135 - 148] MMOL/L; [redacted]20[redacted] (RX DAY 210): NPTST452-MONOCYTES: 0.57 [0.24 - 0.76] 10^3/UL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 180): ENDOSCOPY: FINDINGS CHARACTERISTIC FOR DUODENAL MUCOSITIS.

AE Stopped Rx Day 182

Duration of AE 4 DAYS

Severity Severe

Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	UNKNOWN
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: M15-572

治験責任医師からの報告。本被験者はポーランドの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，十二指腸粘膜炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，胃食道逆流性疾患，変形性脊椎椎間板症，閉経後，乾癬性関節炎，高血圧，喫煙者（1 日に 10 本を 38 年間）及び現飲酒者（2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は十二指腸粘膜炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，十二指腸粘膜炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃痛（心窩部）及び脊椎痛のため入院した。診断検査で十二指腸粘膜炎と一致する結果が得られた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。

投与された薬剤は ospamox，metronidazol 及び controloc であった。

Causality for UPADACITINIB (Blinded)

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1) Small intestinal mucositis (10065710) (Enteritis (10014866)) [v.22.1] [10065710]

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 DUODENAL MUCOSITIS

- Investigator: Unknown

- AbbVie: Risk factors include active smoking status and concomitant therapy with methotrexate.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BASOPHILS:** 0.02 X10**3/MCL (normal 0.01 to 0.08)

[redacted] **BASOPHILS:** 0.3 % (normal 0.1 to 1.2)

[redacted] **CHLORIDE:** 110 MMOL/L (normal 98 to 107)

[redacted] **CREATININE:** 0.83 mg/dL (normal 0.55 to 1.02)

[redacted] **CRP:** 0.80 MG/L (normal 5.0)

[redacted] **EGFR:** 60 >

[redacted] **ENDOSCOPY:** Findings characteristic for duodenal mucositis.

[redacted] **EOSINOPHILS:** 0.06 X10**3/MCL (normal 0.04 to 0.36)

[redacted] **EOSINOPHILS:** 0.9 % (normal 0.7 to 5.8)

[redacted] **ERYTHROCYTES:** 3.78 X10**6/MCL (normal 3.93 to 5.22)

[redacted] **HEMATOCRIT:** 36.3 % (normal 34.1 to 44.9)

[redacted] **INR:** 0.95 (no units) (normal 0.8 to 1.3)

[redacted] **MCHC:** 32.8 G/DL (normal 32.2 to 35.5)

[redacted] **MCV:** 96.0 FL (normal 79.4 to 94.8)

[redacted] **20[redacted] PLATELET LARGE CELL RATIO:** 39.0 (no units)

[redacted] **20[redacted] PLATELETS:** 174 X10**3/MCL (normal 182 to 369)

[redacted] **20[redacted] POTASSIUM:** 4.0 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] SODIUM:** 148.0 MMOL/L (normal 135 to 148)

[redacted] **20[redacted] WEIGHT:** 75.1 KG

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 15 mg QD	2[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: ADENOIDECTOMY	19[redacted]
SURGERY: AMPUTATION OF THE DISTAL PHALANX OF THE LEFT THUMB	20[redacted]
SURGERY: BONE RECONSTRUCTION OF THE DISTAL PHALANX OF THE LEFT THUMB	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 394	225
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 395		

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]
DICLOFENAC	150 mg	QD	Y-M: 20[redacted]
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted] / -220
SHARK-LIVER OIL	570 mg	BID	Y-M: 20[redacted] / -220
DICLOFENAC	75 mg	BID	Y-M: 20[redacted] / -201
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -201
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -201

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
SHARK-LIVER OIL	570 mg	BID	Y-M: 20[redacted] / -220	ONGOING
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted] / -220	Y-M: 20[redacted] / 58
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -201	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -201	ONGOING
COLECALCIFEROL	28 OTHER: DROPS	EVERY WEEK	Y-M: 20[redacted] / 59	ONGOING
ULTRACET	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 73
DURAPATITE	830 mg	BID	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 112

Event #1: Serious Adverse Event

Event Description FRACTURE OF THE BONE RECONSTRUCTION OF THE DISTAL PHALANX OF THE LEFT THUMB

Preferred term 手骨折

AE Onset Date / Rx Day [redacted]20[redacted] / 58

Age at AE Onset 2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 57): XRAY: DETECTION OF FRACTURE OF THE REGENERATE IN THE AMPUTATED THUMB OF THE LEFT HAND; [redacted]20[redacted] (RX DAY 59): CLOSE REDUCTION-INTERNAL FIXATION PROCEDURE: NO COMPLICATIONS; XRAY: SETTING OF FRAGMENTS AND IMPLANTS CORRECT

AE Stopped Rx Day 59

Duration of AE 2 DAYS

Severity Severe

Relation to Study Drug by Investigator No Reasonable Possibility

Investigator Alternative Etiology UNKNOWN

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: M15-572

治験責任医師からの報告。本被験者はポーランドの 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が投与され，左母指末節骨の骨再建部位の骨折の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，左母指末節骨の切断，左母指末節骨の骨再建，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左母指末節骨の骨再建部位の骨折を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左母指末節骨の骨再建部位の骨折は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は骨折の整復及び安定化のため入院した。この骨折は無症候性で，整形外科の経過観察で偶発的に発見されたものであった。20[redacted] 年 [redacted] 月 [redacted] 日，CRIF（徒手整復内部固定術），X 線検査及びキルシュナー鋼線によるフラグメント固定が行われた。入院中に合併症は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。

投与された薬剤は，poltram combo，devikap 及び osteogenon であった。

The patient's past medications include:

OLFEN for PSORIATIC ARTHRITIS (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Fractured thumb (10017313) (Hand fracture (10019114)) [v.22.1] [10017313]

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 FRACTURE OF THE BONE RECONSTRUCTION OF THE DISTAL PHALANX OF THE LEFT THUMB

- Investigator: Unknown

- AbbVie: Event more likely related to past history of amputation of the distal phalanx of the left thumb and bone reconstruction of the distal phalanx of the left thumb.

Relevant Laboratory & Other Diagnostic Tests

Unknown date CHEST X RAY: Normal and Absent

[redacted] **X-RAY:** Setting of fragments and implants correct.

[redacted] **XRAY:** At least One (1) erosion on the hands and feet

[redacted] **XRAY:** DETECTION OF FRACTURE OF THE REGENERATE IN THE AMPUTATED THUMB OF THE LEFT HAND

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: RIGHT ELBOW INJURY	19[redacted]
ASTHMA	19
OTHER: EPILEPSY	19
OTHER: PLAQUE PSORIASIS	19
DRUG ALLERGIES/REACTIONS: AMINOFILIN	19
OTHER: HBV INFECTION	19
HYPERLIPIDEMIA: EXCEEDED LEVELS OF TRIGLYCERIDES AND CHOLESTEROL	20
PARKINSON'S DISEASE	20
OTHER: DEGENERATIVE DISEASE OF THE SPINE	20
OTHER: OVERWEIGHT	20
BENIGN PROSTATIC HYPERPLASIA	20
OTHER: SLEEP DISORDERS	20
OTHER: CONDITION AFTER REMOVAL OF THE GALLBLADDER	20
PSORIATIC ARTHRITIS	20
LIVER DISEASE (EXCLUDING HEPATITIS): DRUG-INDUCED LIVER DAMAGE	20
OSTEOPOROSIS	20

Prior Procedures	Procedure Year
INCREASED CREATINE PHOSPHOKINASE: FRACTIONATED LAB TEST	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	10	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted] / 1	[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted] / 169	[redacted] / 391	223
ABT-494	30 MG	ORAL	QD	[redacted] / 392		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	200 ug	BID	Y-M: 19[redacted]
FENOTEROL	100 ug	PRN	Y-M: 19[redacted]
FORMOTEROL	12 ug	QD	Y-M: 19[redacted]
AMINOPHYLLINE	200 mg	QD	Y-M: 19[redacted]
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]
MADOPAR	125 mg	TID	Y-M: 20[redacted]
DOXAZOSIN	4 mg	QD	Y-M: 20[redacted]
FINASTERIDE	5 mg	QD	Y-M: 20[redacted]
MIANSERIN	30 mg	QD	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
KETOPROFEN	100 mg	PRN	Y-M: 20[redacted]
NAPROXEN	500 mg	PRN	Y-M: 20[redacted]
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted]
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted]
CALCIUM CARBONATE	500 mg	QD	Y-M: 20[redacted]
COLECALCIFEROL	2000 IU	BID	Y-M: 20[redacted]
IBANDRONIC ACID	150 mg	OTHER: EVERY MONTH	Y-M: 20[redacted]
ULTRACET	362.5 mg	BID	Y-M: 20[redacted]
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted] / -341
CICLOSPORIN	100 mg	BID	Y-M: 20[redacted] / -311
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted] / -250
METHYLPREDNISOLONE	4 mg	QD	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
BUDESONIDE	200 ug	BID	Y-M: 19[redacted]	NOT REPORTED

FENOTEROL	100 ug	PRN	Y-M: 19[redacted]	NOT REPORTED
FORMOTEROL	12 ug	QD	Y-M: 19[redacted]	NOT REPORTED
AMINOPHYLLINE	200 mg	QD	Y-M: 19[redacted]	NOT REPORTED
MADOPAR	125 mg	TID	Y-M: 20[redacted]	NOT REPORTED
FINASTERIDE	5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 260
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted]	NOT REPORTED
CALCIUM CARBONATE	500 mg	QD	Y-M: 20[redacted]	NOT REPORTED
IBANDRONIC ACID	150 mg	OTHER: EVERY MONTH	Y-M: 20[redacted]	NOT REPORTED
ULTRACET	362.5 mg	BID	Y-M: 20[redacted]	NOT REPORTED
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted] / -341	NOT REPORTED
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted] / -250	NOT REPORTED
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -97	NOT REPORTED
CIPROFIBRATE	160 mg	QD	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 260
PIRACETAM	800 mg	BID	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 260
DIOSMIN	500 mg	BID	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 260
PHLEBODRIL	150 mg	BID	Y-M: 20[redacted] / 245	Y-M: 20[redacted] / 260
ACETYLSALICYLIC ACID	75 mg	QD	Y-M: 20[redacted] / 260	NOT REPORTED
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted] / 260	NOT REPORTED
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 260	NOT REPORTED
SPIRONOLACTONE	25 mg	QD	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 286
RAMIPRIL	2.5 mg	QD	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 287
DILTIAZEM	60 mg	BID	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 362
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 785
SPIRONOLACTONE	12.5 mg	QD	Y-M: 20[redacted] / 287	Y-M: 20[redacted] / 362
RAMIPRIL	1.25 mg	QD	Y-M: 20[redacted] / 288	NOT REPORTED
DUTASTERIDE	0.5 mg	QD	Y-M: 20[redacted] / 358	Y-M: 20[redacted] / 863

OTHER DRUGS USED IN BENIGN PROSTATIC HYPERTRO	240+150+120+30+0,001+1,4+6+10 +0,0035 mg	QD	Y-M: 20[redacted] / 358	Y-M: 20[redacted] / 863
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / 358	Y-M: 20[redacted] / 863
DILTIAZEM	30 mg	BID	Y-M: 20[redacted] / 362	NOT REPORTED

Event #1: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description	MYOCARDIAL INFARCTION
Preferred term	心筋梗塞
AE Onset Date / Rx Day	[redacted]20[redacted] / 260
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 260): CAROTID ULTRASOUND: ATHEROSCLEROTIC PLAQUES DO NOT CAUSE ACCELERATION OF FLOW VELOCITY; ECHOCARDIOGRAPHY: LVEF 50%,HYPOKINESIS

AE Stopped Rx Day	264
Duration of AE	5 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	THE FIRST MANIFESTATION OF CORONARY HEART DISEASE
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: M15-572

治験責任医師からの報告。本被験者はポーランドの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，心筋梗塞の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，高脂血症（トリグリセリド及びコレステロールの増加），元紙巻タバコ喫煙者（1 日 1 箱を 10 年間），過体重，睡眠障害，兄弟が 6[redacted] 歳時の心筋梗塞による死亡並びに母親の動脈性高血圧であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は心筋梗塞を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，心筋梗塞は消失した。

被験者は [redacted] 月より，疲労及び運動誘発性呼吸困難の増大（約 100 m 歩行後）並びに下腿浮腫の症状を訴えていた。被験者は，これらの症状は，呼吸器科医の指示で抗浮腫薬ステロイドを中止したことと関係していると考えていた。呼吸困難は吸入薬投与後に治まった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は胸痛で救急治療室や救急医療センターを受診するようなことはなかった。しかしながら，本事象の発現前 24 時間以内に狭心症又はそれに相当する症状が出現した。これらの症状の持続時間は，1 時間未満 5 分超であった。被験者は，左冠動脈回旋枝の一次血管形成術と，有糸分裂阻害剤コーティングステント 2 本の植え込みによる治療を受けた。退院時の心エコー検査所見は，LVER 50%及び下壁運動低下であった。頚動脈の超音波検査で壁周囲にアテローム動脈硬化性プラークが認められたが，血流量への影響はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，atoris，tritace，ipp，acard，dilzem，spironol 及びプラビックスであった。

The patient's past medications include:

AMINOFILIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Myocardial infarction (10028596) (Myocardial infarction (10028596)) [v.22.1] [10028596]

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 MYOCARDIAL INFARCTION

- Investigator: The first manifestation of coronary heart disease.

- AbbVie: Risk factors include pre-existing plaque psoriasis, hyperlipidemia and obesity BMI(30.8).

Relevant Laboratory & Other Diagnostic Tests

Unknown date BLOOD PRESSURE: 106/70 mmHg

[redacted] **20[redacted] CAROTID ULTRASOUND:** Paramural atherosclerotic plaques without acceleration of flow velocity

[redacted] **20[redacted] ECG:** Sinus rhythm, regular, of 64/min. Intermediate heart axis. PQ 180 ms. QTc 410 ms. Q wave in III, q in aVF, inverted T wave in III, and flat T wave in aVF.

[redacted] **20[redacted] ECHOCARDIOGRAPHY:** LVEF 50%,hypokinesis of the inferior wall

[redacted] **20[redacted] ECHOCARDIOGRAPHY:** The heart chambers are of normal size. The intraventricular septal wall is slightly thickened. The size of the aorta is normal. Left ventricular global contractility is normal, slight hypokinesis of the basal and mid segments of the lateral wall has been observed. The left ventricular diastolic function is normal. No significant regurgitation found in the valves, and gradients are normal. No thrombi in the cardiac chambers, or pericardial fluid observed. The risk of pulmonary hypertension is low. Visibility of the examined structures is quite good.

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	4[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
PSORIATIC ARTHRITIS	20[redacted]
HYPERTENSION	20[redacted]
OTHER: LEFT LOWERLEG VARICOSE VEINS	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

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-M: 20[redacted]
ACECLOFENAC	100 mg	QD	Y-M: 20[redacted]

MODURETIC	1 OTHER: TABLET	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
RAMIPRIL	5 mg	QD	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -297
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -297

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
ACECLOFENAC	100 mg	QD	Y-M: 20[redacted]	NOT REPORTED
MODURETIC	1 OTHER: TABLET	QD	Y-M: 20[redacted]	NOT REPORTED
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED
RAMIPRIL	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	15 mg	EVERY WEEK	Y-M: 20[redacted] / -297	NOT REPORTED
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -297	NOT REPORTED
AUGMENTIN	UNKNOWN OTHER: UNKNOWN	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 141
CHLORAMPHENICOL	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 141
ENOXAPARIN	UNKNOWN OTHER: UNKOWN	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 141
METAMIZOLE	1 OTHER: AMPULE	PRN	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 141
METRONIDAZOLE	UNKNOWN OTHER: UNKNOWN	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 141
OCTENISEPT	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 141
RANITIDINE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 141
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 146

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

Event Description	RIGHT LOWER LEG ERYSIPELAS
Preferred term	丹毒
AE Onset Date / Rx Day	[redacted]20[redacted] / 134
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 134): Alanine Aminotransferase: 41 [NOT REPORTED - 41] U/L; Eosinophils/Leukocytes: 0.2 [1 - 7] %; Glucose: 6.7 [3.3 - 5.5] MMOL/L; Leukocytes: 12.3 [4 - 11] 10^9/L; Lymphocytes/Leukocytes: 9.1 [25 - 40] %; Monocytes: 1.02 [0 - 1] 10^9/L; NPTST129-C-REACTIVE PROTEIN: 38 [NOT REPORTED - 5] mg/L; NPTST372-IMMATURE GRANULOCYTE ABS: 0.05 [0.01 - 0.03] 10^3/UL; NPTST537-PROTHROMBIN TIME: 12.6 [9.2 - 12.2] SEC; Neutrophils: 10.05 [1.9 - 7.5] 10^9/L; Neutrophils/Leukocytes: 81.8 [50 - 70] %; [redacted]20[redacted] (RX DAY 135): Alanine

Aminotransferase: 62 [0 - 41] U/L; Aspartate Aminotransferase: 42 [0 - 40] U/L; Eosinophils: 0.06 [0.03 - 0.44] 10^9/L; Glucose: 6.2 [4.1 - 5.9] MMOL/L; Leukocytes: 8.6 [4 - 10] 10^9/L; NPTST410-LEUKOCYTES: PRESENT [NOT REPORTED - NOT REPORTED] N/A; NPTST568-RED BLOOD CELL DISTRIBUTION WID: 48.3 [35.1 - 43.9] FL; [redacted]20[redacted] (RX DAY 140): NPTST568-RED BLOOD CELL DISTRIBUTION WID: 47.2 [35.1 - 43.9] FL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 134): HEAD COMPUTED TOMOGRAPHY: NORMAL

AE Stopped Rx Day	146
Duration of AE	13 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はポーランドの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右下肢の丹毒の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，高血圧，元紙巻タバコ喫煙者（1 日 1 箱を 20 年間），左下肢の静脈瘤及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年[redacted] 月[redacted] 日であった。

20[redacted] 年[redacted] 月[redacted] 日，被験者は右下肢の丹毒を発現した。20[redacted] 年[redacted] 月[redacted] 日，右下肢の丹毒は消失した。

20[redacted] 年[redacted] 月[redacted] 日，被験者は右下肢の疼痛及び発赤のため入院した。体温上昇，全身脱力及び失神も認められた。頭部コンピュータ断層撮影（CT）検査が行われたが，中枢神経系の変化は見られなかった。院内治療後，被験者の状態は改善した。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，20 週時来院の際，治験責任医師は，創傷は完全治癒したと判断した。

投与された薬剤は，pyralgin，octanisept，detromycyna，ranigast，クレキサン，メトロニダゾール，amoksiklav 及びドキシサイクリンであった。

The patient's past medications include:

APREMILAST for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Erysipelas (10015145) (Erysipelas (10015145)) [v.21.0] [10015145]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of RIGHT LOWER LEG ERYSIPELAS

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ALANINE AMINO TRANSFERASE:** 41 U/L (normal 0 to 41)

[redacted] 20[redacted] **ALANINE AMINO TRANSFERASE:** 62 U/L (normal 0 to 41)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 42 U/L (normal 0 to 40)

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 38 mg/dL (normal 0 to 5)

[redacted] 20[redacted] **EOSINOPHILS:** 0.2 % (normal 1.0 to 7.0)

[redacted] 20[redacted] **EOSINOPHILS ABSOLUTE:** 0.06 X10**3/MCL (normal 0.03 to 0.44)

[redacted] 20[redacted] **GLUCOSE:** 121 mg/dL (normal 60 to 99)

[redacted] 20[redacted] **GLUCOSE:** 111 mg/dL (normal 74 to 106)

[redacted] 20[redacted] **HEAD COMPUTED TOMOGRAPHY:** NORMAL

[redacted] 20[redacted] **IMMATURE GRANULOCYTE ABSOLUTE:** 0.05 X10**3/MCL (normal 0.01 to 0.03)

[redacted] 20[redacted] **LYMPHOCYTES:** 9.1 % (normal 25 to 40)

[redacted] 20[redacted] **MONOCYTES ABSOLUTE:** 1.02 X10**3/MCL (normal 0.00 to 1.00)

[redacted] 20[redacted] **NEUTROPHILS:** 81.8 % (normal 50.0 to 70.0)

[redacted] 20[redacted] **NEUTROPHILS ABSOLUTE:** 10.05 X10**3/MCL (normal 1.9 to 7.5)

[redacted] 20[redacted] **PROTHROMBIN TIME:** 12.6 SEC (normal 9.2 to 12.2)

[redacted] 20[redacted] **RED BLOOD CELL DISTRIBUTION WIDTH:** 48.3 FL (normal 35.1 to 43.9)

[redacted] 20[redacted] **RED BLOOD CELL DISTRIBUTION WIDTH:** 47.2 FL (normal 35.1 to 43.9)

[redacted] 20[redacted] **URINE LEUKOCYTES:** PRESENT

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 12.29 X10**3/MCL (normal 4 to 11)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 8.56 X10**3/MCL (normal 4.00 to 10.0)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
脳血管発作	X			X

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
HYPERTENSION: ESSENTIAL ARTERIAL HYPERTENSION	19[redacted]
OTHER: PNEUMOFIBROSIS BASALIS	19[redacted]
OTHER: PSORIASIS PLAQUE	20[redacted]
OBESITY: ADIPOSITAS III (BMI-51.5)	20[redacted]
OTHER: MENOPAUSE	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
TUBERCULOSIS: PROPHILACTICALY TREATMENT FOR LATENT WITH ISONIAZID FROM MAR2016 TO 01DEC2016	20[redacted]
OTHER: STRUMA NODOSUM	20[redacted]
CHOLELITHIASIS	20[redacted]
OTHER: HYPERURICAEMIA	20[redacted]

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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 398	230
ADA	40MG	SC	EOW	[redacted]20[redacted] / 399		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]
BI PREDONIUM	5 mg	QD	Y-M: 20[redacted]
DICLOFENAC	150 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
ISONIAZID	300 mg	QD	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED
BI PREDONIUM	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
DICLOFENAC	150 mg	QD	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
PHOSPHOLIPIDS	600 mg	TID	Y-M: 20[redacted] / 406	Y-M: 20[redacted] / 597
ORNITHINE	3000 mg	BID	Y-M: 20[redacted] / 598	NOT REPORTED
SILYBUM MARIANUM	3000 mg	OTHER: TWELVE CAPSULES PER DAY	Y-M: 20[redacted] / 598	NOT REPORTED
PERINDOPRIL	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749	NOT REPORTED
ACETYLSALICYLIC ACID	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 763
AMLODIPINE	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 763
ATORVASTATIN	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 763
DIAZEPAM	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 763
IPIDACRINE	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 763
LIDOCAINE;PYRIDOXINE;THIAMINE;VITAMIN B12 NOS	UNSPECIFIED mL	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 763
MAGNESIUM	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 763
MANNITOL	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 763

MOXONIDINE	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749 - Y-M: 20[redacted] / 763
OMEPRAZOLE	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749 - Y-M: 20[redacted] / 763
RINGER	UNSPECIFIED mg	QD	Y-M: 20[redacted] / 749 - Y-M: 20[redacted] / 763

Event #2: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description	STROKE
Preferred term	脳血管発作
AE Onset Date / Rx Day	[redacted]20[redacted] / 748
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 748): NPTST170-CKMB: 21 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST223-D DIMERS: 0.46 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST235-DIRECT BILIRUBIN: 4.3 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST541-PT: 122 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 750): Alanine Aminotransferase: 119 [NOT REPORTED - NOT REPORTED] U/L; Bilirubin: 8 [5 - 21] UMOL/L; Creatinine: 66 [53 - 97] UMOL/L; Glucose: 6.2 [4.1 - 5.9] MMOL/L; Hematocrit: 42.7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 15 [117 - 160] G/L; NPTST041-AMYLASE: 9.97 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST070-APTL: 25.1 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST209-CRP: 20.8 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST256-ERYTROCITES: 4850000 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST412-LIPASE: 79 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST643-TROMBOCYTES: 269000 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST647-TROPONIN I-HS: 104.5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST662-UREA: 4.8 [NOT REPORTED - NOT REPORTED] mmol/L; Potassium: 3.9 [3.4 - 4.4] MMOL/L; Prothrombin Intl. Normalized Ratio: 0.9 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Sodium: 143 [136 - 145] MMOL/L; Urate: 412 [150 - 350] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 748): COMPUTED TOMOGRAPHY (CT): HYPERACUTE ISCHEMIC PICTURE IN ACM DX BASIN RIGHT FRONTAL AND PARIETAL LOBE ENCLOSED ISCHEMIA NOT VISIBLE AT THE MOMENT. RIGHT SIDE TEMPORAL LOBE SUBARACHNOID CYST; [redacted]20[redacted] (RX DAY 749): COMPUTED TOMOGRAPHY (CT): WITHOUT SIGNIFICANT CHANGES IN DYNAMICS; ECG: SINUS RHYTHM 84X, NON-SPECIFIC ST-T WAVE ABNORMALITY; [redacted]20[redacted] (RX DAY 750): MRI HEAD: HCVN, SMALL ENCEPHALOMALACIA SPOTS IN BOTH CEREBRAL HEMISPHERES IN WHITE CEREBRAL MATTER, PERHAPS WITH VASCULAR GENESIS. REMAINS ARACHNOID CYST IN FRONTAL POLE OF RIGHT TEMPORAL LOBE.; [redacted]20[redacted] (RX DAY 754): CEREBRAL BLOOD VESSELS DOPLEROGRAPHY: ACM, ACA DX BLOOD FLOW REDUCED, SIN NOT REDUCED. A. BASILARIS BLOOD FLOW REMAINED; [redacted]20[redacted] (RX DAY 757): ABDOMINAL ULTRASONOGRAPHY: ABDOMEN USS 14.11: CONCRETES IN THE GALLBLADDER WITHOUT PERIVESICULAR REACTION. LIVER STEATOSIS IN THE US SCENE; BRACHIOCEPHALIC VASCULAR DUPLEX: A. CAROTIS BLOOD FLOW NOT DISTURBED. INTIMA MEDIA NORMAL (0,8MM). A VERTEBRALIS BLOOD FLOW NOT DISTURBED. ATHEROSCLEROTIC PLAQUES NOT FOUND. NO STENOSIS.; CT FOR HEAD ANGIOGRAPHY: CTA NO DATA ABOUT SIGNIFICANT STENOSIS IN INTRA AND EXTRA-CRANIAL MAGISTRAL ARTERIA.

AE Stopped Rx Day	763
Duration of AE	16 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ARTERIAL HYPERTENSION

Discontinued Study Drug Due to the Event NO
SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION, PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はラトビアの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，脳卒中の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，本態性動脈性高血圧，肥満（脂肪過多 III［BMI-51.5］），非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脳卒中を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性虚血性脳卒中のため入院した。アセトリシスで，90 mg，10% ボーラス，灌流速度 81 mL/h にて血栓溶解が行われた。徴候・症状は，急性脳血管障害及び浮動性めまいであった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脳卒中専門の神経科の診察を受けた。症状はあったものの著しい障害はなかった。日常活動や日常動作はすべて問題なくできた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，脳卒中は消失した。

投与された薬剤は，neuromidin，アムロジピン，マグネシウム，moksonidin，ジアゼパム，オメプラゾール，アスピリン，sortis，マンニットール及び prestarium であった。

Causality for UPADACITINIB (Blinded)

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1) Stroke (10042244) (Cerebrovascular accident (10008190)) [v.23.0] [10042244]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, outcome unknown

Alternative Etiology for UPADACITINIB (Blinded)

Event of STROKE

- Investigator: Arterial hypertension

- AbbVie: Risk factors include pre-existing hypertension and obesity. Additionally, cerebrovascular morbidity is increased by 22%, in patients with PsA compared with the general population.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ADOMINAL ULTRASONOGRAPHY:** ABDOMEN USS 14.11: CONCRETES IN THE GALLBLADDER WITHOUT PERIVESICULAR REACTION. LIVER STEATOSIS IN THE US SCENE

[redacted] **20[redacted] ALT:** 119 U/L

20[redacted] ANA IGG: 4 no units (normal 0 to 12)

20[redacted] ANCA P-1: 6 no units (normal 0 to 5)

20[redacted] ANCA PR: 4 no units (normal 0 to 5)

[redacted] **20[redacted] APTL:** 25.1 No unit

[redacted] **20[redacted] BRACHIOCEPHALIC VASCULAR DUPLEX:** A. carotis blood flow not disturbed. Intima media normal (0.8). A vertebralis blood flow not disturbed. Atherosclerotic plaque not found. No stenosis.

[redacted] **20[redacted] CEREBRAL BLOOD VESSLES DOPLEROGRAPHY:** ACM, ACA dx blood flow reduced, sin not reduced. A. basilaris blood flow remained.

[redacted] **20[redacted] CKMB:** 21 no units

[redacted] **20[redacted] CREATININE:** 66.3 umol/l

Unknown date CRO: 7.2 No unit

[redacted] **20[redacted] CT:** WITHOUT SIGNIFICANT CHANGES IN DYNAMICS

[redacted] **20[redacted] CT FOR HEAD:** HYPERACUTE ISCHEMIC PICTURE IN ACM DX BASIN RIGHT FRONTAL AND PARIETAL LOBE ENCLOSED ISCHEMIA NOT VISIBLE AT THE MOMENT. RIGHT SIDE TEMPORAL LOBE SUBARACHNOID CYST

[redacted] **20[redacted] CT FOR HEAD ANGIOGRAPHY:** CTA NO DATA ABOUT SIGNIFICANT STENOSIS IN INTRA AND EXTRA-CRANIAL MAGISTRAL ARTERIA.

[redacted] **20[redacted] D DIMER:** 0.46 no units

[redacted] **20[redacted] DIRECT BILIRUBIN:** 4.3 no units

Unknown date EBV EA IGM: Negative

[redacted] **20[redacted] ECG:** SINUS RHYTHM 84X, NON-SPECIFIC ST-T WAVE ABNORMALITY

[redacted] **20[redacted] GLUCOSE:** 6.15 MMOL/L

[redacted] **20[redacted] HEMATOCRIT:** 42.7 No unit

[redacted] **20[redacted] HEMOGLOBIN:** 14.7 G/L

20[redacted] IMG AGAINST BORRELIA BURGDORFERI: Negative

[redacted] **20[redacted] INR:** 0.9 No unit

[redacted] **20[redacted] MRI FOR HEAD:** HCVN, small encephalomalacia spots in both cerebral hemispheres in white cerebral matter, perhaps with vascular genesis. Remains arachnoid cyst in frontal pole of right temporal lobe.

[redacted] **20[redacted] NA:** 143 MMOL/L

20[redacted] PHOSPHOLIT ANTIBODIES IGG 01: 3 no units (normal 0 to 10)

[redacted] **20[redacted] POTASSIUM:** 3.9 MMOL/L

Unknown date PT: 122 No unit

[redacted] **20[redacted] TOTAL BILIRUBIN:** 8.2 umol/l

[redacted] **20[redacted] TROMBOCYTES:** 269000 No unit

[redacted] **20[redacted] TROPONIN 1-HS:** 104.5 No unit

[redacted] **20[redacted] UREA:** 4.8 MMOL/L

[redacted] **20[redacted] URIN ACID:** 412 No unit (normal 150 to 350)

[redacted] **20[redacted] WEIGHT SCREENING:** 107 KG

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PSORIASIS	19[redacted]
OTHER: HYPERPLASIA ENDOMETRI	20[redacted]
OTHER: MENOMETRORAGIA	20[redacted]
OTHER: UTERINE MYOMA	20[redacted]
OTHER: MENOPAUSE	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: DISLIPIDEMIA	20[redacted]

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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 231	63

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]

FOLIC ACID	5.0 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5.0 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	OVARIAN CYST
Preferred term	卵巣嚢胞
AE Onset Date / Rx Day	[redacted]20[redacted] / 259 (48 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 259): CYSTECTOMIA: NA; [redacted]20[redacted] (RX DAY 574): GYNECOLOGIC ULTRASOUND: NO DATA

AE Stopped Rx Day	259 (48 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAY
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	POSTMENOPAUSE
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: M15-572

治験責任医師からの報告。本被験者はラトビアの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，卵巣嚢胞の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，子宮内膜増殖症，過長過多不規則月経，子宮筋腫及び閉経であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は卵巣嚢胞を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，卵巣嚢胞は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は予定されていた卵巣嚢腫摘出術のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for UPADACITINIB (Blinded)

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1) Ovarian cyst (10033132) (Ovarian cyst (10033132)) [v.22.1] [10033132]

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 OVARIAN CYST

- Investigator: Postmenopause

- AbbVie: EVENT IS COMMON IN THE FEMALE POPULATION.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] **20[redacted] GYNECOLOGIC ULTRASOUND:** NO DATA

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	4[redacted]	MALE	WHITE

Medical History	Onset Year
DEGENERATIVE DISC DISEASE: SPONDILOSIS	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: LEFT KNEE ARTRITIS	20[redacted]
OTHER: GASTRODUODENITIS	20[redacted]
PNEUMONIA	20[redacted]
OTHER: SPONDILOSIS	20[redacted]
DEGENERATIVE DISC DISEASE: ARTROSIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: SPONDILOLISTESIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: ARTROSCOPIA	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)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 396	227
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 397		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	5.0 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]
METHOTREXATE	10.0 mg	EVERY WEEK	Y-M: 20[redacted]-
METHOTREXATE	15.0 mg	EVERY WEEK	Y-M: 20[redacted]-

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5.0 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]	NOT REPORTED
METHOTREXATE	15.0 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]	NOT REPORTED

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

Event Description	APENDICITIS
Preferred term	虫垂炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 303
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 303): Alanine Aminotransferase: 17 [5 - 55] U/L; Creatinine: 107 [64 - 104] UMOL/L; Erythrocytes: 14.2 [4.5 - 5.9] 10^12/L; Glucose: 6.6 [3.9 - 6.1] MMOL/L; Leukocytes: 11.4 [4.5 - 8.5] 10^9/L; NPTST209-CRP: 53.2 [NOT REPORTED - 5] g/dL; [redacted]20[redacted] (RX DAY 331): Platelets: 178 [150 - 400] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 303): APPENDECTOMIA: OPERATION SUCCESSFUL

AE Stopped Rx Day	306
Duration of AE	4 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	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: M15-572

治験責任医師からの報告。本被験者はラトビアの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，虫垂炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，椎間板変性疾患，局面型乾癬，胃十二指腸炎，脊椎症，関節症，乾癬性関節炎，脊椎すべり症，非喫煙者及び非飲酒者であった。

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

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は強い胃の痛みを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。同日，被験者は虫垂切除術を受けた。手術は成功し，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院した。

Causality for UPADACITINIB (Blinded)

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1) Appendicitis (10003011) (Appendicitis (10003011)) [v.22.1] [10003011]

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 APPENDICITIS

- Investigator: Infection

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males and 6.7 percent in females.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 17 U/L (normal 5 to 55)

[redacted] **20[redacted] CREATININE:** 107.1 umol/L

[redacted] **20[redacted] CRP:** 53.2 G/DL (normal 0.5 to 5)

[redacted] **20[redacted] GLUCOSE:** 6.58 MMOL/L (normal 3.85 to 6.1)

[redacted] **20[redacted] PLATELET COUNT:** 178 X10**3/MM**3 (normal 150 to 400)

[redacted] **20[redacted] RED BLOOD CELLS:** 14.2 10^6/mm3

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.43 X10**3/MM**3 (normal 4.5 to 8.5)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	7[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
HYPERTENSION	20[redacted]
OTHER: OSTEOPENIA	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

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)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ADA	40MG	SC	EOW	[redacted]20[redacted] / 170	[redacted]20[redacted] / 392	223
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

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]
CALCIUM CARBONATE	600 mg	QD	Y-M: 20[redacted]
FOLIC ACID	20 mg	EVERY WEEK	Y-M: 20[redacted]

HYDROXYCHLOROQUINE	20 mg	QD	Y-M: 20[redacted]
KETOPROFEN	150 mg	OTHER: AS NEEDED	Y-M: 20[redacted]
METAMIZOLE	500 mg	QD	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -105

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CALCIUM CARBONATE	600 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	20 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
KETOPROFEN	150 mg	OTHER: AS NEEDED	Y-M: 20[redacted]	NOT REPORTED
METAMIZOLE	500 mg	QD	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -105	NOT REPORTED
ISONIAZID	100 mg	QID	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 493
NADROPARIN	5 mL	QD	Y-M: 20[redacted] / 471	NOT REPORTED
CEFUROXIME	750 mg	TID	Y-M: 20[redacted] / 471	Y-M: 20[redacted] / 476

Event #1: Serious Adverse Event

Event Description	INJURY: END OF RADIUS FRACTURE - EXTENSION TYPE, LEFT HAND
Preferred term	橈骨骨折
AE Onset Date / Rx Day	[redacted]20[redacted] / 456
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 471): Alanine Aminotransferase: 33 [3 - 47] U/L; Creatinine: 60 [25 - 42] UMOL/L; Erythrocytes: 4.2 [3.8 - 5.3] 10^12/L; Glucose: 6.4 [3.9 - 5.6] MMOL/L; Hemoglobin: 136 [135 - 180] G/L; Leukocytes: 7.2 [3.8 - 10] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 471): BLOOD NPTST053-ANTI SYPHILLIS: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 471): ANESTHESIOLOGISTS PREOPERATIVE EXAMINATION: NORMAL FINDING; INTERNAL PREOPERATIVE EXAMINATION: NORMAL FINDING; X-RAY: END OF RADIUS FRACTURE - EXTENSION TYPE, LEFT HAND; [redacted]20[redacted] (RX DAY 472): SURGERY - OSTHEOSYNTHESIS: ONGOING RESULT

AE Stopped Rx Day	484
Duration of AE	29 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DUE TO AE FRACTURE OF RADIUS THERE WAS BAD HEALING OF THE FRACTURE SUBJECT WAS INVITED TO PLANNED HOSPITALIZATION [redacted] [redacted] [redacted] 20[redacted]
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: M15-572

治験責任医師からの報告。本被験者はスロバキア共和国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，損傷-橈骨端骨折（伸展型，左手）の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，局面型乾癬，高血圧，骨減少症，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は損傷-橈骨端骨折（伸展型，左手）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，損傷-橈骨端骨折（伸展型，左手）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は森で木を扱う作業中に手を損傷した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は橈骨骨折の治癒不良のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，骨接合術が行われ，術後経過は良好であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は fraxiparine multi 及び cefuroxim kabi であった。

The patient's past medications include:

PLAQUENIL for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Radius fracture (10037802) (Radius fracture (10037802)) [v.22.1] [10037802]

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 INJURY: END OF RADIUS FRACTURE - EXTENSION TYPE, LEFT HAND

- Investigator: DUE TO AE FRACTURE OF RADIUS THERE WAS BAD HEALING OF THE FRACTURE SUBJECT WAS INVITED TO PLANNED HOSPITALIZATION [redacted] 20[redacted]

- AbbVie: EVENT IS MORE LIKELY RELATED TO TRAUMA FROM A HAND INJURY WHILE WORKING. PRE-EXISTING OSTEOPENIA IS AN ADDITIONAL RISK FACTOR.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ANTI-SYPHILLIS ANTIBODY:** Negative

[redacted] 20[redacted] **CREATININE:** 60.3 MCMOL/L (normal 25 to 42)

[redacted] 20[redacted] **GLUCOSE:** 6.44 MMOL/L (normal 3.9 to 5.6)

[redacted] 20[redacted] **HEMOGLOBIN:** 136 G/L (normal 135 to 180)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.18 X10**12/L (normal 3.8 to 5.3)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 7.24 X10**9/L (normal 3.8 to 10)

[redacted] 20[redacted] **X-RAY:** End of radius fracture extension type, left hand

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ブドウ球菌性敗血症	X	X		X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
PSORIATIC ARTHRITIS	19[redacted]
OTHER: ATEROSCLEROTIC HEART DISEASE	20[redacted]
HYPERTENSION: ARTERIAL HYPERTENSION	20[redacted]
KIDNEY DISORDER: CHRONIC KIDNEY DISORDER G2A1	20[redacted]
BENIGN PROSTATIC HYPERPLASIA	20[redacted]
OSTEOPOROSIS: OSTEOPENIA	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]

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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 258	90

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SANDIMMUN NEORAL	150 mg	QD	Y-M: 20[redacted]-

SANDIMMUN NEORAL	125 mg	QD	Y-M: 20[redacted]
TRIAMCINOLONE	4 mg	QD	Y-M: 20[redacted]
FOLIC ACID	20 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted]
TRANDOLAPRIL	2 mg	QD	Y-M: 20[redacted]
TRIAMCINOLONE	6 mg	QD	Y-M: 20[redacted]
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
METHYLPREDNISOLONE	2 mg	QD	Y-M: 20[redacted]
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -227

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	20 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 259
TRANDOLAPRIL	2 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 259
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -227	Y-M: 20[redacted] / 277
CEFUROXIME	500 mg	BID	Y-M: 20[redacted] / 257	ONGOING
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 262	ONGOING
FLUCONAZOLE	100 mg	QD	Y-M: 20[redacted] / 263	ONGOING
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 272	ONGOING
BISOPROLOL	5 mg	QD	Y-M: 20[redacted] / 277	ONGOING
CALTRATE PLUS	1 OTHER: TBL	QD	Y-M: 20[redacted] / 277	ONGOING
ENOXAPARIN	0,4 mL	QD	Y-M: 20[redacted] / 277	ONGOING
HYLAK FORTE	35 gtt	TID	Y-M: 20[redacted] / 277	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 277	ONGOING
SILYBUM MARIANUM	300 mg	BID	Y-M: 20[redacted] / 277	ONGOING
TRAMADOL	15 gtt	TID	Y-M: 20[redacted] / 277	ONGOING
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 278	ONGOING

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

Event Description	STAPHYLOCOCCUS AUREUS SEPSIS
Preferred term	ブドウ球菌性敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 257
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 257): Basophils/Leukocytes: 0,1 [0 - 1] %; Chloride: 107 [101 - 109] UNIT NOT REPORTED; Cholesterol: 3,94 [0 - 5.17] UNIT NOT REPORTED; Creatine Kinase: 2,4 [0 - 2.85] UNIT NOT REPORTED; Creatinine: 54 [59 - 104] UNIT NOT REPORTED; Eosinophils/Leukocytes: 0,1 [1 - 5] %; Glucose: 6,0 [4.1 - 5.9] UNIT NOT REPORTED; Hemoglobin: 107 [140 - 179] UNIT NOT REPORTED; Leukocytes: 9,4 [4.5 - 6] UNIT NOT REPORTED; Lymphocytes/Leukocytes: 2,8 [25 - 46] %; Monocytes/Leukocytes: 7,3 [2 - 10] %; NPTST209-CRP: 248 [0 - 5] UNIT NOT

REPORTED; Neutrophils/Leukocytes: 7,9 [1.4 - 6.5] %; Platelets: 179 [140 - 400] UNIT NOT REPORTED; Potassium: 3,8 [3.5 - 5.1] UNIT NOT REPORTED; Sodium: 137 [136 - 146] UNIT NOT REPORTED; pH: 7,465 [7.36 - 7.44] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 260): BLOOD NPTST319-HEMOCULTIVATION: Positive-STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 257): CHEST XRAY: NORMAL , WITHOUT INFILTRATIVE CHANGES; XRAY OF HANDS: FRACTURE OF BASIS OF RIGHT V. MCP JOINT; [redacted]20[redacted] (RX DAY 260): USG OF DEEP VEIN SYSTEM OF LEFT LEG: WITHOUT SIGNS OF THROMBOSIS, BACER CYST; [redacted]20[redacted] (RX DAY 263): USG OF ABDOMEN: STEATOSIS OF LIVER, CYSTS IN LIVER; [redacted]20[redacted] (RX DAY 265): ECHOCARDIOGRAPHY: HYPERTROPHY OF INTRAVENTRICULAR SEPTUM; [redacted]20[redacted] (RX DAY 266): MR OF LEFT KNEE: INFLAMATORY CHANGES OF KNEE

AE Stopped Rx Day	642 (384 DAYS AFTER LAST TREATMENT)
Duration of AE	386 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, LIFE THREATENING

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はスロバキア共和国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，黄色ブドウ球菌性敗血症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，慢性腎障害（G2A1），骨減少症，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は黄色ブドウ球菌性敗血症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，黄色ブドウ球菌性敗血症は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は車のホイール交換時に右手の外傷性骨折（非重篤）を来した。右手に血腫が出現し，数日後に悪化し始めた。その他の症状は振戦であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。血液培養の結果は黄色ブドウ球菌陽性であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。被験者は部分的に治癒し，抗生物質療法が継続された。本事象により治験薬の投与が完全に中止された。

投与された薬剤は，シプロフロキサシン，entizol，mycomax 及び zinnat であった。

Causality for UPADACITINIB (Blinded)

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1) Staphylococcus aureus septicemia (10054638) (Staphylococcal sepsis (10056430)) [v.23.0] [10054638]

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 STAPHYLOCOCCUS AUREUS SEPSIS

- Investigator: Not applicable

- AbbVie: Event more likely related to preceding trauma to hand.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD CULTURE:** staphylococcus aureus

[redacted] **20[redacted] CHEST X-RAY:** normal, without infiltrative changes

[redacted] **20[redacted] CRP:** 248 no unit (normal 0 to 5)

[redacted] **20[redacted] ECHOCARDIOGRAPHY:** hypertrophy of intraventricular septum

[redacted] **20[redacted] HAND X-RAY:** fracture of basis of right V. MCP joint

[redacted] **20[redacted] LYMPHOCYTES:** 2.8 % (normal 25 to 46)

[redacted] **20[redacted] NEUTROPHILS:** 7.9 % (normal 1.4 to 6.5)

[redacted] **20[redacted] ULTRASOUND OF ABDOMEN:** steatosis of liver, cysts in liver

[redacted] **20[redacted] WBC:** 9.4 no unit (normal 4.5 to 6.0)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 30 mg QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	30	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 393	225
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 394		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CERTOSTAT	2/0.03 mg	QD	Y-M: 20[redacted]
FOLIC ACID	20 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -225

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	20 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -225	Y-M: 20[redacted] / 814
DROSPIRENONE W/ETHINYLESTRADIOL	3/0.02 mg	QD	Y-M: 20[redacted] / 110	NOT REPORTED
SILYBUM MARIANUM	70 mg	TID	Y-M: 20[redacted] / 313	Y-M: 20[redacted] / 330
GABAPENTIN	300 mg	BID	Y-M: 20[redacted] / 338	Y-M: 20[redacted] / 417
SILYBUM MARIANUM	150 mg	BID	Y-M: 20[redacted] / 338	Y-M: 20[redacted] / 417
ULTRACET	37.5/325 mg	BID	Y-M: 20[redacted] / 338	Y-M: 20[redacted] / 417
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 341	Y-M: 20[redacted] / 345
METAMIZOLE	500 mg	TID	Y-M: 20[redacted] / 341	Y-M: 20[redacted] / 345

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

Event Description HERPES ZOSTER THORACIS LOCALIZED

Preferred term 帯状疱疹

AE Onset Date / Rx Day [redacted]20[redacted] / 338

Age at AE Onset 4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 341): Alanine Aminotransferase: 1.68 [NOT REPORTED - NOT REPORTED] ukat/L; Alkaline Phosphatase: 0.75 [NOT REPORTED - NOT REPORTED] ukat/L; Aspartate Aminotransferase: 1.15 [NOT REPORTED - NOT REPORTED] ukat/L; Basophils/Leukocytes: 0.4 [0 - 2] %; Bilirubin: 6 [5 - 21] UMOL/L; Calcium: 2.29 [2.15 - 2.5] MMOL/L; Chloride: 104 [98 - 107] MMOL/L; Creatinine: 56 [53 - 97] UMOL/L; Eosinophils/Leukocytes: 0.6 [1 - 4] %; Erythrocytes: 4.2 [3.8 - 5.3] 10^12/L; Hemoglobin: 137 [117 - 160] G/L; Leukocytes: 4.6 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 61.7 [20 - 44] %; Monocytes/Leukocytes: 8.3 [2 - 9] %; NPTST209-CRP: 85.4 [NOT REPORTED - NOT REPORTED] mg/L; Neutrophils/Leukocytes: 29 [50 - 70] %; Platelets: 100 [150 - 400] 10^9/L; Potassium: 4.6 [3.4 - 4.4] MMOL/L; Sodium: 136 [136 - 145] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 342): OTHER LARYNGEAL SWAB NPTST023-AEROBAL CULTIVATION: Not applicable-STREPTOCCCUS SALLIVARIUS, NEISSERIA CATARRHALIS; OTHER TONSILLAR SWAB NPTST024-AEROBEAL CULTIVATION: Not applicable-STREPTOCOCCUS SALIVARIUS, NEISSERIA CATARRHALIS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 341): XRAY OF CHEST: NORMAL, WITHOUT INFILTRATIVE CHANGES

AE Stopped Rx Day 417

Duration of AE 80 DAYS

Severity Moderate

Relation to Study Drug by Investigator Reasonable Possibility

Investigator Alternative Etiology NOT REPORTED

Discontinued Study Drug Due to the Event NO

SAE Criteria REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はスロバキア共和国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，限局性胸郭帯状疱疹の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，喫煙者（1 日 1 箱を 30 年間）及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は限局性胸郭帯状疱疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，限局性胸郭帯状疱疹は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹の出現を自覚した。帯状疱疹は 20[redacted] 年 [redacted] 月 [redacted] 日に悪化した。被験者はその後，感染症専門医を受診し，病院に搬送された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は非経口的治療のため入院した。徴候・症状は，帯状疱疹性湿疹及び疼痛であった。帯状疱疹との診断は，病歴及び身体的診察の結果に基づいて下された。病変は 2 つの皮膚分節（T3 及び T4）に及んでいた。血清学的検査で軽度の炎症活性増加及び肝酵素増加が認められた。抗ウイルス療法が開始された。高い臨床効果が見られ，炎症活性は低下した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

水疱瘡及び帯状疱疹の病歴並びに帯状疱疹ワクチン接種歴の記載はなかった。

投与された薬剤は，novalgin，herpesin，ガバペンチン，tramapran 及び lagosa であった。

The patient's past medications include:

FLAVOBION for HEPATOPROTECTION ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Herpes zoster dermatitis (10019977) (Herpes zoster (10019974)) [v.22.0] [10019977]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of HERPES ZOSTER THORACIS LOCALIZED

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ALANINE AMINOTRANSFERASE:** 1.68 MCKAT/L

[redacted] **ALKALINE PHOSPHATASE:** 0.75 MCKAT/L

[redacted] **ASPARTATE AMINOTRANSFERASE:** 1.15 MCKAT/L

[redacted] **ASPARTATE AMINOTRANSFERASE:** 1.15 MCKAT/L

[redacted] **CHEST X-RAY:** NORMAL, WITHOUT INFILTRATIVE CHANGES

[redacted] **CRP:** 85.4 MG/L

[redacted] **LARYNGEAL SWAB:** STREPTOCCCUS SALLIVARIUS, NEISSERIA CATARRHALIS

[redacted] **LYMPHOCYTES:** 61.7 %

[redacted] **PLATELET COUNT:** 100 X10**9/L

[redacted] **TONSILLAR SWAB:** STREPTOCCCUS SALLIVARIUS, NEISSERIA CATARRHALIS

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 30 mg QD	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: HERPES ZOSTER THORACIS (LOCALIZED)	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OBESITY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HERNIOTOMY OF UMBILICAL HERNIA	20[redacted]
SURGERY: LISTESIS L5/S1	20[redacted]

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

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] / 28	28

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CICLOSPORIN	50 mg	BID	Y-M: 20[redacted]
CICLOSPORIN	100 mg	BID	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]

NUVARING	1 OTHER: PIECE	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
NUVARING	1 OTHER: PIECE	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]	ONGOING
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 8	Y-M: 20[redacted] / 12
MYDOCALM	150 mg	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 34
NADROPARIN	0.8 mL	BID	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 63
RIVAROXABAN	20 mg	QD	Y-M: 20[redacted] / 64	ONGOING

Event #2: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description	DEEP VEIN THROMBOSIS OF LEFT SHIN
Preferred term	深部静脈血栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 32 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 46): Alanine Aminotransferase: 0.23 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Aspartate Aminotransferase: 0.19 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Bilirubin: 2.7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Chloride: 104.8 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Creatinine: 51.1 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Erythrocytes: 4.76 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: 6.67 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 140 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 7.5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST226-D-DIMERS: 2.94 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 480 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 3.9 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Prothrombin Intl. Normalized Ratio: 1.06 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Sodium: 139 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 46): ABDOMINAL USG: CALCIFICAT IN LIVER WITH MAXIMAL SIZE OF 10MM; ABDOMINAL XRAY: NORMAL; CHEST XRAY: NORMAL; [redacted]20[redacted] (RX DAY 47): USG OF VEIN OF LEGS: DEEP VENOUS SYSTEM: SIGNS OF FLEBOTHROMBOSIS OF MUSCULAR VEINS IN MEDIAL PART OF LEFT SHINE

AE Stopped Rx Day	105 (77 DAYS AFTER LAST TREATMENT)
Duration of AE	74 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	NO Reasonable Possibility
Investigator Alternative Etiology	COMBINATION OF HORMONAL CONTRACEPTION PLUS NIKOTINISM
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: M15-572

治験責任医師からの報告。本被験者はスロバキア共和国の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左脛の深部静脈血栓症の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，肥満，喫煙者（1 日 1 箱を 10 年間），非飲酒者，パイプ喫煙者及び噛みタバコ喫煙者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左脛の深部静脈血栓症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左脛の深部静脈血栓症は消失した。

本事象発現前，20[redacted] 年 [redacted] 月 [redacted] 日，腰痛症の悪化（非重篤）の事象により治験薬の投与が完全に中止された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左脛の腫脹及び圧痛の発現を来した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者によると，呼吸困難はなかった。右腓腹は 38 cm，左腓腹は 40 cm と測定され，足底の圧痛及びホーマンズ徴候が認められた。被験者は左脛の筋静脈血栓症と診断された。抗凝固療法が開始され，高い効果が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。

投与された薬剤は，イグザレルト，fraxiparine 及び novalgin であった。

Causality for UPADACITINIB (Blinded)

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

Causality as 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 DEEP VEIN THROMBOSIS OF LEFT SHIN

- Investigator: Combination of hormonal contraception plus nicotinism.

- AbbVie: Risk factors include current smoking status of 1PPD for 10 years, concomitant use of nuva ring, and obesity (BMI 30).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Liver of adequate size, echo reflection with dorsal shadow in the right lobe subcapsularly – a calcification with a size up to 10 mm. Normal volume of the gallbladder, echo-empty. Bile ducts are not dilated. No focal changes in the pancrea and spleen. Both kidneys of adequate size, parenchyma without reduction and focal changes. No fluid accumulation bilaterally. The urinary bladder is echo empty. No free fluid intraperitoneally. Calcification in the liver.

[redacted] **20[redacted] BLOOD PRESSURE:** 124/85 mmHg

[redacted] **20[redacted] BODY MASS INDEX:** 30 kg/m**2

[redacted] **20[redacted] CHEST XRAY:** Lungs: Normal diaphragms, costophrenic angles are free. Normal width of hilar shadows, extended lung parenchyma, no new infiltrative or focal changes. Normal heart and mediastinal shadow. No pathological changes in intrathoracic organs in X-ray image.

[redacted] **20[redacted] D DIMER:** 2.94 no unit

[redacted] **20[redacted] INTERNATIONAL NORMALIZED RATIO:** 1.06 no unit

[redacted] **20[redacted] PLATELET COUNT:** 480 no unit

[redacted] **20[redacted] PLATELETS:** 317 GI/L (normal 140 to 400)

[redacted] **20[redacted] PT:** 89 no units

[redacted] **20[redacted] PTT:** 53 no units

[redacted] **20[redacted] ULTRASOUND OF VEIN OF LEGS:** Common femoral vein, superficial femoral vein and popliteal vein are compressible, with preserved response to augmentation. Signs of phlebothrombosis of muscular veins on the medial side of the calf – veins of wider calibre, non-compressible with more echo content.

[redacted] **20[redacted] URINE:** Specific Gravity 1.012 (1.003-1.035) pH 5.5 (5.0-8.0) Protein Negative Glucose Normal Ketones Negative Bilirubin Negative Urobilirubin Normal Blood +1 (Negative-Trace) Nitrite Negative Leukocyte Negative WBC 1 (0-12/hpf)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 15 mg QD	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: CHRONIC LOW BACK PAIN	20[redacted]
PERIPHERAL NERVE DISORDER: POLYNEUROPATHY	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
HYPERTENSION: ARTERIAL HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HEMILAMINECTOMY DISCI L4/L5	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)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 169	169
ABT-494	15 MG	ORAL	QD	[redacted] / 170	[redacted] / 393	224
ABT-494	15 MG	ORAL	QD	[redacted] / 394		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	10 mg	EVERY WEEK	Y-M: [redacted]
CICLOSPORIN	100 mg	BID	Y-M: [redacted]
CICLOSPORIN	50 mg	BID	Y-M: [redacted]
CICLOSPORIN	150 mg	BID	Y-M: [redacted]
BISOPROLOL	5 mg	QD	Y-M: [redacted]
FOLIC ACID	20 mg	EVERY WEEK	Y-M: [redacted]
METHOTREXATE	5 mg	EVERY WEEK	Y-M: [redacted]
GABAPENTIN	100 mg	OTHER: 1-0-3	Y-M: [redacted]
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: [redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: [redacted] / -309
METHOTREXATE	15 mg	EVERY WEEK	Y-M: [redacted] / -233

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
BISOPROLOL	5 mg	QD	Y-M: [redacted]	NOT REPORTED
FOLIC ACID	20 mg	EVERY WEEK	Y-M: [redacted]	NOT REPORTED
GABAPENTIN	100 mg	OTHER: 1-0-3	Y-M: [redacted]	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: [redacted] / -233	NOT REPORTED
METAMIZOLE	500 mg	OTHER: UNK	Y-M: [redacted] / 286	Y-M: [redacted] / 287

Event #1: Serious Adverse Event

Event Description	METAL FOREING BODY IN SUBCUTTIS OF FOREHEAD
Preferred term	体内異物
AE Onset Date / Rx Day	[redacted]20[redacted] / 223
Age at AE Onset	5[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 223): XRAY OF HEAD: SMALL 2MM METAL SATURATED SHADE IN FRONTAL SCALP;
[redacted]20[redacted] (RX DAY 287): SURGICAL EXTRACTION OF FOREIGN METAL BODY: WITHOUT COMPLICATION

AE Stopped Rx Day	287
Duration of AE	65 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	REPEATED TRAUMA OF HEAD IN CHILDHOOD
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: M15-572

治験責任医師からの報告。本被験者はスロバキア共和国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，前額部皮下組織内の金属製体内異物の事象を発現した。

Event 1 の臨床経過：

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。記録によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は前額部皮下組織内の金属製体内異物を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，前額部皮下組織内の金属製体内異物は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は前額部の金属製体内異物を除去するため入院した。入院時の病歴聴取及び身体診察の結果，被験者の状態は良好であり，症状は特になかった。入院後，金属製体内異物が外科的に除去された。合併症は

認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，novalgin であった。

Causality for UPADACITINIB (Blinded)

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1) Foreign body (10070245) (Foreign body (10070245)) [v.23.0] [10070245]

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 METAL FOREIGN BODY IN SUBCUTTIS OF FOREHEAD

- Investigator: Repeated trauma of head in childhood.

- AbbVie: Event is more likely related to trauma to head in childhood as reported by PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] XRAY OF HEAD:** Small 2 mm metal saturated shade in frontal scalp.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腰髄神経根障害	X			

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

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: CHRONIC TONSILLITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 398	230
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 399		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETORICOXIB	60 mg	QD	Y-M: 20[redacted] / -357
METHYLPREDNISOLONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -299
VELOSALIC	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -299
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -259
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -259
LEFLUNOMIDE	10 mg	QD	Y-M: 20[redacted] / -126
VITAMIN D NOS	6000 IU	QD	Y-M: 20[redacted] / -78

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
ETORICOXIB	60 mg	QD	Y-M: 20[redacted] / -357	NOT REPORTED
LEFLUNOMIDE	10 mg	QD	Y-M: 20[redacted] / -126	NOT REPORTED
DICLOFENAC	150 mg	QD	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 486
PARACETAMOL	1000 g	TID	Y-M: 20[redacted] / 486	Y-M: 20[redacted] / 489
GABAPENTIN	300 mg	TID	Y-M: 20[redacted] / 489	Y-M: 20[redacted] / 490

Event #1: Serious Adverse Event

Event Description L5 LUMBAR RADICULOPATHY ON THE LEFT SIDE
Preferred term 腰髄神経根障害
AE Onset Date / Rx Day [redacted]20[redacted] / 450
Age at AE Onset 4[redacted]
Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 491): LUMBAR MRI SCAN: DEGENERATIVE CHANGES IN L4/5, L5/S1 INTERVERTEBRAL DISCS, PRONOUNCED HERNIATIONS. SLIGHT ARTHROTIC CHANGES IN FASSET JOINTS. SIZABLE L4/5 LEFT- CENTRAL, L5/S1 RIGHT- CENTRAL EXTRUSIONS WITH NERVE ROOTCOMPRESSION. SPINAL CORD WITH NORMAL FINDINGS.; [redacted]20[redacted] (RX DAY 492): L4/5 LAMINECTOMY, DISCECTOMY: RESOLVED
AE Stopped Rx Day 492
Duration of AE 43 DAYS
Severity Severe
Relation to Study Drug by Investigator No Reasonable Possibility
Investigator Alternative Etiology PADDLING
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: M15-572

治験責任医師からの報告。本被験者はエストニアの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左側 L5 の腰髄神経根障害の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，非喫煙者及び現飲酒者（2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左側 L5 の腰髄神経根障害を発現した。

[redacted] 月から背部痛が続いていた。背部痛は（ボート等を）こいでいるときに初めて出現した。20[redacted] 年 [redacted] 月以降，neurontin，ジクロフェナク，アセトアミノフェンの服用や理学療法にもかかわらず，背部痛は重度となり，放射状に拡がった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は神経外科病棟に入院した。診察時，被験者によると不全麻痺はなかったが，重度の腰痛で可動域が制限されていた。下肢伸展挙上検査の結果，左 10 度陽性，右 60 度陽性であった。L4/5 椎弓・椎間板切除術が行われた。背部痛は軽減され，神経根障害は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，neurontin，ジクロフェナク及びアセトアミノフェンであった。

The patient's past medications include:

ADVANTAN CREAM for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ELOSALIC OINTMENT for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TREXAN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Lumbar radiculopathy (10050219) (Lumbar radiculopathy (10050219)) [v.23.0] [10050219]

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 L5 LUMBAR RADICULOPATHY ON THE LEFT SIDE

- Investigator: paddling

- AbbVie: Event is more likely related to paddling (rowing) activity in [redacted] 20[redacted] as noted by PI. Additional risk factor includes pre-existing psoriatic arthritis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] **20[redacted] LUMBAR MRI:** DEGENERATIVE CHANGES IN L4/5, L5/S1 INTERVERTEBRAL DISCS, PRONOUNCED HERNIATIONS. SLIGHT ARTHROTIC CHANGES IN FASSET JOINTS. SIZABLE L4/5 LEFT- CENTRAL, L5/S1 RIGHT- CENTRAL EXTRUSIONS WITH NERVE ROOT COMPRESSION. SPINAL CORD WITH NORMAL FINDINGS.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
鉄欠乏性貧血	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: VITILIGO	19[redacted]
OTHER: SARCOIDOSIS	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
PSORIATIC ARTHRITIS	20[redacted]
HYPERTENSION	20[redacted]

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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1[redacted]	20[redacted] / 72	72

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]
FOLIC ACID	5.0 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	25.0 mg	EVERY WEEK	Y-M: 20[redacted]
LEFLUNOMIDE	20.0 mg	QD	Y-M: 20[redacted] / -286
INDAPAMIDE	1.25 mg	QD	Y-M: 20[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 / Stop Year-Month / RX Day	
			RX Day	Day
LEFLUNOMIDE	20.0 mg	QD	Y-M: 20[redacted] / -286	Y-M: 20[redacted] / 72
INDAPAMIDE	1.25 mg	QD	Y-M: 20[redacted] / -19	NOT REPORTED
PERINDOPRIL	5.0 mg	QD	Y-M: 20[redacted] / 13	NOT REPORTED
AMOXICILLIN	500.0 mg	TID	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 84
AZITHROMYCIN	500.0 mg	QD	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84
AZITHROMYCIN	250.0 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 88
ERGOCALCIFEROL	4000 IU	QD	Y-M: 20[redacted] / 91	NOT REPORTED

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

Event Description	IRON DEFICIENT ANAEMIA
Preferred term	鉄欠乏性貧血
AE Onset Date / Rx Day	[redacted]20[redacted] / 90 (18 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 73): NPTST129-C-REACTIVE PROTEIN: 28 [0.1 - 5] MG/L; [redacted]20[redacted] (RX DAY 87): NPTST129-C-REACTIVE PROTEIN: 16.4 [0.1 - 5] MG/L; [redacted]20[redacted] (RX DAY 90): Eosinophils: 0.12 [0.01 - 0.4] 10^9/L; Erythrocyte Sedimentation Rate: 73 [1 - 20] MM/H; Erythrocytes: 3.2 [4.2 - 5.7] 10^12/L; Hemoglobin: 95 [134 - 170] G/L; Leukocytes: 5 [4.5 - 10.4] 10^9/L; Lymphocytes: 1.45 [1 - 3.5] 10^9/L; Monocytes: 0.49 [0.2 - 1] 10^9/L; NPTST209-CRP: 6.5 [0.1 - 5] MG/L; NPTST638-TRANSFERRIN SOLUBLE RECEPTORS: 2.31 [0.76 - 1.76] MG/L; Neutrophils: 2.9 [1.8 - 7.8] 10^9/L; Platelets: 257 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 91): NPTST689-VIT D: 13 [50 - NOT REPORTED] NMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 84): BLOOD NPTST133-C. PNEUMONIAE IGA, IGM, IGG: Negative; BLOOD NPTST420-M. PNEUMONIAE IGA AND IGM: Negative; BLOOD NPTST421-M. PNEUMONIAE IGG: Positive-136.5; [redacted]20[redacted] (RX DAY 91): BLOOD NPTST172-CMV IGG: Positive->500.0; BLOOD NPTST173-CMV IGM: Negative; BLOOD NPTST241-EBV IGM: Negative; URINE NPTST408-LEGIONELLA PNEUMOPHILA ANTIGEN: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 83): X-RAY CHEST: NORMAL FINDING; [redacted]20[redacted] (RX DAY 84): US ABDOMEN: METEORISM, OTHERWISE NORMAL FINDING; [redacted]20[redacted] (RX DAY 90): CT NECK, CHEST, ABDOOMEN, PELVIS: NO SIGNS OF POSSIBLE INFECTION OR TUMOR; [redacted]20[redacted] (RX DAY 91): GASTROSCOPY: LIPOMA IN DUODENUM (BIOPSY TAKEN), DIAMETER 1 CM, OTHERWISE NORMAL FINDING BIOPSY RESULT: LIPOMA; [redacted]20[redacted] (RX DAY 92): ECHOCARDIOGRAPHY: NORMAL FINDING; [redacted]20[redacted] (RX DAY 97): COLOSCOPY: VARICES EXTERNI ET INTERNI, OTHERWISE NORMAL FINDING

AE Stopped Rx Day	143 (71 DAYS AFTER LAST TREATMENT)
Duration of AE	54 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はエストニアの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，鉄欠乏性貧血の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，サルコイドーシス，局面型乾癬，乾癬性関節炎，高血圧，非喫煙者及び現飲酒者（1 日 2～4 杯）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は鉄欠乏性貧血を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，鉄欠乏性貧血は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は体調が優れず，発熱があり，詳細不明の感染症（非重篤）と診断された。被験者はかかりつけ医を受診した。CRP が 28 mg/L であった。この非重篤の事象により治験薬の投与が休止された。抗生物質療法が開始され，体温は 38°C に低下した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は貧血及び最近の原因不明の発熱についてさらなる検査を受けるため入院した。被験者は脱力，疲労，悪心，皮膚蒼白及び 38°C～39°C の発熱を発現した。ウイルス感染や細菌感染は認められず，被験者の全般的な全身状態は問題ないと考えられた。肺・心音聴診及びリンパ節・筋肉・関節触診の結果は正常範囲内と判断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

FOLVERLAN for TREXAN TOXICITY PREVENTION (20[redacted] - 20[redacted])

TREXAN for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

ARAVA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AMOXICILLIN for UNSPECIFIED INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

SUMAMED for UNSPECIFIED INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Iron deficiency anemia (10022974) (Iron deficiency anaemia (10022972)) [v.23.0] [10022974]

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 IRON DEFICIENT ANAEMIA

- Investigator: Not Applicable.

- AbbVie: Risk factors include recent infection, preexisting sarcoidosis and psoriatic arthritis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **BIOPSY:** (Gastroscopy): lipoma

20[redacted] **BODY TEMPERATURE:** [redacted] / [redacted] 38-39C

[redacted] 20[redacted] **C. PNEUMONIAE IGG:** negative

[redacted] 20[redacted] **C. PNEUMONIAE IGA:** negative

[redacted] 20[redacted] **CHEST XRAY:** normal

[redacted] 20[redacted] **CMV IGM:** negative

[redacted] 20[redacted] **COLONOSCOPY:** VARICES EXTERNAL AND INTERNAL, OTHERWISE NORMAL FINDING

[redacted] 20[redacted] **CRP:** 28 MG/L

[redacted] **20[redacted] CRP:** 18 MG/L

[redacted] **20[redacted] CRP:** 6.5 MG/L (normal 0.1 to 5)

[redacted] **20[redacted] CT SCAN:** CT neck, chest, abdomen, pelvis- no signs of possible infection or tumor

[redacted] **20[redacted] EBV IGM:** negative

[redacted] **20[redacted] ECHOCARDIOGRAPHY:** normal finding

[redacted] **20[redacted] ERYTHROCYTE SED RATE:** 73 mm/h (normal 1 to 20)

[redacted] **20[redacted] GASTROSCOPY:** lipoma in duodenum (biopsy taken), diameter 1 cm, otherwise normal finding.

[redacted] **20[redacted] HEMATOCRIT:** 44 % (normal 39 to 54)

[redacted] **20[redacted] HEMATOCRIT:** 43 % (normal 39 to 54)

[redacted] **20[redacted] HEMATOCRIT:** 40 % (normal 39 to 54)

[redacted] **20[redacted] HEMATOCRIT:** 35 % (normal 39 to 54)

[redacted] **20[redacted] HEMOGLOBIN:** 143 G/DL (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 145 G/DL (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 138 G/DL (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 119 G/DL (normal 127 to 181)

[redacted] **20[redacted] HEMOGLOBIN:** 95 G/DL (normal 134 to 170)

[redacted] **20[redacted] LEGIONELLA PNEUMOPHILA ANTIGEN URINE:** negative

[redacted] **20[redacted] M. PNEUMONIAE IGA AND IGM:** negative

[redacted] **20[redacted] M. PNEUMONIAE IGG:** Positive: 136.5

[redacted] **20[redacted] M. PNEUMONIAE IGG:** Positive: >500.0

[redacted] **20[redacted] PLATELET COUNT:** 257 X10**9/L (normal 150 to 450)

[redacted] **20[redacted] RBC:** 3.2 X10**12/L (normal 4.2 to 5.7)

[redacted] **20[redacted] TRANSFERRIN SOLUBLE RECEPTORS:** 2.31 MG/L (normal 0.76 to 1.76)

[redacted] **20[redacted] ULTRASOUND OF ABDOMEN:** meteorism, otherwise normal

[redacted] **20[redacted] VIT D:** 13 MMOL/L (normal >50)

[redacted] **20[redacted] WBC:** 5.0 X10**9/L (normal 4.5 to 10.4)

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

Reason for Narrative

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

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

Medical History	Onset Year
CHOLELITHIASIS	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: CHRONIC TONSILLITIS	20[redacted]
OBESITY	20[redacted]
OTHER: TOENAILS INGROWN	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CHOLECYSTECTOMY	20[redacted]
SURGERY: TONSILLECTOMY	20[redacted]
SURGERY: LAPAROSCOPIC SLEEVE GASTRECTOMY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 399	231
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 400		

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]
SULFASALAZINE	1 g	BID	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -318
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[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
MELOXICAM	15 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -101	NOT REPORTED
LIDOCAINE	10 mL	QD	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 79

Event #1: Serious Adverse Event

Event Description TOENAILS INGROWN WORSENING

Preferred term 嵌入爪

AE Onset Date / Rx Day [redacted]20[redacted] / 79

Age at AE Onset 4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 79): PARTIAL RESECTION OF BOTH TOENAILS AND NAILBEDS:; X-RAY OF FEET: RIGHT TOE DISTAL PHALANX MARGINAL OSTEITIS (NONSEPTIC)

AE Stopped Rx Day 232

Duration of AE 154 DAYS

Severity Moderate

Relation to Study Drug by Investigator No Reasonable Possibility

Investigator Alternative Etiology REPETITIVE PRESSURE TO THE FEET

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: M15-572

治験責任医師からの報告。本被験者はエストニアの 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が投与され，嵌入爪の悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，肥満，嵌入爪及び現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は嵌入爪の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，嵌入爪の悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は嵌入爪（両側母趾）の外科治療のため入院した。入院時に，足指爪周囲の疼痛，発赤及び腫脹が見られた。同日，足指爪及び爪床の部分切除術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤はリドカインであった。

The patient's past medications include:

SALAZOPYRIN for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Ingrown toe nail (10022015) (Ingrowing nail (10022013)) [v.22.1] [10022015]

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 TOENAILS INGROWN WORSENING

- Investigator: Repetitive pressure to the feet.

- AbbVie: Event is more likely related to pre-existing history of toenails ingrown.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] FOOT X-RAY:** Right toe distal phalanx marginal osteitis (nonseptic).

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

Reason for Narrative

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

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

Medical History	Onset Year
MIGRAINE HEADACHE	NOT REPORTED
OTHER: PLAQUE PSORIASIS	19[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: RIGHT MEDIAN NEUROLYSIS	20[redacted]
OTHER: LEFT MEDIAN NEUROLYSIS	20[redacted]
OTHER: HEAD TRAUMA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HERNIATED DISC SURGERY	19[redacted]
SURGERY: KNEE RIGHT MENISCECTOMY	19[redacted]
SURGERY: SYNOVECTOMY	19[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	18	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 393	224
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 394	[redacted]20[redacted] / 782	389

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
LEFLUNOMIDE	10 mg	QD	Y-M: 20[redacted] / -347
NIMESULIDE	100 mg	PRN	Y-M: 20[redacted] / -55
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -55
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -31

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
NIMESULIDE	100 mg	PRN	Y-M: 20[redacted] / -55	ONGOING
COLECALCIFEROL	25000 IU	EVERY 2 WEEKS	Y-M: 20[redacted] / 1	ONGOING
ACICLOVIR	5 %	OTHER: THREE TIMES AT DAY	Y-M: 20[redacted] / 478	Y-M: 20[redacted] / 485
BRIVUDINE	125 mg	QD	Y-M: 20[redacted] / 478	Y-M: 20[redacted] / 485
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / 729	ONGOING
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 782	Y-M: 20[redacted] / 789
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 783	Y-M: 20[redacted] / 789
METRONIDAZOLE	250 mg	BID	Y-M: 20[redacted] / 790	Y-M: 20[redacted] / 790
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 802	ONGOING
METRONIDAZOLE	250 mg	BID	Y-M: 20[redacted] / 803	ONGOING

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

Event Description DIVERTICULITIS

Preferred term 憩室炎

AE Onset Date / Rx Day [redacted]20[redacted] / 782

Age at AE Onset 5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 782): Blood Urea Nitrogen: 14,2 [9 - 23] mg/dL; Creatinine: 68 [62 - 115] UMOL/L; Erythrocytes: 4.1 [4.5 - 6] 10^12/L; Glucose: 86,5 [70 - 100] mg/dL; Hematocrit: 37,1 [40 - 52] %; Hemoglobin: 126 [140 - 175] G/L; Leukocytes: 11,57 [4 - 10] 10^3/uL; NPTST525-PROCALCITONINE: 0.05 [0.01 - 0.5] NG/ML; Platelets: 310 [150 - 450] 10^9/L; Potassium: 3.5 [3.5 - 5.5] MMOL/L; Sodium: 139,3 [132 - 146] mmol/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 782): CHEST X-RAY: NORMAL; [redacted]20[redacted] (RX DAY 783): CT ABDOMEN: DIVERTICULITIS

AE Stopped Rx Day ONGOING

Duration of AE ONGOING

Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はイタリアの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，憩室炎の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，乾癬性関節炎，元喫煙者（1 日 2 箱を 18 年間）及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は憩室炎を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は異常高熱及び左側腹痛で入院した。抗生物質療法が開始され，腹部 CT 検査により憩室炎との診断が確定した。同日，詳細不明の外科的検査が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，症状が消失し，被験者は退院した。

本事象により治験薬の投与が完全に中止された。

投与された薬剤は，metronidazolo 及びセフトリアキソンであった。

The patient's past medications include:

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

LEFLUNOMIDE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Diverticulitis (10013538) (Diverticulitis (10013538)) [v.23.0] [10013538]

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 DIVERTICULITIS

- Investigator: Not applicable.

- AbbVie: Risk factors include concomitant use of NSAIDs and Prednisone increasing the risk of developing diverticulitis, high BMI(>25) and increasing age. The prevalence of diverticulosis increases with age from less than 20 percent at age 40 to 60 percent by age 60.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ABDOMINAL CT:** Diverticulitis.

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 14.2 mg/dL (normal 9 to 23)

[redacted] 20[redacted] **BMI:** 25.31 kg/m2

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

[redacted] 20[redacted] **CREATININE:** 0.77 mg/dL (normal 0.70 to 1.30)

[redacted] 20[redacted] **GLUCOSE:** 86.5 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **HEMATOCRIT:** 37.1 % (normal 40 to 52)

[redacted] **20[redacted] HEMOGLOBIN:** 12.6 G/DL (normal 14 to 17.5)

[redacted] **20[redacted] PLATELET COUNT:** 310 X10**3/MCL (normal 150 to 450)

[redacted] **20[redacted] POTASSIUM:** 3.5 MMOL/L (normal 3.5 to 5.5)

[redacted] **20[redacted] PROCALCITONINE:** 0.05 NG/ML (normal 0.01 to 0.50)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.13 X10**6/MCL (normal 4.5 to 6)

[redacted] **20[redacted] SODIUM:** 139.5 MMOL/L (normal 132 to 146)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.57 X10**3/MCL (normal 4 to 10)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
尿路性敗血症	X	X		X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	8[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: GONARTHROSIS	NOT REPORTED
OTHER: PLAQUE PSORIASIS	19[redacted]
HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: UROSEPSIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: RIGHT LEG AMPUTATION	1987

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	30	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 10	[redacted]20[redacted] / 46	46

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
RAMIPRIL	2.5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
LEFLUNOMIDE	20 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -96
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -35

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
RAMIPRIL	2.5 mg	QD	Y-M: 20[redacted]	ONGOING
LEFLUNOMIDE	20 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]	Y-M: 20[redacted] / 47
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -96	ONGOING
ALENDRONIC ACID	70 mg	EVERY WEEK	Y-M: 20[redacted] / 14	ONGOING
COLECALCIFEROL	25000 IU	EVERY WEEK	Y-M: 20[redacted] / 14	ONGOING
PRAVASTATIN	20 mg	QD	Y-M: 20[redacted] / 36	ONGOING
PARACETAMOL	1000 mg	BID	Y-M: 20[redacted] / 47	ONGOING
CEFIXIME	400 mg	QD	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 50

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

Event Description	UROSEPSIS
Preferred term	尿路性敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 47 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	8[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 51): NPTST525-PROCALCITONINE: 0.92 [0.05 - 0.5] NG/ML; [redacted]20[redacted] (RX DAY 64): Calcium: 2.05 [2.07 - 2.64] MMOL/L; Creatinine: 53 [62 - 115] UMOL/L; Erythrocytes: 2.8 [4.5 - 6] 10^12/L; Hematocrit: 0.26 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 88 [140 - 175] G/L; Leukocytes: 4 [10 - 10.7] 10^9/L; NPTST127-C REACTIVE PROTEIN: 10 [0.02 - 0.5] MG/DL; NPTST141-CALCITONINE: 0.11 [0.05 - 0.5] NG/ML; NPTST662-UREA: 8 [5 - 23] MG/DL; Platelets: 471 [150 - 450] 10^9/L; Potassium: 3.9 [3.5 - 5.5] MMOL/L; Sodium: 136 [132 - 146] MMOL/L; Urate: 166.56 [202.25 - 416.39] UMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 52): BLOOD NPTST025-AEROBI HEMOCOLTURE: Negative; [redacted]20[redacted] (RX DAY 58): URINE NPTST670-URINE CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 50): CHEST X-RAY: NORMAL

AE Stopped Rx Day	66 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	20 DAYS
Severity	Mild
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: M15-572

治験責任医師からの報告。本被験者はイタリアの 8[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，尿路性敗血症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元喫煙者（1 日 1 箱を 30 年間），局面型乾癬，高血圧，乾癬性関節炎，尿路性敗血症，変形性膝関節症及び現飲酒者（1 日 2～4 杯）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は尿路性敗血症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，尿路性敗血症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は異常高熱及び排尿困難で入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，tachipirina 及びセフィキシムであった。

Causality for UPADACITINIB (Blinded)

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1) Urosepsis (10048709) (Urosepsis (10048709)) [v.22.1] [10048709]

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 UROSEPSIS

- Investigator: Not applicable

- AbbVie: Risk factors include advanced age and past history of urosepsis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BLOOD CULTURE:** Negative

[redacted] **C REACTIVE PROTEIN:** 10 mg/dL (normal 0.02 to 0.50)

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

[redacted] **CREATININE:** 0.6 mg/dL (normal 0.7 to 1.30)

[redacted] **HEMATOCRIT:** 25.5 % (normal 40 to 52)

[redacted] **HEMOGLOBIN:** 8.8 G/L (normal 14 to 17.5)

[redacted] **PLATELET COUNT:** 471 X10**3/MCL (normal 150 to 450)

[redacted] **RED BLOOD CELLS:** 2.79 X10**6/MCL (normal 4.5 to 6)

[redacted] **WHITE BLOOD CELLS:** 4 X10**3/MM**3 (normal 10 to 10.7)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ニューモシスチス・イロベチイ肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: PROSTATE ABSCESS	20[redacted]
BENIGN PROSTATIC HYPERPLASIA	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDICECTOMY	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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SILODOSIN	8 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -168
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -92

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
SILODOSIN	8 mg	QD	Y-M: 20[redacted]	ONGOING
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -92	Y-M: 20[redacted] / 64
COLECALCIFEROL	100000 IU	OTHER: EVERY MONTH	Y-M: 20[redacted] / 14	ONGOING
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 64
FONDAPARINUX	2.5 mg	QD	Y-M: 20[redacted] / 63	ONGOING
FOLIC ACID	10 mg	QD	Y-M: 20[redacted] / 65	ONGOING
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted] / 65	ONGOING
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 82
BACTRIM	6 OTHER: CAPSULES	QD	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 86
PREDNISONE	12.5 mg	QD	Y-M: 20[redacted] / 83	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zoster

Event Description	PNEUMOCYSTOSIS
Preferred term	ニューモシスチス・イロベチイ肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 50
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 65): Chloride: 104 [99 - 109] MMOL/L; Creatinine: 111 [62 - 115] UMOL/L; Glucose: 180,3 [60 - 110] mg/dL; Hematocrit: 38,3 [40 - 52] %; Hemoglobin: 130 [140 - 175] G/L; NPTST127-C REACTIVE PROTEIN: 3.2 [0 - 0.5] MG/DL; NPTST525-PROCALCITONINE: 0,10 [NOT REPORTED - NOT REPORTED] ng/mL; Potassium: 4.2 [3.5 - 5.5] MMOL/L; Sodium: 140 [132 - 146] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 65): BLOOD NPTST081-B-GLUCAN: Positive-PNEUMOCYSTIS JIROVECI; [redacted]20[redacted] (RX DAY 70): OTHER BRONCHOSCOPY NPTST212-CULTURE FOR AEROBIC AND FUNGAL: Negative; OTHER BRONCHOSCOPY NPTST236-DIRECT MICROSCOPIC EXAMINATION: Negative; [redacted]20[redacted] (RX DAY 73): OTHER BRONCHOLALVEOLAR LAVAGE NPTST284-GALACTOMANNAN DOSAGE FOR ASPERG: Negative-ASPERGILLUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 64): CT OF THE CHEST: PRESENCE OF SHADED GROUND GLASS AREAS WITH DISTRIBUTION PREVALENT IN THE MIDDLE AND UPPER FIELDS; [redacted]20[redacted] (RX DAY 66): BRONCHOSCOPY: NEGATIVE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はイタリアの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，ニューモシスチス症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はニューモシスチス症を発現した。

入院前，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は白血球減少症（非重篤）及びリンパ球減少症（非重篤）と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は表在性静脈血栓症（非重篤）とも診断され，超音波検査で診断が確定した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は発熱及び呼吸困難の徴候・症状を呈し，入院した。20[redacted] 年 [redacted] 月 [redacted] 日，気管支鏡検査が行われ，培養結果は好気性菌及び真菌陰性であった。直接顕微鏡検査でもマイコバクテリア陰性であった。ニューモシスチス肺炎が疑われた。抗生物質の静脈内投与が行われ，症状の改善が見られた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，自宅で抗生物質療法を行うこととなった。

ニューモシスチス症，白血球減少症（非重篤）及びリンパ球減少症（非重篤）の事象により治験薬の投与が完全に中止された。

退院時サマリーによると，被験者は，その他の症状としてこの 1 週間，軽労作時呼吸困難も呈しており，CD4 陽性リンパ球数が約 200/IU との結果が得られていた。診断のための臨床検査及び画像検査が行われた。投与された薬剤は，抗生物質及びステロイドであった。20[redacted] 年 [redacted] 月 [redacted] 日，血中 β-D-グルカンの検査結果が陽性であったことから診断が確定した。入院中，被験者に発熱は見られず，軽労作時呼吸困難は改善した。

投与された薬剤は，アジスロマイシン，bactrim 及び deltacortene であった。

The patient's past medications include:

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pneumocystosis (10035662) (Pneumocystis jirovecii pneumonia (10073755)) [v.22.1] [10035662]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMOCYSTOSIS

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BASOPHILS:** 1.2 %

[redacted] **20[redacted] BLOOD BETA-D-GLUCAN:** Positive, Pneumocystis Jiroveci

[redacted] **20[redacted] BLOOD GLUCOSE:** 180.3 mg/dL (normal 60 to 110)

[redacted] **20[redacted] BRONCHOAVLVEOLAR LAVAGE:** GALACTOMANNAN DOSAGE FOR ASPERGILLUS- Negative Aspergillus identified.

[redacted] **20[redacted] BRONCHOSCOPY:** Pneumocystis - Negative

[redacted] 20[redacted] **BRONCHOSCOPY:** CULTURE FOR AEROBIC ANDFUNGAL BACTERIA- Negative DIRECT MICROSCOPIC EXAMINATION- Negative

[redacted] 20[redacted] **CD 4 POSITIVE LYMPHOCYTES:** 200 cells/IU

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

[redacted] 20[redacted] **CHEST XRAY:** NORMAL

[redacted] 20[redacted] **CHEST XRAY:** NORMAL

[redacted] 20[redacted] **CREATININE:** 1.25 mg/dL (normal 0.7 to 1.3)

[redacted] 20[redacted] **CRP:** 3.99 mg/dL

[redacted] 20[redacted] **CRP:** 3.20 mg/dL (normal 0 to 0.5)

[redacted] 20[redacted] **CT CHEST:** Presence of shaded ground glass areas with parallel distribution prevalent in the middle and upper fields.

[redacted] 20[redacted] **DIRECT MICROSCOPIC EXAMINATION:** Pneumocystis Jirovecii : Negative

[redacted] 20[redacted] **EOSINOPHIL:** 0.3 %

[redacted] 20[redacted] **GALACTOMANNAN TEST:** FOR ASPERGILLUS: POSITIVE VALUE COMPATIBLE WITH PNEUMOCYSTIS

[redacted] 20[redacted] **HEMATOCRIT:** 38.3 % (normal 40 to 52)

[redacted] 20[redacted] **HGB:** 13 G/DL (normal 14 to 17.5)

[redacted] 20[redacted] **LEUKOCYTES:** 4.78 X10**3/MCL

[redacted] 20[redacted] **LEUKOCYTES:** 14.4 X10**3/MCL

[redacted] 20[redacted] **LYMPHOCYTES:** 26.5 %

[redacted] 20[redacted] **LYMPHOCYTES:** 1.26 X10**3/MM**3

[redacted] 20[redacted] **LYMPHOCYTES:** 4.98 X10**3/MM**3

[redacted] 20[redacted] **MONOCYTES:** 8.3 %

[redacted] 20[redacted] **NEUTROPHILS:** 63.7 %

[redacted] 20[redacted] **PCR:** negative for mycobacterium tuberculosis

[redacted] 20[redacted] **PHARYNGEAL SWAB:** Rhinovirus A/B/C : Positive

[redacted] 20[redacted] **PLATELETS:** 398 X10**3/MCL

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
良性前立腺肥大症	X	X		

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: HYPER CHOLESTEROLEMY	NOT REPORTED
PEPTIC ULCER DISEASE: PEPTISCH ULCUS	NOT REPORTED
OTHER: PSORISIS	20[redacted]
OTHER: CARPAL TUNNEL GRADE1 RIGHT	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: PROSTATE HYPERTROPHY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CARPAL TUNNEL RELEASE LEFT	20[redacted]
SURGERY: CARPAL TUNNEL RELEASE RIGHT	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.75 PACK	35	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 240	72

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
COLECALCIFEROL	25000 IU	OTHER: 1/MONTH	Y-M: 20[redacted]-[redacted]

PIROXICAM	20 mg	PRN	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -279
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -278
ETORICOXIB	90 mg	PRN	Y-M: 20[redacted] / -98
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -98
SIMVASTATIN	40 mg	QD	Y-M: 20[redacted] / -47
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / -25

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
COLECALCIFEROL	25000 IU	OTHER: 1/MONTH	Y-M: 20[redacted]	ONGOING
PIROXICAM	20 mg	PRN	Y-M: 20[redacted]	ONGOING
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]	ONGOING
ETORICOXIB	90 mg	PRN	Y-M: 20[redacted] / -98	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -98	ONGOING
SIMVASTATIN	40 mg	QD	Y-M: 20[redacted] / -47	ONGOING
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / -25	ONGOING
TEMOCILLIN	1 g	QD	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 253
VANCOMYCIN	500 mg	QD	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 253
LEVOFLOXACIN	20 mg	QD	Y-M: 20[redacted] / 254	ONGOING

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

Event Description	WORSENING HYPERTROPHY PROSTATE
Preferred term	良性前立腺肥大症
AE Onset Date / Rx Day	[redacted]20[redacted] / 225
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 248): OTHER CELLS OF PROSTATE NPTST148-CARCINOMA TEST: Negative; BLOOD NPTST447-MICROMIOLOGY: Positive-ENTEROCOCCUS FAECALIS AND PROTEUS MIRABILIS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 247): T.U.R.P: NO DISURIA

AE Stopped Rx Day	254 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	30 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	INSUFFICIENT WORKING OFF TAMSULOSINE
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: M15-572

治験責任医師からの報告。本被験者はベルギーの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，前立腺肥大悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，乾癬，乾癬性関節炎，前立腺肥大，消化性潰瘍，高コレステロール血症，喫煙者（1 日 0.75 箱を 35 年間）及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は前立腺肥大悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，前立腺肥大悪化は消失した。

被験者は排尿困難を来していた。泌尿器科医は経尿道的前立腺切除術（TURP）を行うため 2 日間の入院を予定することとした。20[redacted] 年 [redacted] 月 [redacted] 日，全身麻酔下で前立腺切除術が行われた。手術は順調に進んだ。術後 1 日目，被験者は最高 40°C の高熱を来し，抗生物質による治療が必要となった。Negaban が投与され，次いでバンコマイシンが追加された。その後レボフロキサシンの投与が開始され，発熱が治まった。20[redacted] 年 [redacted] 月 [redacted] 日，膀胱カテーテルが問題なく抜去された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。被験者はレボフロキサシンによる治療を約 20 日間継続することとなった。20[redacted] 年 [redacted] 月 [redacted] 日，治験薬の投与が完全に中止された。

投与された薬剤は，バンコマイシン，レボフロキサシン及び negaban であった。

The patient's past medications include:

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Prostatic hypertrophy (10036962) (Benign prostatic hyperplasia (10004446)) [v.22.1] [10036962]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING HYPERTROPHY PROSTATE

- Investigator: Insufficient working of Tamsulosine.

- AbbVie: Risk factor includes pre-existing prostate hypertrophy,

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CARCINOMA TEST:** Cells of prostate: Negative

[redacted] **20[redacted] MICROBIOLOGY (BLOOD):** Positive: Enterococcus faecalis and Proteus mirabilis

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
コロナウイルス感染	X			X

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: ELBOW FRACTURE	19[redacted]
OTHER: HIGH CHOLESTEROL	20[redacted]
OTHER: PSORIASIS PLAQUES	20[redacted]
OTHER: PROSTATIC HYPERTROPHY	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: LUMBAL SURGERY	19[redacted]
SURGERY: ARTHROSCOPY LEFT KNEE	19[redacted]
SURGERY: CARPAL TUNNEL RIGHT	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ADA	40MG	SC	EOW	[redacted]20[redacted] / 170	[redacted]20[redacted] / 393	224
ADA	40MG	SC	EOW	[redacted]20[redacted] / 394		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	80 mg	QD	Y-M: 20[redacted]
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted]
DICLOFENAC	75 mg	PRN	Y-M: 20[redacted] / -204
SULFASALAZINE	1000 mL	BID	Y-M: 20[redacted] / -204

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
ACETYLSALICYLIC ACID	80 mg	QD	Y-M: 20[redacted]	NOT REPORTED
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED
DICLOFENAC	75 mg	PRN	Y-M: 20[redacted] / -204	NOT REPORTED
SULFASALAZINE	500.0 mg	BID	Y-M: 20[redacted] / 345	NOT REPORTED
SPEKTRAMOX	875/125 mg	TID	Y-M: 20[redacted] / 465	Y-M: 20[redacted] / 468
AZITHROMYCIN	500.0 mg	QD	Y-M: 20[redacted] / 469	Y-M: 20[redacted] / 472
CEFTRIAXONE	1.0 g	QD	Y-M: 20[redacted] / 469	Y-M: 20[redacted] / 472
SPEKTRAMOX	850/125 mg	TID	Y-M: 20[redacted] / 472	Y-M: 20[redacted] / 475

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

Event Description COVID-19 POSITIVE INFECTION

Preferred term コロナウイルス感染

AE Onset Date / Rx Day [redacted]20[redacted] / 461

Age at AE Onset 7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 468): Alanine Aminotransferase: 125 [0 - 41] U/L; Aspartate Aminotransferase: 74 [0 - 40] U/L; Leukocytes: 3.7 [4.5 - 11] 10^9/L; NPTST209-CRP: 47.6 [0 - 5] MG/L; NPTST225-D-DIMEREN: 4 [0 - 0.5] UG FIB.EQ./ML; [redacted]20[redacted] (RX DAY 470): Aspartate Aminotransferase: 109 [0 - 41] U/L; Aspartate Aminotransferase: 56 [0 - 40] U/L; Leukocytes: 4.4 [4.5 - 11] 10^9/L; NPTST209-CRP: 26.8 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 468): OTHER NASOPHARYNGEAL SPECIMEN NPTST584-RT-PCR: Positive-SARS-COV-2 VIRUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 468): RX-THORAX: PERI-BRONCHIAL INFILTRATES, WITH AN IMPRESSION OF SCATTERED FROSTED GLASS ASPECT ACROSS BOTH LUNG FIELDS. UNDERLYING VIRAL PNEUMONIA POSSIBLE. NO SIGNS OF ACUTE THRUST. NO SIGNS OF PNEUMOTHORAX OR PLEURAL FLUID; [redacted]20[redacted]

(RX DAY 469): ECG: SINUSAL, 1ST DEGREE AV BLOCK, VOLTAGE CRITERIA FOR LEFT VENTRICLE HYPERTROPHY, QTC 406 MSEC

AE Stopped Rx Day	475
Duration of AE	15 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	VIRAL INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はベルギーの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，新型コロナウイルス感染症陽性の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，コレステロール高値，乾癬性関節炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は新型コロナウイルス感染症陽性を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，新型コロナウイルス感染症陽性は消失した。

10 日前から胃痛及び呼吸困難が生じていた。20[redacted] 年 [redacted] 月 [redacted] 日から抗生物質の投与が開始されていた。食欲減退が見られたが，水分補給は十分に行っていた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 37°C の発熱，呼吸困難及び腹痛のため入院した。胸郭痛はなく，咳嗽もそれほどなかった。重複感染の可能性とモビリゼーションで，経鼻酸素投与と経験的抗生物質療法（セフトリアキソン及びアジスロマイシン）による治療が開始された。それにより，好ましい進展が見られた。20[redacted] 年 [redacted] 月 [redacted] 日，咳嗽などの呼吸器症状，息切れ，38°C の発熱が見られた。CRP は 47 mg/L に増加しており，酸素飽和度は 92%であった。被験者はオーグメンチン 7 日分を処方され，2 週間

の自宅待機を指示された。被験者は完全に治癒した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，オーグメンチン，amoxiclav，セフトリアキソン及びアジスロマイシンであった。

Causality for UPADACITINIB (Blinded)

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1) Corona virus infection (10053983) (Coronavirus infection (10051905)) [v.23.0] [10053983]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 POSITIVE INFECTION

- Investigator: viral infection

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY (SCREENING):** normal

[redacted] **20[redacted] CRP:** 47.6 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] CRP:** 47 MG/L

[redacted] **20[redacted] CRP:** 26.8 MG/L (normal 0 to 5.0)

[redacted] **20[redacted] D-DIMER:** >4.0 (099¥¥ug fib.eq./mL)

[redacted] **20[redacted] ECG:** Sinusal, 1st degree AV block, voltage criteria for left ventricle hypertrophy, QTc 406 msec

[redacted] **20[redacted] GOT (AST):** 74.0 U/L (normal 0.0 to 0.0)

[redacted] **20[redacted] GOT (AST):** 56.0 U/L (normal 0.0 to 40.0)

[redacted] **20[redacted] GPT (ALT):** 125.0 U/L (normal 0 to 41)

[redacted] **20[redacted] GPT (ALT):** 109 U/L (normal 0 to 41)

20[redacted] NASOPHARYNGEAL SWAB: Positive COVID-19

[redacted] **20[redacted] RT-PCR:** SARS-COV-2 VIRUS positive (sputum)

[redacted] **20[redacted] RX THORAX:** Peri-bronchial infiltrates, with an impression of scattered frosted glass aspect across both lung fields. Underlying viral pneumonia possible. No signs of acute thrust. No signs of pneumothorax or pleural fluid.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3.7 10^3/uL (normal 4.5 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.4 10^3/uL (normal 4.5 to 11.0)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
神経内分泌癌	X	X		X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: NAIL PSORIASIS	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: DIABETES	20[redacted]
DIVERTICULITIS: LEFT COLON	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: KNEE PROTHESE BILATERAL	20[redacted]
SURGERY: STENTING CARDIAC CORONARY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	35	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PSORALENS FOR SYSTEMIC USE	NOT REPORTED	OTHER: 3/WEEK	Y-M: 19[redacted]
METFORMIN	500 mg	QD	Y-M: 20[redacted]
ACITRETIN	25 mg	OTHER: 3/WEEK	Y-M: 20[redacted]
DAIVOBET	50 ug	PRN	Y-M: 20[redacted]

PROPYSALIC NF	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
XAMIOL	50 ug	PRN	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
ACETYLSALICYLIC ACID	80 mg	QD	Y-M: 20[redacted] / -126
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted] / -126
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / -126
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -126
PNEUMOCOCCAL VACCINE	1 mL	OTHER: ONCE	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
METFORMIN	500 mg	QD	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	80 mg	QD	Y-M: 20[redacted] / -126	ONGOING
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted] / -126	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / -126	ONGOING
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -126	ONGOING
CARBOPLATIN W/ETOPOSIDE	UN OTHER: UN	QD	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 93

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 NEURO-ENDOCRIENE CARCINOMA OF UNKNOWN PRIMARY SITE

Preferred term 神経内分泌癌

AE Onset Date / Rx Day [redacted]20[redacted] / 37

Age at AE Onset 7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 72): NPTST147-CARCINO EMBRYONIC ANTIGEN (CEA): 1.3 [0 - 3] UG/L; NPTST467-NEURON SPECIFIC ENOLASE TUMOR M: 634.5 [0 - 16.9] UG/L; NPTST527-PROSTATE SPECIFIC ANTIGEN (PSA): 2.88 [0 - 4] UG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 43): CT THORAX: MULTIPLE MEDISTINAL ADENOPATHIES; RX THORAX FACE PROFILE: NODULAR MEDIASTINAL WIDENING PARAMEDISTINAL RIGHT-SIDED ADENOPATHIES; [redacted]20[redacted] (RX DAY 54): PET CT: MULTIPLE MEDISTINAL ADENOPATHIES; [redacted]20[redacted] (RX DAY 75): CT UROGRAPHY: EXTENSIVE TRANSITIONAL CELL CARCINOMA OF THE LATERAL BLADDER WALL AND UPPER BLADDER; [redacted]20[redacted] (RX DAY 77): SUPRA CLAVIVLAR GLAND LEFT: SMALL CELL CARCINOMA; [redacted]20[redacted] (RX DAY 79): BLADDER BIOPTIE: SMALL CELL CARCINOMA; [redacted]20[redacted] (RX DAY 83): CT ABDOMEN: MULTIPLE ADENOPATHIES RETROPERITONEAL, RETROCRURAL AND LOW MEDIASTINAL. TUMOR ENCASEMENT OF THE LEFT VENA ILIACA COMMUNIS AND EXTEMA; [redacted]20[redacted] (RX DAY 86): NMR PROSTATE: PATHALOGICAL TRANSFORMATION OF SEMINAL VESICLES LEFT WITH DIFFUSION RESTRICTION HYPO-INTENSE NODULE IN THE PERIPHERAL PROSTATE LEFT; [redacted]20[redacted] (RX DAY 91): PORT-A-CATH: NONE

AE Stopped Rx Day ONGOING

Duration of AE ONGOING

Severity Severe

Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	AGE
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: M15-572

治験責任医師からの報告。本被験者はベルギーの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，原発巣不明の神経内分泌癌の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，爪乾癬，局面型乾癬，元喫煙者（1 日 2 箱を 35 年間），糖尿病，乾癬性関節炎及び現飲酒者（1 日 2～4 杯）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は原発巣不明の神経内分泌癌を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は，腹痛，頻尿，排尿困難及び排尿時灼熱感を呈していた。カテーテルが留置され，化学療法が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。被験者には本事象に関連する家族歴はなかった。

投与された薬剤はカルボプラチン／エトポシドであった。

The patient's past medications include:

PUVA for PSORIASIS (19[redacted] - 20[redacted])

NEOTIGASON for PSORIASIS (20[redacted] - 20[redacted])

DOVOBET for PSORIASIS (20[redacted] - [redacted] 20[redacted])

SALICYLACID 4% CLOBETASOLPROPIANATE 0.05% WITH SORBITANSESQUIOLEATE for PSORIASIS (20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Neuroendocrine carcinoma (10057270) (Neuroendocrine carcinoma (10057270)) [v.22.1] [10057270]

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 NEURO-ENDOCRINE CARCINOMA OF UNKNOWN PRIMARY SITE

- Investigator: AGE

- AbbVie: Weak temporal relationship, with only approximately 1 month of study drug exposure prior to the onset of the event. Event's etiology remains unknown at this time in the medical literature.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLADDER BIOPSY:** SMALL CELL CARCINOMA

[redacted] **20[redacted] CARCINO EMBRYONIC ANTIGEN (CEA) TUMOR MARKER:** 1.30 MCG/L (normal 0 to 4)

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

[redacted] **20[redacted] CT ABDOMEN:** Multiple adenopathies retroperitoneal, retrocrural and low mediastinal. Tumor encasement of the left vena iliaca communis and externa.

[redacted] **20[redacted] CT THORAX:** multiple medistinal adenopathies

[redacted] **20[redacted] CT UROGRAPHY:** Extensive transitional cell carcinoma of e lateral bladder wall and upper bladder

[redacted] 20[redacted] NEURON SPECIFIC ENOLASE TUMOR MARKER: 634.5 MCG/L (normal 0 to 16.9)

[redacted] 20[redacted] NMR PROSTATE: pathological transformation of seminal vesicles with diffusion restriction. Hypo-intense nodule in the peripheral prostate left.

[redacted] 20[redacted] PET SCAN: multiple medistinal adenopathies

[redacted] 20[redacted] PROSTATE SPECIFIC ANTIGEN: 2.88 MCG/L (normal 0 to 4)

[redacted] 20[redacted] RIGHT THORAX FACE PROFILE: nodular mediastinal widening paramedistinal right-sided adenopathies

[redacted] 20[redacted] SUPRA CLAVIVLAR GLAND LEFT: SMALL CELL CARCINOMA

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
PEPTIC ULCER DISEASE: ULCER OF STOMACH	20[redacted]
HYPERTENSION	20[redacted]
OTHER: POST-MENOPAUSAL	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 396	227
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 397	[redacted]20[redacted] / 651	255

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	0.5 g	QID	Y-M: 20[redacted]
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -320
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -320
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -139
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -78

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -320	NOT REPORTED
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -78	NOT REPORTED

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	LEFT BREAST CANCER
Preferred term	乳癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 627
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 631): BIOPSY OF BREAST: LEFT BREAST IIA T2N0M0G3, LUMINAL B, HER2-NEGATIVE; ULTRASOUND EXAMINATION OF THE BREASTS AND REGIONAL AREAS: IN THE LEFT AND RIGHT BREASTS, SONOGRAPHIC FINDINGS ARE CONSISTENT WITH INVOLUTION AND DIFFUSE FIBROCYSTIC BREAST CHANGES WITH SIGNS OF LINEAR MAMMARY DUCT ECTASIA TO 3 MM AND FEW CYSTS. THE DUCTS THEMSELVES SHOWS NO LESIONS

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Mild
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はロシア連邦の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左乳癌の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，閉経後，乾癬性関節炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左乳癌を発現した。

20[redacted] 年 [redacted] 月末，被験者は左乳房に腫瘤を発見した。被験者は，その際，詳細な検査を受けた。

医療記録の要約：

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，被験者自身が 2 週間前に発見した左乳房の腫瘤病変について，がん専門医を受診した。診察所見は，乳房が左右均等でなく，一見すると左乳房が右乳房よりも小さかった。乳輪乳頭部は正常に発達しており，乳頭からの分泌物は見られなかった。触診所見は，両側乳房は軟らかく弾力があり，びまん性硬結が認められた。さらに，左乳房外側下部に境界不明瞭な病変（3×2 cm）があった。所属リンパ節は触診不能であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，別のがん専門医を受診した。被験者は，左乳癌，病期 IIA，T2N0M0G3，luminal B（her2 陰性）と診断された。診察所見は，乳房は左右均等で，変形は見られなかった。乳頭からの分泌物は見られなかった。左乳房の外側上部と外側下部との境界に，最大 3.5 cm の結節性領域があった。結節性領域は高密度で，適度に可動性があり，痛みはなかった。触診で，両側の区域にも結節性病変は認められなかった。

本事象により治験薬の投与が完全に中止された。

The patient's past medications include:

SULFASALAZINE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MOVALIS for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Breast cancer (10006187) (Breast cancer (10006187)) [v.23.0] [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 LEFT BREAST CANCER

- Investigator: Not applicable.

- AbbVie: Breast cancer is themost common diagnosed cancer in Russia and the leading cause of oncological mortality in Russian women.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BIOPSY OF BREAST:** LEFT BREAST IIA T2N0M0G3, LUMINAL B, HER2-NEGATIVE

20[redacted] CYTOLOGY: Reveals cells that are suspicious for being cancer cells.

[redacted] **20[redacted] MAMMOGRAPHY:** A lesion (20 x 25 mm) in the left breast.

[redacted] **20[redacted] ULTRASOUND EXAMINATION OF THE BREASTS AND REGIONAL AREAS:** In the left and right breasts, sonographic findings are consistent with involution and diffuse fibrocystic breast changes with signs of linear mammary duct ectasia to 3 mm and few cysts. The ducts themselves shows no lesions. Sonographic signs of a nodular lesion in the left breast - BIRADS - 5. At the moment of the examination, the regional areas show no abnormalities in the presence of involution and fibrocystic mastopathy.

[redacted] **20[redacted] ULTRASOUND EXAMINATION OF THE BREASTS AND REGIONAL LYMPH NODES:** A lesion with microcalcifications (28 x 220 x 20 mm) in the lower outer quadrant of the left breast. The supraclavicular, subclavian and axillary lymph nodes show no abnormalities.

20[redacted] WHOLE-BODY PET-CT SCAN: Not available.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
胃腸出血	X			
H1N1 インフルエンザ	X	X		X
肺塞栓症	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OSTEOPOROSIS	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
DEPRESSION: NO FUTHER SPECIFICATION AVAILABLE ACCEPT THE USE OF AMYTRIPTTILINE AND PSYCHOLOGICAL CARE	20[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]
HYPERLIPIDEMIA: USE OF SIMVASTATINE	20[redacted]
HYPERTENSION	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	44	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 205	36

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
AMITRIPTYLINE	50 MORNING 100 AFTERNOON mg	BID	Y-M: 20[redacted]
COLECALCIFEROL	25.000 OTHER: IE/ML	EVERY WEEK	Y-M: 20[redacted]
SIMVASTATIN	40 mg	QD	Y-M: 20[redacted]
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted] / -51

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 205
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 205
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 209
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]	ONGOING
AMITRIPTYLINE	50 MORNING 100 AFTERNOON mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 205
COLECALCIFEROL	25.000 OTHER: IE/ML	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 205
SIMVASTATIN	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 205
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted] / -51	ONGOING
AMOXICILLIN	1000 mg	QID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 206
CEFOTAXIME	1000 mg	QID	Y-M: 20[redacted] / 206	Y-M: 20[redacted] / 208
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / 206	Y-M: 20[redacted] / 208
BACTRIM	1920 mg	BID	Y-M: 20[redacted] / 206	Y-M: 20[redacted] / 211
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 209	ONGOING
ANIDULAFUNGIN	100 mg	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 243
VORICONAZOLE	3 mg/kg	BID	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 243
AMPHOTERICIN B	50 mg	QD	Y-M: 20[redacted] / 213	Y-M: 20[redacted] / 237
HEPARIN	1100 OTHER: IE/HOUR	OTHER: ALL DAY	Y-M: 20[redacted] / 213	Y-M: 20[redacted] / 243

BACTRIM	480 mg	QD	Y-M: 20[redacted]- / 226	ONGOING
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted]- / 226	ONGOING

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

Event Description	H1N1 INFLUENZA
Preferred term	H1N1 インフルエンザ
AE Onset Date / Rx Day	[redacted]20[redacted] / 205
Age at AE Onset	6[redacted]
Laboratory Testing	

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 206): BLOOD NPTST390-INFLUENZA TYPE A: Positive-NO OTHER RELEVANT FINDINGS; BLOOD NPTST485-ONFLUENZA TYPE A H1MEXICO: Positive-NO OTHER RELEVANT FINDINGS; BLOOD NPTST518-PNEUMOCYTIS JIROVECII PCR: Negative; [redacted]20[redacted] (RX DAY 221): BLOOD NPTST075-ASPERGILLUS PCR: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 204): CHEST X RAY: POSSIBLE LITTLE INFILTRATION; [redacted]20[redacted] (RX DAY 206): BAL: RESOLVED; CHEST X RAY: MULTIPLE INFILTRATION; MECHANICAL VENTILATION: RESOLVED; STOMAC TUBE PLACEMENT: RESOLVED; [redacted]20[redacted] (RX DAY 207): CHEST X RAY: INCREASE IN INFILTRATIONS; CONTINUOUS VENO-VENOUS HEMOFILTRATION: RESOLVED; [redacted]20[redacted] (RX DAY 209): GASTROSCOPY: GASTRO-INTESTINAL BLEEDING. CLIPPED. RESULT: BLEEDING STOPPED, AT [redacted] 20[redacted]; [redacted]20[redacted] (RX DAY 213): CT-THORAX: PULMONARY EMBOLISM; [redacted]20[redacted] (RX DAY 226): CHEST CT: AREAS OF CONSOLIDATION; [redacted]20[redacted] (RX DAY 227): CT CEREBRUM: NO MENINGITIS; EEG: NO EPILEPSY; LUMBAR PUNCTURE: NO MENINGITIS

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, PERSIST OR SIGNIF DISABILITY/INCAPACITY, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

Event #3: Serious Adverse Event

Event Description	GASTRO INTESTINAL BLEEDING
Preferred term	胃腸出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 209 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 209): GASTOSCOPIC CLIPPING ADF A VESSEL IN THE STOMAC: BLEEDING STOPPED 2 DAYS LATER

AE Stopped Rx Day	211 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CONCOMMITENT MEDICATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	LIFE THREATENING

Event #5: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 213 (8 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 207): CHEST CT: SUBSEGMENTAL PULMOARY EMBOLISM; [redacted]20[redacted] (RX DAY 213): CHEST X RAY: UNKNOWN, INFORMATION NOT AVAILABLE

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, LIFE THREATENING

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はオランダの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，H1N1 インフルエンザ，肺塞栓症及び胃腸出血の事象を発現した。

Event 2，3 及び 5 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，高血圧，喫煙者（1 日 1 箱を 44 年間）現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は H1N1 インフルエンザを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃腸出血を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胃腸出血は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺塞栓症を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，咳嗽，呼吸困難及び最高 38.8°C の発熱のため，救急治療室を受診した。被験者は重複感染を伴う A 型インフルエンザと診断されて入院した。血清学的検査の結果は A 型インフルエンザ陽性であった。胸部 X 線検査で肺炎に見られるような陰影が認められたため，まずアモキシシリンの投与が開始された。呼吸不全が認められたため，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に ICU に入院した。抗生物質はセフォタキシム及びシプロフロキサシンに変更され，それと同時に Optiflow による呼吸補助が行われた。呼吸不全が続いたため，挿管及び機械的換気が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，気管支鏡検査及び気管支肺胞洗浄検査が行われた。PJP 及びアスペルギルス症の疑いに対する治療が行われた。持続的な酸素化障害のため，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に他の医療センターに転院となった。被験者は，A 型インフルエンザ，肺炎及び侵襲性アスペルギルス症疑いによる呼吸不全を来していた。ICU にて被験者が急性呼吸不全に陥ったため，カテーテルが留置され，継続的な静脈-静脈血液ろ過が行われた。CT スキャン検査で亜区域性肺塞栓症が明らかとなり，ヘパリンの静脈内投与が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は上部消化管出血を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胃内視鏡検査及びクリッピングが行われた。出血は 2 日後に止まった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺アスペルギルス症（非重篤）を発現した。この被験者の治験薬の投与は完全に中止された。20[redacted] 年 [redacted] 月 [redacted] 日，依然として人工呼吸下にあった被験者は，他院の ICU に転院となった。20[redacted] 年 [redacted] 月 [redacted] 日，胸部 CT 検査で感染症と一致する結果が認められた。投与された薬剤は，prednisone 及び cotrimoxazole であった。鎮静剤の漸減後，攣縮及び頚部硬直を伴うグラスゴー昏睡尺度の変動が認められた。腰椎穿刺検査及び頭部 CT 検査で髄膜炎は認められなかった。脳波検査でてんかんは認められなかった。神経症状はボリコナゾールの副作用であると考えられた。20[redacted] 年 [redacted] 月 [redacted] 日，気管カニューレが抜去された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，理学療法を受けるため，ICU から回復室に移された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

医療記録より：中心静脈カテーテル及び動脈カテーテルが留置された。大動脈内バルーンポンプが留置され，継続的な静脈-静脈血液ろ過／透析が行われた。気管切開が行われ，換気が開

始された。血液製剤が投与された。担当医によると，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，細菌重複感染を伴うインフルエンザによる入院後に肺診療科から転科した。その日の夕方，被験者の状態が悪化し，MEWS のいくつかの項目のスコアが高く，低酸素血症が進行し（15 L で 92%），40°C の発熱が見られた。胸部 X 線検査で著しい両側斑点形成が認められ，両側性肺炎が示唆された。診察所見は，両膝関節に斑点形成あり，腹部軟で圧痛なし，腓腹部軟で浮腫なし，肺胞呼吸音は両肺で強い捻髪音，血行動態安定，頻脈なし，血圧良好であった。この 24 時間で 4 L の輸液が投与された。その日の夕方に被験者の状態が悪化したため，「EMV」は最大値となった。気管支痙攣は認められず，酸素飽和度に改善が見られた。心電図検査の結果は正常で，血行動態も安定していた。被験者は，細菌重複感染を伴う A 型インフルエンザによる呼吸不全のため，Optiflow 装着下の状態にあった。「LD」増加によりニューモシスチス・イロベチイ肺炎の鑑別診断も行われた。PJP 及びアスペルギルスの培養検査が行われた。

投与された薬剤は，カリウム，プレドニゾロン，cotrim，cotrimoxazole，anidulafungin，ボリコナゾール，ヘパリン，pantoprazol，anidulafungine，クラフォラン，ciproxin，co trimoxazol，エリスロマイシン，ボリコナゾール及びアモキシシリンであった。

Causality for UPADACITINIB (Blinded)

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1) H1N1 influenza (10069767) (H1N1 influenza (10069767)) [v.22.0] [10069767]

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

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

Dechallenge: No

2) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.22.0] [10037377]

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

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

Dechallenge: Not Applicable

3) Gastro intestinal bleeding (10017871) (Gastrointestinal haemorrhage (10017955)) [v.22.0] [10017871]

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 H1N1 INFLUENZA

- Investigator: INFLUENZA SEASON IN THE NETHERLANDS

- AbbVie: COMMON SEASONAL VIRAL INFECTION IN THE GENERAL POPULATION. SUBJECT'S EXTENSIVE SMOKING HISTORY (1 PPD FOR 44 YEARS) IS AN ADDITIONAL RISK FACTOR FOR AN INFLUENZA INFECTION THAT IS MORE SEVERE AND ASSOCIATED WITH AN INCREASE IN COMPLICATIONS.

Event of PULMONARY EMBOLISM

- Investigator: Not applicable

- AbbVie: Risk factor includes current hospitalization for influenza infection which required mechanical ventilation with subsequent immobilization.

Event of GASTRO INTESTINAL BLEEDING

- Investigator: Concomitant medication

- AbbVie: Risk factor includes current ICU hospitalization for influenza infection which required mechanical ventilation.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ASPERGILLOSIS PCR:** Negative

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

[redacted] **CHEST CT:** subsegmental pulmonary embolism

[redacted] **CHEST CT:** No cavities seen, areas of consolidation in particular sub-pleural, most pronounced in the fields appropriate to an infection or an organizing pneumonia; no signs of sub segmental PE visible

[redacted] **20[redacted] CHEST X-RAY:** bilateral heavy mottling and suggestive of bilateral pneumonia

[redacted] **20[redacted] CHEST XRAY:** pulmonary shadow

[redacted] **20[redacted] CHEST XRAY:** Multiple infiltration

[redacted] **20[redacted] CHEST XRAY:** Increase in infiltration

[redacted] **20[redacted] CT HEAD:** No meningitis

[redacted] **20[redacted] CT THORAX:** Pulmonary embolism

[redacted] **20[redacted] EEG:** Epilepsy

[redacted] **20[redacted] EKG:** Normal

[redacted] **20[redacted] GASTROSCOPY:** erosions

[redacted] **20[redacted] INFLUENZA A SEROLOGY EST:** Positive

[redacted] **20[redacted] INFLUENZA TYPE A H1MEXICO:** Positive

[redacted] **20[redacted] LUMBAR PUNCTURE:** No meningitis

[redacted] **20[redacted] PJP PCR:** Negative

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
黄疸	X			X
遠隔転移を伴う膵癌	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	MALE	WHITE

Medical History	Onset Year
HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: ERECTIL DYSFUNCTION	20[redacted]
OTHER: ACTIVE PLAQUE PSORIASIS	20[redacted]
OTHER: HYPERGLYCEMIA	20[redacted]
OTHER: HEMATURIA	20[redacted]
OTHER: PROTEINURIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: RIGHT KNEE BALLL JOINT SURGICAL REMOVED	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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 167	167
ADA	40MG	SC	EOW	[redacted]20[redacted] / 168	[redacted]20[redacted] / 391	224
ADA	40MG	SC	EOW	[redacted]20[redacted] / 392	[redacted]20[redacted] / 502	111

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DICLOFENAC	50 mg	PRN	Y-M: 20[redacted] / -354
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -173
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -173
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -173
NAPROXEN	500 mg	BID	Y-M: 20[redacted] / -173
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -173

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
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -173	Y-M: 20[redacted] / 514
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -173	Y-M: 20[redacted] / 514
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -173	Y-M: 20[redacted] / 514
NAPROXEN	500 mg	BID	Y-M: 20[redacted] / -173	Y-M: 20[redacted] / 514
HYDROCORTISONE	10 OTHER: MG/G	TID	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 514
METFORMIN	500 mg	BID	Y-M: 20[redacted] / 225	Y-M: 20[redacted] / 514
RAMIPRIL	5 mg	BID	Y-M: 20[redacted] / 295	Y-M: 20[redacted] / 514
CYCLOBENZAPRINE	5 mg	QD	Y-M: 20[redacted] / 483	Y-M: 20[redacted] / 514
I.V. SOLUTIONS	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / 515	Y-M: 20[redacted] / 516
CALCIUM FOLINATE W/FLUOROURACIL/IRI	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 555	ONGOING

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 PRIMARY METASTATIC PANCREAS NEOPLASIA

Preferred term 遠隔転移を伴う膵癌

AE Onset Date / Rx Day [redacted]20[redacted] / 474

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 392): NPTST548-QUANTIFERON GOLD INTER: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST549-QUANTIFERON GOLD MITOGEN: >10.00 [NOT REPORTED - NOT REPORTED] IU/mL; NPTST550-QUANTIFERON GOLD NIL: 0.07 [NOT REPORTED - NOT REPORTED] IU/mL; NPTST551-QUANTIFERON GOLD TB1: 1.13 [NOT REPORTED - NOT REPORTED] IU/mL; NPTST552-QUANTIFERON GOLD TB2: 1.00 [NOT REPORTED - NOT REPORTED] IU/mL; [redacted]20[redacted] (RX DAY 400): NPTST548-QUANTIFERON GOLD INTER: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST549-QUANTIFERON GOLD MITOGEN: >10.00 [NOT REPORTED - NOT REPORTED] IU/mL; NPTST550-QUANTIFERON GOLD NIL: 0.06 [NOT REPORTED - NOT REPORTED] IU/mL; NPTST551-QUANTIFERON GOLD TB1: 0.34 [NOT REPORTED - NOT REPORTED] IU/mL; NPTST552-QUANTIFERON GOLD TB2: 0.50 [NOT REPORTED - NOT REPORTED] IU/mL; [redacted]20[redacted] (RX DAY 501): NPTST017-ACTIVATED PARCIAL PROTHROMBIN T: 28.4 [23 - 38] SEC; NPTST537-PROTHROMBIN TIME: 13.5 [0 - 14] SEC; NPTST542-PT / APTT: 0.9 [0 - 1.2] RATIO; Prothrombin Intl. Normalized Ratio: 1.3 [0.8 - 1.1] RATIO

Microbiology

[redacted]20[redacted] (RX DAY 501): BLOOD NPTST461-MYCOBACTERIAL CULTURAL EXAMINAT: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 474): THORACOABDOMINOPELVIC CT: PRIMARY METASTATIC PANCREAS NEOPLASIA; [redacted]20[redacted] (RX DAY 507): PANCREATIC BIOPSY: INSUFFICIENT SAMPLE BUT FAVORS PANCREATIC CARCINOMA

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Event #2: Serious Adverse Event, Event of Interest - Hepatic Disorder

Event Description	JAUNDICE
Preferred term	黄疸
AE Onset Date / Rx Day	[redacted]20[redacted] / 514 (17 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 514): Alanine Aminotransferase: 234 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Alkaline Phosphatase: 290 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Aspartate Aminotransferase: 139 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Bilirubin: 6.84 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Creatinine: 0.61 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 119 [131 - 172] G/L; Leukocytes: 6200 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST041-AMYLASE: 28 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST209-CRP: 2.75 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST662-UREA: 26 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 193000 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 4.29 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Sodium: 136 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 515): Alanine Aminotransferase: 161 [NOT REPORTED - 41] U/L; Albumin: 41 [35 - 52] G/L; Aspartate Aminotransferase: 99 [0 - 40] U/L; Basophils/Leukocytes: 0.8 [0 - 2] %; Bilirubin: ++ [NOT REPORTED - NOT REPORTED] POSITIVE; Bilirubin: 6.79 [NOT REPORTED - 1.4] mg/dL; Calcium: 2.4 [2.2 - 2.55] MMOL/L; Chloride: 98 [98 - 107] MMOL/L; Creatine Kinase: 43 [0 - 190] U/L; Creatinine: 50 [62 - 106] UMOL/L; Eosinophils/Leukocytes: 2.2 [1 - 6] %; Erythrocytes: 4 [4.4 - 5.9] 10^12/L; Glucose: 0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: 5.8 [4.1 - 5.9] MMOL/L; Hematocrit: 0.35 [0.41 - 0.5] FRACTION OF 1; Hemoglobin: 114 [130 - 170] G/L; Hemoglobin: + [NOT REPORTED - NOT REPORTED] POSITIVE; Leukocytes: 4.8 [4 - 10] 10^9/L; Lymphocytes/Leukocytes: 15.3 [20 - 40] %; Monocytes/Leukocytes: 11.7 [2 - 11.7] %; NPTST016-AC VHC: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST071-APTT: 30.1 [23 - 38] SEC; NPTST129-C-REACTIVE PROTEIN: 2.54 [NOT REPORTED - 0.5] mg/dL; NPTST298-GGT: 683 [10 - 71] U/L; NPTST397-KETONE BODIES: POSITIVE [NOT REPORTED - NOT REPORTED] POSITIVE; NPTST405-LDH: 175 [135 - 225] U/L; NPTST412-LIPASE: 33 [13 - 60] U/L; NPTST422-MAGNESIUM: 1.8 [1.6 - 2.4] MG/DL; NPTST631-TOTAL AMYLASE: 26 [NOT REPORTED - 110] U/L; NPTST655-TSH: 0.3 [0.27 - 4.2] UIU/ML; NPTST662-UREA: 25 [17 - 49] MG/DL; Neutrophils/Leukocytes: 70 [40 - 80] %; Phosphate: 0.87 [0.81 - 1.45] MMOL/L; Platelets: 179 [150 - 400] 10^9/L; Potassium: 3.9 [3.5 - 5.1] MMOL/L; Protein: 69 [64 - 83] G/L; Protein: 0.15-0.25 [NOT REPORTED - NOT REPORTED] G/L; Prothrombin Intl. Normalized Ratio: 1.4 [0.8 - 1.1] RATIO; Sodium: 138 [136 - 145] MMOL/L; Specific Gravity: 1.026 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; pH: 7.434 [7.35 - 7.45] UNIT NOT REPORTED; pH: 6.5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 516): Alanine Aminotransferase: 147 [NOT REPORTED - 41] U/L; Albumin: 41 [35 - 52] G/L; Aspartate Aminotransferase: 90 [NOT REPORTED - 40] U/L; Basophils/Leukocytes: 1 [0 - 2] %; Bilirubin: 116.79 [NOT REPORTED - 23.94] umol/L; Chloride: 100 [98 - 107] MMOL/L; Creatinine: 50 [62 - 106] UMOL/L; Eosinophils/Leukocytes: 2.2 [1 - 6] %; Erythrocytes: 4 [4.4 - 5.9] 10^12/L; Hematocrit: 0.34 [0.41 - 0.5] FRACTION OF 1; Hemoglobin: 115 [130 - 170] G/L; Leukocytes: 4.4 [4 - 10] 10^9/L; Lymphocytes/Leukocytes: 12.3 [20 - 40] %; Monocytes/Leukocytes: 11.2 [2 - 11.7] %; NPTST127-C REACTIVE PROTEIN: 3.00 [NOT REPORTED - 0.5] mg/dL; NPTST298-GGT: 660 [10 - 71] U/L; Neutrophils/Leukocytes: 73.3 [40 - 80] %; Platelets: 182 [150 - 400] 10^9/L; Potassium: 3.6 [3.5 - 5.1] MMOL/L; Sodium: 136 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 514): ABDOMINAL CT: LIVER OF CONSERVED DIMENSIONS, REGULAR OUTLINES AND HETEROGENEOUS OPACIFICATION BY THE CONTRAST SUBSTANCE WITH SOME HYPODENSE AREAS IN PROBABLE RELATION WITH FATTY AREAS, AT LEAST 4 HYPODENSE NODULESIN ITS PARENCHYMA, THE LARGEST WITH 40MM IN SEGMENT VI. PATENT LEFT INTRAHEPATIC BILE DUCTS. PANCREAS WITH HYPODENSE AREA WITH ABOUT 6 CM OF MAJOR AXIS IN THE TAIL, WITHOUT CLEAVAGE PLANE WITH LEFT KIDNEY OR ADRENAL. HYPODENSE NODULE ABOUT 7MM IN THE RIGHT ADRENAL GLAND. SMALL LOMBOAORTIC ADENOPATHIES.; [redacted]20[redacted] (RX DAY 515): ABDOMINAL ULTRASOUND: MILD ECTASIA OF INTRAHEPATIC BILE DUCTS FROM LEFT LOBE AND MAIN BILE DUCT. LIVER OF ENLARGED DIMENSIONS AND HETEROGENEOUS STRUCTURE CONDITIONED BY GEOGRAPHIC STEATOSIS AND MULTIPLE HYPOECHOGENIC NODULES THAT CAN BE RELATED WITH THE REFERRED SECONDARY LESIONS; ECG:; PELVIC AND BLADDER ULTRASOUND: BLADDER IN MODERATE REPLETION WITHOUT ASPECTS TO HIGHLIGHT; RENAL ULTRASOUND: KIDNEYS OF INCREASED DIMENSIONS WITH NO EVIDENCE OF SPATIAL LESIONS.; TORAX X-RAY:

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はポルトガルの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，黄疸及び原発性転移性膵臓新生物の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，高血圧，乾癬性関節炎，活動性局面型乾癬，高血糖，血尿，蛋白尿，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は原発性転移性膵臓新生物を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は黄疸を発現した。

被験者は無力症，食欲不振及び体重減少の症状を呈していた。被験者はクォンティフェロン検査で二度にわたって陽性と判定（非重篤の潜伏結核と診断）されたため，20[redacted] 年 [redacted] 月 [redacted] 日に胸腹部 CT スキャン検査が行われ，肝転移を伴う転移性新生物が見つかった。一次治療として緩和的化学療法が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は全身倦怠，悪心，食欲不振，腹痛及び黄疸のため救急治療室を受診した。20[redacted] 年 [redacted] 月 [redacted] 日，点滴静注による水分補給が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は無症状であり，水分補給と休養を指示されて退院した。

投与された薬剤は，folfirinox であった。

The patient's past medications include:

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Jaundice (10023126) (Jaundice (10023126)) [v.23.0] [10023126]

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

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

Dechallenge: Not Applicable

2) Pancreas neoplasm malignant metastatic (10033590) (Pancreatic carcinoma metastatic (10033610)) [v.23.0] [10033590]

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 JAUNDICE

- Investigator: Not applicable

- AbbVie: Event is more likely related to concurrent event of Primary metastatic pancreas neoplasm with hepatic metastases seen on thoracoabdominal CT scan as noted by the PI.

Event of PRIMARY METASTATIC PANCREAS NEOPLASIA

- Investigator: Not Applicable

- AbbVie: Weak temporal association. Study drug exposure is for approximately 15.5 months prior to event onset. Per Johns Hopkins researchers, conservative estimates are that an average of 11.7 years elapses before the first cancer cell develops within a high grade pancreatic lesion, then another 6.8 years as the cancer grows and at least one cell has the potential to spread.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL CT:** Liver of conserved dimensions, regular outlines and heterogeneous opacification by the contrast substance with some hypodense areas in probable relation with fatty areas, at least 4 hypodense nodules in its parenchyma, the largest with 40mm in segment VI. Patent left intrahepatic bile ducts. Pancreas with hypodense area with about 6 cm of major axis in the tail, without cleavage plane with left kidney or adrenal. Hypodense nodule about 7mm in the right adrenal gland. Small lomboaortic adenopathies.

[redacted] **ABDOMINAL ECOGRAPHY:** mild ectasia of intrahepatic bile ducts from left lobe and main bile duct. liver of enlarged dimensions and heterogeneous structure conditioned by geographic steatosis and multiple hypoechogenic nodules that can be related with the referred secondary lesions

[redacted] **AC VHC:** Negative

[redacted] **ACTIVATED PARTIAL PROTHROMBIN TIME:** 28.4 SEC (normal 23 to 38)

[redacted] **ALANINE AMINO TRANSFERASE:** 234 No units

[redacted] **ALANINE AMINO TRANSFERASE:** 147 U/L (normal <41)

[redacted] **ALBUMIN:** 4.1 G/DL (normal 3.5 to 5.2)

[redacted] **ALBUMIN:** 4.1 G/DL (normal 3.5 to 5.2)

[redacted] **ALKALINE PHOSPHATASE:** 290 No units

[redacted] **APTT:** 30.1 SEC (normal 23 to 38)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 139 No units

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 161 U/L (normal <41)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 99 U/L (normal 0 to 40)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 90 U/L (normal <40)

[redacted] **20[redacted] BASOPHILS:** 0.8 % (normal 0 to 2.0)

[redacted] **20[redacted] BASOPHILS:** 1.0 % (normal 0 to 2)

[redacted] **20[redacted] BILIRUBIN:** 116.79 umol/L (normal <23.94)

[redacted] **20[redacted] BIOPSY:** Pancreatic biopsy: insufficient sample that favors pancreatic carcinoma

[redacted] **20[redacted] BLOOD PH:** 7.434 pH (normal 7.350 to 7.450)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 2.54 mg/dL (normal <0.5)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 3.00 mg/dL (normal <0.5)

[redacted] **20[redacted] CALCIUM:** 9.6 MMOL/L (normal 8.8 to 10.2)

[redacted] **20[redacted] CHLORIDE:** 98 MMOL/L (normal 97 to 107)

[redacted] **20[redacted] CHLORIDE:** 100 MMOL/L (normal 98 to 5.10)

[redacted] **20[redacted] CREATINE KINASE:** 43 U/L (normal <190)

[redacted] **20[redacted] CREATININE:** 0.61 No units

[redacted] **20[redacted] CREATININE:** 0.56 mg/dL (normal 0.7 to 1.20)

[redacted] **20[redacted] CREATININE:** 0.57 mg/dL (normal 0.7 to 1.20)

[redacted] **20[redacted] CRP:** 2.75 No units

[redacted] **20[redacted] ECG:** Results pending

[redacted] **20[redacted] EOSINOPHILS:** 2.2 % (normal 1.0 to 6.0)

[redacted] **20[redacted] EOSINOPHILS:** 2.2 % (normal 1 to 6)

[redacted] **20[redacted] GGT:** 683 U/L (normal 10 to 71)

[redacted] **20[redacted] GGT:** 660 U/L (normal 10 to 71)

[redacted] **20[redacted] GLUCOSE:** 104 mg/dL (normal 74 to 106)

[redacted] **20[redacted] HEMATOCRIT:** 34.8 % (normal 40.6 to 50.4)

[redacted] 20[redacted] **HEMATOCRIT:** 0.343 fraction of 1 (normal 0.406 to 0.504)

[redacted] 20[redacted] **HEMOGLOBIN:** 11.9 G/DL

[redacted] 20[redacted] **HEMOGLOBIN:** 11.4 G/DL (normal 13 to 17)

[redacted] 20[redacted] **HEMOGLOBIN:** 11.5 G/DL (normal 13 to 17)

[redacted] 20[redacted] **INR:** 1.4 RATIO

[redacted] 20[redacted] **INTERNATIONAL NORMALIZED RATIO:** 1.3 ratio

[redacted] 20[redacted] **LDH:** 175 U/L (normal 135 to 225)

[redacted] 20[redacted] **LYMPHOCYTES:** 15.3 % (normal 20 to 40)

[redacted] 20[redacted] **LYMPHOCYTES:** 12.3 % (normal 20.0 to 40)

[redacted] 20[redacted] **MONOCYTES:** 11.7 % (normal 2.0 to 11.7)

[redacted] 20[redacted] **MONOCYTES:** 11.2 % (normal 2.0 to 11.7)

[redacted] 20[redacted] **MYCOBACTERIAL BLOOD CULTURE:** negative

[redacted] 20[redacted] **NEUTROPHILS:** 70 % (normal 40 to 80)

[redacted] 20[redacted] **NEUTROPHILS:** 73.3 % (normal 40.0 to 80.0)

[redacted] 20[redacted] **PELVIC ULTRASOUND:** bladder in moderate repletion without aspects to highlight

[redacted] 20[redacted] **PLATELET COUNT:** 193000 No units

[redacted] 20[redacted] **PLATELET COUNT:** 179 X10**9/L (normal 150 to 400)

[redacted] 20[redacted] **PLATELET COUNT:** 182 X10**9/L (normal 150 to 400)

[redacted] 20[redacted] **POTASSIUM:** 4.29 No units

[redacted] 20[redacted] **POTASSIUM:** 3.86 MMOL/L (normal 3.5 to 5.10)

[redacted] 20[redacted] **POTASSIUM:** 3.60 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **PROTHROMBIN TIME:** 13.5 SEC (normal 0 to 14)

[redacted] 20[redacted] **PT / APTT:** 0.9 ratio (normal 0 to 1.2)

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

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

[redacted] 20[redacted] **RBC:** 4.00 X10**12/L (normal 4.41 to 5.9)

[redacted] **20[redacted] RBC:** 3.96 X10**12/L (normal 4.41 to 5.9)

[redacted] **20[redacted] RENAL ULTRASOUND:** kidneys of increased dimensions with no evidence of spatial lesions

[redacted] **20[redacted] SODIUM:** 138 MMOL/L (normal 136 to 145)

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

[redacted] **20[redacted] THORACOABDOMINOPELVIC CT:** PRIMARY METASTATIC PANCREAS NEOPLASIA: pancreatic tail carcinoma with multiple liver metastases.

[redacted] **20[redacted] THORAX XRAY:** Results pending

[redacted] **20[redacted] TOTAL BILIRUBIN:** 6.84 No units

[redacted] **20[redacted] TOTAL BILIRUBIN:** 6.79 mg/dL (normal <1.4)

[redacted] **20[redacted] TOTAL PROTEIN:** 6.9 G/DL (normal 6.4 to 8.3)

[redacted] **20[redacted] URINE BILIRUBIN:** ++

[redacted] **20[redacted] URINE GLUCOSE:** 0

[redacted] **20[redacted] URINE HEMOGLOBIN:** +

[redacted] **20[redacted] URINE KETONE:** positive

[redacted] **20[redacted] URINE PH:** 6.5 No units

[redacted] **20[redacted] URINE PROTEIN:** 0.15-0.25 G/L (normal reference range: n/a)

[redacted] **20[redacted] WBC:** 6200 No units

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.8 X10**9/L (normal 4.0 to 10)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.4 X10**9/L (normal 4.0 to 10.0)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
門脈血栓症	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PORTAL VEIN THROMBOSIS	19[redacted]
OTHER: THROMBOCYTOSIS ESSENTIAL	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: POSTMENOPAUSAL	20[redacted]

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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 133	133

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	UNKNOWN mg	OTHER: UNKNOWN	Y-M: 19[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ENOXAPARIN	60 mg	BID	Y-M: 20[redacted] / 133	ONGOING
PROPRANOLOL	5 mg	TID	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 142

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

Event Description	PORTAL VEIN THROMBOSIS
Preferred term	門脈血栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 133 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 133): Bilirubin: 29 [2 - 21] UMOL/L; Creatinine: 42 [53 - 97] UMOL/L; Hemoglobin: 121 [117 - 155] G/L; Leukocytes: 6.9 [4 - 11] 10^9/L; Lymphocytes: 0.9 [1.2 - 3] 10^9/L; NPTST209-CRP: 25.34 [0.03 - 5] MG/L; Neutrophils: 5.6 [1.4 - 6] 10^9/L; Platelets: 203 [150 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 134): NPTST503-PCO2-AR: 31.3 [35 - 46] MMHG; NPTST520-PO2-AR: 52 [70 - 100] MMHG; [redacted]20[redacted] (RX DAY 138): NPTST149-CARDIOLIPIN IGG: 1.6 [5 - 8] IU/ML; NPTST150-CARDIOLIPIN IGM: 0.7 [5 - 8] IU/ML; NPTST394-JAK2 V617 MUTATION: POSITIVE [NOT REPORTED - NOT REPORTED] PCR METHOD

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 133): CHEST X-RAY: NO EVIDENCE OF CONGESTION; CT ABDOMEN: PORTAL VEIN THROMBOSIS WITH MULTIPLE HEPATOCELLULAR PORTO-SYSTEMIC COLTERALS, ESOPHAGEAL AND GASTRIC VARICOSE VEINS, SPLEEN AND LARGE SPLENORRHEA SHUNT.; ECG: SINUS, REGULAR(74), WITHOUT SIGNS OF ACUTE ISCHEMIA; [redacted]20[redacted] (RX DAY 141): GASTROSCOPY: VARICOSE GRADE 4.

AE Stopped Rx Day	142 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	10 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はイスラエルの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，門脈血栓症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，門脈血栓症，本態性血小板増加症（JAK2+），局面型乾癬，乾癬性関節炎，閉経後，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は門脈血栓症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，門脈血栓症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃痛，息切れ，悪心，嘔吐，便秘及び臍周囲痛の悪化（主に右下腹部）のため入院した。CT スキャン検査で胃・食道静脈瘤が明らかとなった。ヘパリン点滴静注及び deralin の投与が開始された。胃内視鏡検査が行われ，グレード 4 の静脈瘤が確認された。JAK2 変異は陽性，APLA（抗リン脂質抗体）は陰性であった。また，乾癬が悪化していた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，治験薬の投与が完全に中止された。

医療記録より：被験者は，母親の死後 2 ヵ月あまり食欲不振で，体重が 3～5 kg 減少したと報告した。被験者は，約 1 週間に及ぶ呼吸困難，悪心及び嘔吐を伴う持続性の臍周囲・右上腹部痛，「チクチクする感じ」及び灼熱感を訴えた。入院前 24 時間にわたり，痛みが悪化し（10/10），痛みの部位の変化はなかった。また，出血を伴わない嘔吐が複数回（10 回超）出現し，下痢も認められた。痛みは食事後に悪化し，鎮痛薬で軽減された。また被験者によると，便秘が約 2 週間続いていた。便の色に変化はなく，鮮血も見られなかった。救急治療室にて便通はあった。被験者によると，発熱及び寝汗はなかったが，入院日に悪寒があったと報告された。救急治療室にて，呼吸困難，蒼白及び発汗は認められなかった。幾度か疼痛発作が出現した。腹部は軟らかく，主に上腹部に軽度の広汎性圧痛及び腹部膨満が認められた。反跳や抵抗はなく，触知可能な腫瘤や嵌頓ヘルニアはなかった。NG 及び導尿カテーテルの留置が再度試みられたが成功せず，ヘパリンの投与が開始された。また，完全な臨床検査値モニタリングが行われた。治療開始後，著しい臨床的改善が見られ，腹痛は軽減された。治療は，抗 10a 抗体価に基づき，クレキサン皮下投与に切り替えられた。

血液学的検査が行われ，骨髄増殖性疾患と一致する臨床像であることが確認された。JAK2 は陽性，APLA は陰性であった。後日，骨髄検査を受けることが勧められた。消化器の診察で，切歯列から 22 cm の食道胃接合部から食道中央部にかけて，グレード 4 の静脈瘤が認められ，接合線に隣接する 2 本の静脈瘤柱に発赤所見が認められた。活動性出血は見られなかった。胃に発赤

所見を伴うグレード 2 の静脈瘤が認められた。Deralin の投与が開始され，今後行う可能性のある治療についての説明が行われた。

入院中，乾癬の悪化も認められた。皮膚科医が診察を行った。推奨されたのは局所療法のみであった。体用に daviobet 軟膏，顔用にエリデルの投与が開始された。

退院日，被験者の全身状態は良好で，バイタルサインも正常であった。被験者から腹部膨満が報告されたが，腹痛はなかった。診察所見は，触診で腹部軟・圧痛なし，蠕動正常であった。

投与された薬剤は，ヘパリン，deralin 及びクレキサンであった。

The patient's past medications include:

METHOTREXATE for PSORIATIC ARTHRITIS (19[redacted] - 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Portal vein thrombosis (10036206) (Portal vein thrombosis (10036206)) [v.22.0] [10036206]

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 PORTAL VEIN THROMBOSIS

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing essential thrombocytosis (JAK2+) and prior history of portal vein thrombosis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20**[redacted] **ACTUAL BASE EXCESS VENOUS:** -3 (Normal -2 - 2)

[redacted] **20**[redacted] **ALBUMIN:** 34.0 no units (normal 35.0 to 50.0)

[redacted] **20**[redacted] **ALBUMIN:** 29.0 no units (normal 35.0 to 50.0)

[redacted] **20**[redacted] **ALKALINE PHOSPHATASE:** 91.00 no units (normal 46.00 to 116.00)

[redacted] **20**[redacted] **ALT (GPT):** 10 no units (normal 8 to 35)

[redacted] **20**[redacted] **ALT (GPT):** 16 no units (normal 8 to 35)

[redacted] **20**[redacted] **AMYLASE:** 47 no units (normal 20 to 104)

[redacted] **20**[redacted] **ANION GAP, AR:** 13 no units (normal 8 to 16)

[redacted] **20**[redacted] **ANISOCYTOSIS, FILM:** Positive

[redacted] **20**[redacted] **ANTIPHOSPHOLIPID ANTIBODIES:** NEGATIVE

[redacted] **20**[redacted] **AST (GOT):** 16 no units (normal 7 to 40)

[redacted] **20**[redacted] **AST (GOT):** 27 no units (normal 7 to 40)

[redacted] **20**[redacted] **BAND %:** 1 no units

[redacted] **20**[redacted] **BASE EXCESS/DEFICIT ARTERIAL:** -3.9 (normal -2.0 - 3.0)

[redacted] **20**[redacted] **BASOPHILS #:** 0.0 no units (normal 0.0 to 0.2)

[redacted] **20**[redacted] **BASOPHILS #:** 0.1 no units (normal 0.0 to 0.2)

[redacted] **20**[redacted] **BASOPHILS %:** 0.6 no unit (normal 0.0 to 1.9)

[redacted] **20**[redacted] **BASOPHILS %:** 1.3 no units (normal 0.0 to 1.9)

[redacted] **20**[redacted] **BETA2-GLYCOPROTEIN IGG:** 1.8 no units

[redacted] **20**[redacted] **BETA2-GLYCOPROTEIN IGM:** 0.8 no units

[redacted] **20**[redacted] **BILIRUBIN, DIRECT:** 0.59 no units (normal 0.1 to 0.30)

[redacted] **20**[redacted] **BILIRUBIN, DIRECT:** 0.23 no units (normal 0.1 to 0.30)

[redacted] **20**[redacted] **BILIRUBIN, INDIRECT:** 1.12 no units (normal 0.00 to 0.60)

[redacted] **20**[redacted] **BILIRUBIN, INDIRECT:** 0.19 no units (normal 0.00 to 0.60)

[redacted] **20**[redacted] **BILIRUBIN, TOTAL:** 1.71 no units (normal 0.1 to 1.20)

[redacted] **20**[redacted] **BLOOD PRESSURE:** 122/75

[redacted] [redacted] 20[redacted] **BUN (BLOOD):** <5 (Normal <5-25)

[redacted] [redacted] 20[redacted] **BUN (BLOOD):** 8 No units

[redacted] [redacted] 20[redacted] **CALCIUM, IONIZED ARTERIAL:** 1.12 no units (normal 1.15 to 1.35)

[redacted] [redacted] 20[redacted] **CALCIUM, TOTAL:** 8.00 no units (normal 8.50 to 10.50)

[redacted] [redacted] 20[redacted] **CALCIUM, TOTAL:** 7.40 no units (normal 8.50 to 10.50)

[redacted] [redacted] 20[redacted] **CARBOXYHEMOGLOBIN:** 1.1 no units (normal 0.0 to 2.0)

[redacted] [redacted] 20[redacted] **CARBOXYHEMOGLOBIN, QUANTITATIVE ARTERIAL:** 0.5 no units (normal <2.0)

[redacted] [redacted] 20[redacted] **CHLORIDE:** 105 no units (normal 95 to 110)

[redacted] [redacted] 20[redacted] **CHLORIDE:** 108 no units (normal 95 to 110)

[redacted] [redacted] 20[redacted] **CHLORIDE ARTERIAL:** 104 no units (normal 95 to 105)

[redacted] [redacted] 20[redacted] **CHOLESTEROL, TOTAL:** 112 no units (normal 120 to 200)

[redacted] [redacted] 20[redacted] **CREATININE:** 0.47 no units (normal 0.60 to 1.10)

[redacted] [redacted] 20[redacted] **CREATININE:** 0.40 no units (normal 0.60 to 1.10)

[redacted] [redacted] 20[redacted] **CREATININE KINASE:** 23 no units (normal 34 to 145)

[redacted] [redacted] 20[redacted] **CREATININE KINASE:** 31 no units (normal 34 to 145)

[redacted] [redacted] 20[redacted] **CRP:** 25.34 no unit (normal 0.03 to 5.00)

[redacted] [redacted] 20[redacted] **CRP:** 9.53 no unit (normal 0.03 to 5.00)

[redacted] [redacted] 20[redacted] **CT SCAN:** Known portal vein thrombosis with formation of multiple porto-systemic collaterals in the hepatic hilum, varices in the esophageal and gastric wall, in the splenic hilum and a large splenorenal shunt. The is a component of acute thrombosis in SMV and its branches with infiltration in its periphery. The liver is of normal size and texture. The spleen is enlarged to 19.8 cm, with no significant change. Intestinal loops - mesenteric congestion, thickening of the ileum loops wall in the right abdomen and minimal thickening of the colon walls, most probably secondary to the increased portal pressure. Small quantity of free fluid near the liver, in the right gutter and pelvis. No free air was demonstrated in the abdomen or pelvis.

[redacted] [redacted] 20[redacted] **DESOXYHEMOGLOBIN, QUANTITATIVE AR:** 11.5 no units (normal 0.0 to 5.0)

[redacted] [redacted] 20[redacted] **ECG:** Sinus, regular (74), with no signs of acute ischemia.

[redacted] [redacted] 20[redacted] **EOSINOPHILS #:** 0.1 no unit (normal 0.0 to 0.4)

[redacted] [redacted] 20[redacted] **EOSINOPHILS %:** 1.3 no unit (normal 0.0 to 6.0)

[redacted] [redacted] 20[redacted] **GASTROSCOPY:** VARICOSITIES GRADE 4

[redacted] **20**[redacted] **GGT:** 27 no unit (normal 6 to 28)

[redacted] **20**[redacted] **GGT:** 45 no unit (normal 6 to 28)

[redacted] **20**[redacted] **GLOBULIN:** 22.0 no units (normal 23.0 to 35.0)

[redacted] **20**[redacted] **GLUCOSE:** 74 no units (normal 60 to 100)

[redacted] **20**[redacted] **GLUCOSE:** 118 no units (normal 70 to 110)

[redacted] **20**[redacted] **GLUCOSE, DIRECT:** 95 no units (normal 70 to 115)

[redacted] **20**[redacted] **GLUCOSE, QUANTITATIVE ARTERIAL:** 111.0 no units (normal 70.0 to 100.0)

[redacted] **20**[redacted] **HCO3 ARTERIAL:** 20.4 no units (normal 212.0 to 26.0)

[redacted] **20**[redacted] **HCT:** 27 no units (normal 35 to 45)

[redacted] **20**[redacted] **HCT, ARTERIAL:** 32.0 no units (normal 37.0 to 52.0)

[redacted] **20**[redacted] **HEART RATE:** 82 /min

[redacted] **20**[redacted] **HEMATOCRIT:** 36 no unit (normal 35 to 45)

[redacted] **20**[redacted] **HEMATOCRIT:** 27 no unit (normal 35 to 45)

[redacted] **20**[redacted] **HEMOGLOBIN:** 12.1 no unit (normal 11.7 to 15.5)

[redacted] **20**[redacted] **HEMOGLOBIN:** 9.4 no unit (normal 11.7 to 15.5)

[redacted] **20**[redacted] **HEMOGLOBIN, TOTAL ARTERIAL:** 11.0 no units (normal 12.0 to 18.0)

[redacted] **20**[redacted] **HEPARIN NEUTRALIZATION:** 0.38 no units

[redacted] **20**[redacted] **HEPARIN NEUTRALIZATION:** 0.49 no units

[redacted] **20**[redacted] **HYPOCHROMIA, FILM:** Positive

[redacted] **20**[redacted] **IGG:** CARDIOLIPIN IgG: 1.6 IU/mL (range: >5 - <8)

[redacted] **20**[redacted] **IGM:** CARDIOLIPIN IgM: 0.7IU/mL (range: 5 - 8)

[redacted] **20**[redacted] **INR:** 1.16 no unit (normal 0.97 to 1.19)

[redacted] **20**[redacted] **INR:** 1.24 no unit (normal 0.97 to 1.19)

[redacted] **20**[redacted] **LACTIC ACID ARTERIAL:** 0.90 no units (normal 0.00 to 1.80)

[redacted] **20**[redacted] **LDH:** 389 no units (normal 208 to 378)

[redacted] **20**[redacted] **LIPASE:** 41 no units (normal 9 to 51)

[redacted] 20[redacted] **LYMPHOCYTES #:** 0.8 no units (normal 1.2 to 3.0)

[redacted] 20[redacted] **LYMPHOCYTES %:** 19.1 no units (normal 20.0 to 40.0)

[redacted] 20[redacted] **LYMPHOCYTES %, FILM:** 4 no units (normal 20.0 to 40.0)

[redacted] 20[redacted] **MAGNESIUM:** 1.80 no units (normal 1.80 to 2.55)

[redacted] 20[redacted] **MEAN PLATELET VOLUME:** 9.6 no unit (normal 7.0 to 12.0)

[redacted] 20[redacted] **MEAN PLATELET VOLUME:** 8.7 no units (normal 7.0 to 12.0)

[redacted] 20[redacted] **METAMYELOCYTES %:** 1 no units

[redacted] 20[redacted] **METHEMOGLOBIN, QUANTITATIVE AR:** 0.2 no units (normal 0.0 to 1.5)

[redacted] 20[redacted] **MICROCYTOSIS TEST:** Positive

[redacted] 20[redacted] **MONO %:** 4.7 no unit (normal 2.0 to 13.0)

[redacted] 20[redacted] **MONO %:** 7.4 no units (normal 2.0 to 13.0)

[redacted] 20[redacted] **MONOCYTES #:** 0.3 no units (normal 0.0 to 1.3)

[redacted] 20[redacted] **NEUTROPHILS #:** 5.6 no unit (normal 1.4 to 6.0)

[redacted] 20[redacted] **NEUTROPHILS #:** 2.9 no units (normal 1.4 to 6.0)

[redacted] 20[redacted] **NEUTROPHILS %:** 80.7 no unit (normal 40.0 to 75.0)

[redacted] 20[redacted] **NEUTROPHILS %:** 66.9 no units (normal 40.0 to 75.0)

[redacted] 20[redacted] **NRBC/100 WBC:** 0.0 no units

[redacted] 20[redacted] **O2 SATURATION (ROOM AIR):** 98 %

[redacted] 20[redacted] **O2 SATURATION ARTERIAL:** 92.5 no units (normal <96)

[redacted] 20[redacted] **O2 SATURATION VENOUS:** 73 no units (normal 70 to 75)

[redacted] 20[redacted] **OVALOCYTES:** Positive

[redacted] 20[redacted] **OXYHEMOGLOBIN, QUANTITATIVE AR:** 87.8 no units (normal <95.0)

[redacted] 20[redacted] **P02 ARTERIAL:** 52.0 no units (normal 70.0 to 100.0)

[redacted] 20[redacted] **PCO2, ARTERIAL:** 31.4 no units (normal 35.0 to 45.0)

[redacted] 20[redacted] **PCR:** JAK2 V617 MUTATION: POSITIVE

[redacted] 20[redacted] **PH, AR:** 7.399 no units (normal 7.320 to 7.420)

[redacted] [redacted] **20**[redacted] **PHOSPHORUS:** 2.73 no units (normal 2.50 to 4.50)

[redacted] [redacted] **20**[redacted] **PHOSPHORUS:** 3.48 no units (normal 2.50 to 4.50)

[redacted] [redacted] **20**[redacted] **PLATELET COUNT:** 203 no unit (normal 150 to 450)

[redacted] [redacted] **20**[redacted] **PLATELET COUNT:** 168 no unit (normal 150 to 450)

[redacted] [redacted] **20**[redacted] **POTASSIUM:** 3.65 no units (normal 3.50 to 5.30)

[redacted] [redacted] **20**[redacted] **POTASSIUM:** 4.18 no units (normal 3.50 to 5.30)

[redacted] [redacted] **20**[redacted] **POTASSIUM, ARTERIAL:** 3.84 no units (normal 3.60 to 4.80)

[redacted] [redacted] **20**[redacted] **PROTEIN, TOTAL:** 59.0 no units (normal 64.0 to 83.0)

[redacted] [redacted] **20**[redacted] **PROTEIN, TOTAL:** 51.0 no units (normal 64.0 to 83.0)

[redacted] [redacted] **20**[redacted] **PT:** 11.90 SEC (normal 10.03 to 12.43)

[redacted] [redacted] **20**[redacted] **PT:** 12.80 SEC (normal 10.03 to 12.43)

[redacted] [redacted] **20**[redacted] **PTT:** 28.90 SEC (normal 25.00 to 34.00)

[redacted] [redacted] **20**[redacted] **PTT:** 30.60 SEC (normal 25.00 to 34.00)

[redacted] [redacted] **20**[redacted] **RBC:** 4.7 no units (normal 3.8 to 5.1)

[redacted] [redacted] **20**[redacted] **RBC:** 3.5 no units (normal 3.8 to 5.1)

[redacted] [redacted] **20**[redacted] **SODIUM:** 139.0 no units (normal 135.0 to 146.0)

[redacted] [redacted] **20**[redacted] **SODIUM:** 138.0 no units (normal 135.0 to 146.0)

[redacted] [redacted] **20**[redacted] **SODIUM, ARTERIAL:** 133.9 no units (normal 135.00 to 145.00)

[redacted] [redacted] **20**[redacted] **TCO2 ARTERIAL:** 19.6 no units (normal 23.0 to 28.0)

[redacted] [redacted] **20**[redacted] **TEMPERATURE:** 36.7 Degrees C

[redacted] [redacted] **20**[redacted] **TRIGLYCERIDES:** 110 no units (normal 50 to 150)

[redacted] [redacted] **20**[redacted] **URIC ACID:** 3.30 no units (normal 2.30 to 6.00)

[redacted] [redacted] **20**[redacted] **URIC ACID:** 2.30 no units (normal 2.30 to 6.00)

[redacted] [redacted] **20**[redacted] **WBC:** 6.9 no unit (normal 4.0 to 11.0)

[redacted] [redacted] **20**[redacted] **WBC:** 4.3 no units (normal 4.0 to 11.0)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
HYPERLIPIDEMIA	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: BENIGH HYPERTROPHY PROSTATE	20[redacted]
OTHER: SPINAL STENOSIS	20[redacted]
OTHER: HYPERURICEMIA	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
INCREASED CREATINE PHOSPHOKINASE: NOT DONE	NOT REPORTED

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	10	19[redacted]
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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]
ALLOPURINOL	300 mg	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]

ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	2 g	QD	Y-M: 20[redacted]
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -270
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted] / -270

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
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted]	ONGOING
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]	ONGOING
ALLOPURINOL	300 mg	QD	Y-M: 20[redacted]	ONGOING
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted]	ONGOING
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -270	ONGOING
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted] / -270	ONGOING
AUGMENTIN	1 g	TID	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 43
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / 41	Y-M: 20[redacted] / 43
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 71

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

Event Description	BACTEREMIA
Preferred term	菌血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 37
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 58): Creatine Kinase: 3825 [20 - 200] U/L; Hemoglobin: 118 [135 - 175] G/L; [redacted]20[redacted] (RX DAY 85): Creatine Kinase: 83 [20 - 200] U/L

Microbiology

[redacted]20[redacted] (RX DAY 62): BLOOD NPTST105-BLOOD CULTURE: Positive-POSITIVE FOR STREPTOCCOCUS PARASANGUINIS.; [redacted]20[redacted] (RX DAY 64): SPUTUM NPTST607-SPUTUM CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 62): CT CHEST: MILD LYMPHADENOPATHY, NON SPECIFIC BILAT. INTERSTITIAL LUNG CHANGES.; [redacted]20[redacted] (RX DAY 64): BRONCHOSCOPY: BRONCHOSCOPY WAS NORMAL . NO PATHOGENS WERE IDENTIFIED ON SPUTUM CULTURE.; [redacted]20[redacted] (RX DAY 65): ECHOCARDIOGRAM -: TRANSESOPHAGEAL WAS NORMAL WITH NO VAGETATIONS.

AE Stopped Rx Day	71 (15 DAYS AFTER LAST TREATMENT)
Duration of AE	35 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者はイスラエルの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，菌血症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元紙巻タバコ喫煙者（1 日 2 箱を 10 年間），良性前立腺肥大，高尿酸血症，乾癬性関節炎及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は菌血症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，菌血症は消失した。

被験者は 3 週間に及ぶ発熱のため病院を受診し，20[redacted] 年 [redacted] 月 [redacted] 日に入院した。全身及び筋骨格系の診察では，軽度の腋窩リンパ節腫大を除き，異常は認められなかった。心内膜炎の徴候は認められなかった。被験者はストレプトコッカス・パラサングイニスによる菌血症と診断された。被験者は抗生物質による 1 コースの治療を完了し，菌血症は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師によると，被験者に，最近の旅行歴，人工器具移植歴及び最近の歯科治療歴はなかった。治験責任医師によると，本事象発現前に被験者の妻が発熱を来していた。

投与された薬剤はセフトリアキソンであった。

The patient's past medications include:

SALAZOPIRIN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Bacteremia (10003999) (Bacteraemia (10003997)) [v.22.0] [10003999]

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 BACTEREMIA

- Investigator: Not applicable

- AbbVie: Viridans group streptococcus is more likely to be contaminant especially in patients who do not have prosthetics or central venous catheters.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD CULTURE:** POSITIVE FOR STREPTOCCOCUS PARASANGUINIS

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

[redacted] **20[redacted] BODY TEMPERATURE:** 38.9 Degrees C

[redacted] **20[redacted] BRONCHOSCOPY:** BRONCHOSCOPY WAS NORMAL . NO PATHOGENS WERE IDENTIFIED ON SPUTUM CULTURE.

[redacted] **20[redacted] CT CHEST:** MILD LYMPHADENOPATHY, NON SPECIFIC BILATERAL. INTERSTITIAL LUNG CHANGES.(not considered serious event by the investigator)

[redacted] **20[redacted] ECHOCARDIOGRAM:** TRANSESOPHAGEAL WAS NORMAL WITH NO VEGETATIONS.

[redacted] **20[redacted] HEMOGLOBIN:** 11.8 G/DL (normal 13.5 to 17.5)

[redacted] **20[redacted] VIRAL PANEL:** negative

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
レンサ球菌性肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: SKIN PSORIATIC PLAQUES - ELBOWS, ABDOMEN, BACK	19[redacted]
OTHER: INSOMNIA	20[redacted]
HYPERTENSION	20[redacted]
OTHER: POST MENOPAUSAL	20[redacted]
EYE DISEASE/DISORDER: BIFOCAL GLASSES	20[redacted]
OTHER: SINUSITIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
DEPRESSION: MILD DEPRESSION	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
EYE DISEASE/DISORDER: RIGHT EYE CATARACT	20[redacted]

Prior Procedures	Procedure Year
SURGERY: BUNIONS REMOVED BOTH FEET	19[redacted]
SURGERY: SPINAL FUSIONS	19[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	4	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 170	170
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 171	[redacted]20[redacted] / 182	12

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
AMITRIPTYLINE	50 mg	OTHER: NOCTE	Y-M: 20[redacted]
FLUOXETINE	20 mg	QD	Y-M: 20[redacted]
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
SULFASALAZINE	500 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted]
PARACETAMOL	1 g	TID	Y-M: 20[redacted]
SULFASALAZINE	1 g	BID	Y-M: 20[redacted]
TRAMADOL	100 mg	TID	Y-M: 20[redacted]
AMLODIPINE	10 mg	QD	Y-M: 20[redacted] / -226
BECLOMETASONE	1 OTHER: SPRAY	TID	Y-M: 20[redacted] / -226
DICLOFENAC	50 mg	TID	Y-M: 20[redacted] / -226
ERGOCALCIFEROL	50000 IU	EVERY WEEK	Y-M: 20[redacted] / -226
CETIRIZINE	10 mg	OTHER: NOCTE	Y-M: 20[redacted] / -85
ENALAPRIL	10 mg	QD	Y-M: 20[redacted] / -85
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted] / -85

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]	ONGOING
AMITRIPTYLINE	50 mg	OTHER: NOCTE	Y-M: 20[redacted]	Y-M: 20[redacted] / 188
FLUOXETINE	20 mg	QD	Y-M: 20[redacted]	ONGOING
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 190
PARACETAMOL	1 g	TID	Y-M: 20[redacted]	ONGOING
TRAMADOL	100 mg	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 188
BECLOMETASONE	1 OTHER: SPRAY	TID	Y-M: 20[redacted] / -226	ONGOING
DICLOFENAC	50 mg	TID	Y-M: 20[redacted] / -226	ONGOING
ERGOCALCIFEROL	50000 IU	EVERY WEEK	Y-M: 20[redacted] / -226	ONGOING
AMLODIPINE	10 mg	QD	Y-M: 20[redacted] / -226	Y-M: 20[redacted] / 195
CETIRIZINE	10 mg	OTHER: NOCTE	Y-M: 20[redacted] / -85	ONGOING
ENALAPRIL	10 mg	QD	Y-M: 20[redacted] / -85	Y-M: 20[redacted] / 188
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted] / -85	Y-M: 20[redacted] / 188
SALBUTAMOL	2 OTHER: PUFFS	BID	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 179
TRAMADOL	50 mg	BID	Y-M: 20[redacted] / 189	ONGOING
ENALAPRIL	5 mg	BID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 195
AUGMENTIN	1.2 g	TID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 198
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 198
FLUCONAZOLE	200 mg	QD	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 198
ENOXAPARIN	60 mg	BID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 199

AMITRIPTYLINE	10 mg	OTHER: NOCTE	Y-M: 20[redacted] / 190	ONGOING
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / 196	ONGOING

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

Event Description	MULTILOBAR PNEUMONIA(GRAM POSITIVE STREPTOCOCCUS)
Preferred term	レンサ球菌性肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 189 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 189): Erythrocytes: 3.2 [3.9 - 5.4] 10^12/L; Hematocrit: 0.3 [0.34 - 0.48] FRACTION OF 1; Hemoglobin: 93 [116 - 164] G/L; Leukocytes: 6 [3.9 - 12.6] 10^9/L; NPTST128-C- REACTIVE PROTEIN: 195 [0 - 10] MG/L; Neutrophils: 1.25 [1.6 - 8.3] 10^9/L; Platelets: 490 [186 - 454] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 189): BLOOD NPTST086-BACTERIAL CULTURE: Positive-GRAM POSITIVE COCCI;
[redacted]20[redacted] (RX DAY 216): SPUTUM NPTST619-TB CULTURE: Positive-MYCOBACTERIUM TUBERCULOSIS COMPLEX

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 190): CHEST X RAY: MULTILOBAR PNEUMONIA; CPAP (CONTINUOUS POSITIVE AIRWAY PRESSURE: RESOLVED

AE Stopped Rx Day	198 (16 DAYS AFTER LAST TREATMENT)
Duration of AE	10 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は南アフリカの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，多葉性肺炎（グラム陽性レンサ球菌）の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，高血圧，閉経後，元喫煙者（1 日 0.5 箱を 4 年間），乾癬性関節炎，胃食道逆流性疾患，軽度のうつ病及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は多葉性肺炎（グラム陽性レンサ球菌）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，多葉性肺炎（グラム陽性レンサ球菌）は消失した。

本事象発現前，20[redacted] 年 [redacted] 月，被験者は呼吸困難（非重篤な事象）及びリンパ球減少症（非重篤な事象）を発現した。リンパ球減少症（非重篤な事象）により治験薬の投与が中止された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，1 週間に及ぶ呼吸困難及び乾性咳嗽のため救急科（ED）を受診し，診察でチアノーゼを伴う肺底部異常音が聴取された。胸部 X 線検査及び血液検査で肺炎が確定した。被験者は ED で抗生物質による治療を受け，治療及びさらなる検査のため同日入院した。20[redacted] 年 [redacted] 月 [redacted] 日，CPAP（持続的気道陽圧）が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，クレキサン，フルコナゾール，アジスロマイシン及びオーグメンチン（co-amoxyclav）であった。

The patient's past medications include:

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALAZOPYRINE for PSORIATIC ARTHRITIS ([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) Pneumonia due to Streptococcus (10035694) (Pneumonia streptococcal (10035735)) [v.22.1] [10035694]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of MULTILOBAR PNEUMONIA (GRAM POSITIVE STREPTOCOCCUS)

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD BACTERIAL CULTURE:** GRAM POSITIVE COCCI- positive

[redacted] **20[redacted] C- REACTIVE PROTEIN:** 195 MG/L (normal 0 to 10)

[redacted] **20[redacted] CHEST X RAY:** MULTILOBAR PNEUMONIA

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

[redacted] **20[redacted] HEMOGLOBIN:** 9.3 G/DL (normal 11.6 to 16.4)

[redacted] **20[redacted] NEUTROPHILS ABS:** 1.25 X10**9/L (normal 1.60 to 8.30)

[redacted] **20[redacted] PLATELET COUNT:** 490 X10**9/L (normal 186 to 454)

[redacted] **20[redacted] SPUTUM CULTURE:** Mycobacterium tuberculosis complex

[redacted] **20[redacted] WHITE BLOOD CELLS:** 6.02 X10**9/L (normal 3.90 to 12.60)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 15 mg QD	3[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: ILIOTIBIAL BAND SYNDROME	20[redacted]
OTHER: SCIATICA LEFT LEG	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: HAIR LOSS	20[redacted]
OTHER: LATENT TB	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	4	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 391	223
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 392		

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]

CELECOXIB	100.00 mg	BID	Y-M: 20
CENTRUM	1 OTHER: TAB	QD	Y-M: 20
CLOBETASOL	1 OTHER: APP	PRN	Y-M: 20
COMMIPHORA MUKUL W/GLYCYRRHIZA GLABRA/MORINGA	1 OTHER: TAB	QD	Y-M: 20
FISH OIL	1 OTHER: TAB	QD	Y-M: 20
FOLIC ACID	5 mg	OTHER: 4 TIMES WEEKLY	Y-M: 20
MAGNESIUM	1 OTHER: TAB	QD	Y-M: 20
PROBIOTICS	1.00 OTHER: TAB	QD	Y-M: 20
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20
VIMOVO	1 OTHER: TAB	BID	Y-M: 20
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20
METHOTREXATE	20.00 mg	EVERY WEEK	Y-M: 20
PREDNISONE	5.0 mg	QD	Y-M: 20
ETORICOXIB	90.00 mg	QD	Y-M: 20
PNEUMOCOCCAL VACCINE	0.5 mL	OTHER: STAT	Y-M: 20
BIOTIN W/CALCIUM PANTOTHENATE/COPPER GLUCONAT	1 OTHER: TAB	QD	Y-M: 20 / - 108
INFLUENZA VACCINE	1.00 OTHER: AMP	OTHER: STAT	Y-M: 20 / - 23
ISONIAZID	300 mg	QD	Y-M: 20 / - 22
PYRIDOXINE	25 mg	QD	Y-M: 20 / - 22

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
CENTRUM	1 OTHER: TAB	QD	Y-M: 20	NOT REPORTED
FISH OIL	1 OTHER: TAB	QD	Y-M: 20	NOT REPORTED
FOLIC ACID	5 mg	OTHER: 4 TIMES WEEKLY	Y-M: 20	NOT REPORTED
MAGNESIUM	1 OTHER: TAB	QD	Y-M: 20	NOT REPORTED
VIMOVO	1 OTHER: TAB	BID	Y-M: 20	NOT REPORTED
METHOTREXATE	20.00 mg	EVERY WEEK	Y-M: 20	Y-M: 20 / 449
ISONIAZID	300 mg	QD	Y-M: 20 / - 22	Y-M: 20 / 251
PYRIDOXINE	25 mg	QD	Y-M: 20 / - 22	Y-M: 20 / 251
CLOBAZAM	10 mg	QD	Y-M: 20 / 309	NOT REPORTED
ESCITALOPRAM	10 mg	QD	Y-M: 20 / 309	Y-M: 20 / 342
ZOLPIDEM	10 mg	OTHER: NOCTE	Y-M: 20 / 313	NOT REPORTED
MIRTAZAPINE	7.5 mg	OTHER: NOCTE	Y-M: 20 / 394	NOT REPORTED
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20 / 450	Y-M: 20 / 464

METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / 465	Y-M: 20[redacted] / 506
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / 507	ONGOING
BENZYDAMINE	1 OTHER: MOUTH FULL	PRN	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 655
SUPRAGESIC	2 OTHER: CAPSULES	PRN	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 655
CLARITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 659
CO-ADVIL	2 OTHER: TABLETS	BID	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 659
OSELTAMIVIR	75 mg	BID	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 659
FLUTICASONE	1 OTHER: SPRAY	QD	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 685
AUGMENTIN	1 g	BID	Y-M: 20[redacted] / 812	Y-M: 20[redacted] / 822
ENTIRO	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 812	Y-M: 20[redacted] / 822

Event #2: Serious Adverse Event

Event Description	RECURRING DEPRESSIVE DISORDER
Preferred term	うつ病
AE Onset Date / Rx Day	[redacted]20[redacted] / 309
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PERSONAL ISSUES
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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，うつ病性障害の再発の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，喫煙者（1 日 1 箱を 4 年間）及び現飲酒者（2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はうつ病性障害の再発を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はうつ病エピソードを発現した。自殺思考，不眠症及び泣きといった症状が見られた。治験責任医師によると，本事象に関連する危険因子は，状況的離婚，不眠症及び金銭的ストレスであった。被験者はさらなる評価及び治療のため精神科医に紹介された。

20[redacted] 年 [redacted] 月 [redacted] 日，精神科医の判断で被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，ゾルピデム，lexamil 及び urbanol であった。

The patient's past medications include:

CELEBREX for PSORIATIC ARTHRITIS (20[redacted] - [redacted] [redacted] 20[redacted])

DOVATE for PSORIASIS (20[redacted] - [redacted] [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

ARCOXIA for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Recurrent depressive disorder (10066589) (Depression (10012378)) [v.23.0] [10066589]

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 RECURRING DEPRESSIVE DISORDER

- Investigator: PERSONAL ISSUES

- AbbVie: PER PI, EVENT IS MORE LIKELY RELATED TO PERSONAL ISSUES OF DIVORCE, INSOMNIA, AND FINANCIAL STRESS.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
後天性鉤爪趾	X			
背部痛	X			

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
HYPOTHYROIDISM	20[redacted]
OTHER: POSTMENOPAUSAL	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: LUMBAR SPONDYLOSIS	20[redacted]
DRUG ALLERGIES/REACTIONS: IMIDAZOLE ALLERGY	20[redacted]
OTHER: INCREASED BODY MASS INDEX	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: SENSORY PERIPHERAL NEUROPATHY	20[redacted]
OTHER: VASCULITITS	20[redacted]
OTHER: HAIR LOSS	20[redacted]
OTHER: BRONCHOSPASM	20[redacted]
OSTEOARTHRITIS	20[redacted]
TUBERCULOSIS: LATENT TUBERCULOSIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: HYSTERECTOMY	19[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]
SURGERY: LUMBAR 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	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

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]
DAIVOBET	1 OTHER: APP	PRN	Y-M: 20[redacted]
LEVOTHYROXINE	100 OTHER: MCG	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	1 OTHER: APP	PRN	Y-M: 20[redacted]
ESTRADIOL	2 mg	QD	Y-M: 20[redacted]
AMITRIPTYLINE	20 mg	OTHER: NOCTE	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted]
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
TRAMADOL	100 mg	OTHER: BD/PRN	Y-M: 20[redacted]
ETORICOXIB	90 mg	QD	Y-M: 20[redacted]
PREGABALIN	75 mg	BID	Y-M: 20[redacted]
METHOTREXATE	22.5 mg	EVERY WEEK	Y-M: 20[redacted]
PREDNISONE	50 mg	QD	Y-M: 20[redacted]
AMITRIPTYLINE	25 mg	OTHER: NOCTE	Y-M: 20[redacted]
PREGABALIN	150 mg	BID	Y-M: 20[redacted] / -336
BUDESONIDE W/FORMOTEROL FUMARATE	160 OTHER: MCG	BID	Y-M: 20[redacted] / -117
LEVOTHYROXINE	125 OTHER: MCG	QD	Y-M: 20[redacted] / -117
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -117
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -17
PYRIDOXINE	25 mg	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
ESTRADIOL	2 mg	QD	Y-M: 20[redacted]	NOT REPORTED
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
TRAMADOL	100 mg	OTHER: BD/PRN	Y-M: 20[redacted]	NOT REPORTED
ETORICOXIB	90 mg	QD	Y-M: 20[redacted]	NOT REPORTED

AMITRIPTYLINE	25 mg	OTHER: NOCTE	Y-M: 20[redacted]	NOT REPORTED
PREGABALIN	150 mg	BID	Y-M: 20[redacted] / -336	Y-M: 20[redacted] / 523
BUDESONIDE W/FORMOTEROL FUMARATE	160 OTHER: MCG	BID	Y-M: 20[redacted] / -117	NOT REPORTED
LEVOTHYROXINE	125 OTHER: MCG	QD	Y-M: 20[redacted] / -117	NOT REPORTED
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -117	Y-M: 20[redacted] / 646
SPIRONOLACTONE	25 mg	QD	Y-M: 20[redacted] / 149	NOT REPORTED
CEFAZOLIN	2000 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
DEXAMETHASONE	8 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
DROPERIDOL	2 mL	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
DROPERIDOL	2.5 mg	OTHER: PC PUMP	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
GLYCOPYRRONIUM	2 mL	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
LIDOCAINE	5 mL	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
MORPHINE	10 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
MORPHINE	60 mg	OTHER: PC PUMP	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
NEOSTIGMINE	2.5 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
ONDANSETRON	4 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
PHENYLEPHRINE	10 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
PROPOFOL	20 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
REMIFENTANIL	5 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
TRANEXAMIC ACID	500 mg	OTHER: STAT	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 523
CEFAZOLIN	2000 mg	TID	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 524
FUROSEMIDE	10 mg	OTHER: 3 DOSES BETWEEN BLOOD	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 524
PARACETAMOL	1000 mg	QID	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 524
PARECOXIB	40 mg	BID	Y-M: 20[redacted] / 523	Y-M: 20[redacted] / 525
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 524	Y-M: 20[redacted] / 524
ZOLPIDEM	12.5 mg	QD	Y-M: 20[redacted] / 524	Y-M: 20[redacted] / 526

ENOXAPARIN	60 mg	QD	Y-M: 20[redacted] / 524	Y-M: 20[redacted] / 527
MOVICOL	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 524	Y-M: 20[redacted] / 527
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 524	Y-M: 20[redacted] / 527
PANADEINE CO	2 OTHER: TABLETS	QID	Y-M: 20[redacted] / 525	Y-M: 20[redacted] / 526
STILPANE	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / 525	Y-M: 20[redacted] / 527
TARGIN	10 mg	BID	Y-M: 20[redacted] / 525	Y-M: 20[redacted] / 527
PREGABALIN	150 mg	BID	Y-M: 20[redacted] / 558	ONGOING

Event #1: Serious Adverse Event

Event Description	BACK PAIN
Preferred term	背部痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 378
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 523): LUMBO-SACARAL SPINAL FUSION: SURGERY SUCCESFUL	
AE Stopped Rx Day	527
Duration of AE	150 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	PREVIOUS SPINAL SURGERY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	CLAW TOE LEFT FOOT SECOND DIGIT
Preferred term	後天性鉤爪趾
AE Onset Date / Rx Day	[redacted]20[redacted] / 652
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	725 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	74 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility

Investigator Alternative Etiology	PSORIATIC ARTHRITIS
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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，背部痛の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，閉経後，乾癬性関節炎，腰椎症，腰椎手術，ボディ・マス・インデックス増加，末梢性感覚ニューロパチー，変形性関節症，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月，被験者は背部痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，背部痛は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，左下肢の神経根痛及び L4/S1 皮節のしびれ感のため入院した。同日，腰仙部固定術が行われた。手術は成功し，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。退院後は理学療法下で経過観察が行われた。

投与された薬剤は，rayzon，dolorol forte，リリカ，synaleve，targinact 及び perfalgan であった。

The patient's past medications include:

COXFLAM for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

IMIDAZOLE for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Back pain (10003988) (Back pain (10003988)) [v.23.0] [10003988]

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 BACK PAIN

- Investigator: Previous spinal surgery.

- AbbVie: Event of back pain is more likely related to pre-existing lumbar spondylosis and history of lumbar surgery.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は南アフリカの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左第 2 趾の鉤爪趾の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，ボディ・マス・インデックス増加，末梢性感覚ニューロパチー，変形性関節症，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左第 2 趾の鉤爪趾を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左第 2 趾の鉤爪趾は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左足部痛で入院した。左第 2 趾（鉤爪趾）の矯正手術が行われた。左足はギプス包帯で固定されていたが，被験者は十分に回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

ADVANTAN for PSORIASIS (20[redacted] - [redacted] 20[redacted])

DOVOBET for PSORIASIS (20[redacted] - [redacted] 20[redacted])

COXFLAM for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

ISONIAZID for TB PROPHYLAXIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PYRIDOXINE for TB PROPHYLAXIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

IMIDAZOLE for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Claw toe (acquired) (10009248) (Acquired claw toe (10057689)) [v.23.0] [10009248]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of CLAW TOE LEFT FOOT SECOND DIGIT

- Investigator: Psoriatic Arthritis

- AbbVie: Risk factors include pre-existing psoriatic arthritis and osteoarthritis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 41.23 kg/m2

[redacted] **20[redacted] BODY WEIGHT:** 115.0 KG

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
変形性関節症	X			

Treatment Group	Age at Study Start	Sex	Race
ADA 40 mg EOW	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: POST MENOPAUSAL	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: DEGENERATIVE OSTEOARTHRITIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
PEPTIC ULCER DISEASE: NO ULCERS CURRENTLY	20[redacted]
TUBERCULOSIS: LATENT TUBERCULOSIS	20[redacted]
OTHER: BAKERS CYSTS	20[redacted]

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 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ADA	40MG	SC	EOW	[redacted]20[redacted] / 393		

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]
CALTRATE PLUS	2 OTHER: TABS	QD	Y-M: 20[redacted]
ULTRACET	2 OTHER: TAB	OTHER: TDS/PRN	Y-M: 20[redacted]
VIMOVO	1 OTHER: TAB	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]
NATTO K2 OSTEO	1 OTHER: TAB	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	OTHER: ALTERNATE DAYS	Y-M: 20[redacted]
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]
MAGNESIUM	450 mg	QD	Y-M: 20[redacted]
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted]
MAGNESIUM	900 mg	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	OTHER: ALTERNATE DAYS	Y-M: 20[redacted]
PREGABALIN	50 mg	OTHER: NOCTE	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	1 OTHER: APPLY	QD	Y-M: 20[redacted]
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -99
PNEUMOCOCCAL VACCINE	0.5 mL	OTHER: STAT	Y-M: 20[redacted] / -84
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -71
PYRIDOXINE	25 mg	QD	Y-M: 20[redacted] / -71
ALCOPHYLLEX	10 mL	PRN	Y-M: 20[redacted] / -58
ASCORBIC ACID	1 g	QD	Y-M: 20[redacted] / -58
DEMACOLIN	1 OTHER: TAB	TID	Y-M: 20[redacted] / -58
AUGMENTIN SR	1 OTHER: TAB	BID	Y-M: 20[redacted] / -49
TOCOPHEROL	2 OTHER: TAB	QD	Y-M: 20[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
NATTO K2 OSTEO	1 OTHER: TAB	QD	Y-M: 20[redacted]	NOT REPORTED
MAGNESIUM	900 mg	QD	Y-M: 20[redacted]	NOT REPORTED
MELOXICAM	15 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 452
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -99	Y-M: 20[redacted] / 74
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -71	Y-M: 20[redacted] / 222
PYRIDOXINE	25 mg	QD	Y-M: 20[redacted] / -71	Y-M: 20[redacted] / 222
TOCOPHEROL	2 OTHER: TAB	QD	Y-M: 20[redacted] / -38	NOT REPORTED

ENTIRO	1 OTHER: TAB	QD	Y-M: 20[redacted] / 1	NOT REPORTED
ESOMEPRAZOLE	40 mg	PRN	Y-M: 20[redacted] / 253	NOT REPORTED
METHYLPREDNISOLONE	1 OTHER: APP	PRN	Y-M: 20[redacted] / 253	NOT REPORTED
KANTREXIL	3 OTHER: TABLETS	QID	Y-M: 20[redacted] / 363	Y-M: 20[redacted] / 365
ALPRAZOLAM	0.5 mg	OTHER: STAT	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
BUPIVACAINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
DEXAMETHASONE	4 mg	OTHER: X 2 VIALS	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
GRANISETRON	1 mg	OTHER: STAT	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
LIDOCAINE	NOT REPORTED	OTHER: STAT	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
MIDAZOLAM	5 mg	OTHER: STAT	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
PROPOFOL	20 mL	OTHER: DURING SURGERY	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
TRANEXAMIC ACID	500 mg	OTHER: STAT X 2 VIALS	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 453
CEFAZOLIN	1000 mg	OTHER: 8 HOURLY	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 454
ONDANSETRON	4 mg	OTHER: 8 HOURLY PRN	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 454
PARACETAMOL	1000 mg	OTHER: 6 HOURLY	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 454
TRANEXAMIC ACID	1000 mg	QD	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 454
BUPRENORPHINE	5 mg	QD	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 455
ZOLPIDEM	12.5 mg	OTHER: NOCTE	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 455
APREPITANT	80 mg	QD	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 456
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 456
PROBIOTICS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 453	Y-M: 20[redacted] / 456
PARECOXIB	40 mg	BID	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 455
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 456
MEROKEN NEW	1 OTHER: SACHET	BID	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 456
PANADEINE CO	2 OTHER: TABLETS	QID	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 470
ETORICOXIB	120 mg	QD	Y-M: 20[redacted] / 455	Y-M: 20[redacted] / 456

ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / 456	Y-M: 20[redacted] / 470
RIVAROXABAN	10 mg	QD	Y-M: 20[redacted] / 457	Y-M: 20[redacted] / 470
VIMOVO	500/20 mg	BID	Y-M: 20[redacted] / 479	NOT REPORTED
OXYBUTYNIN	5.00 mg	QD	Y-M: 20[redacted] / 561	ONGOING
FUSIDIC ACID	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 610	Y-M: 20[redacted] / 615

Event #1: Serious Adverse Event

Event Description	WORSENING OSTEOARTHRITIS LEFT KNEE
Preferred term	変形性関節症
AE Onset Date / Rx Day	[redacted]20[redacted] / 86
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 453): TOTAL LEFT KNEE REPLACEMENT: SUCCESFUL SURGERY	
AE Stopped Rx Day	453
Duration of AE	368 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	OSTEOARTHRITIS
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	WORSENING OSTEOARTHRITIS RIGHT KNEE
Preferred term	変形性関節症
AE Onset Date / Rx Day	[redacted]20[redacted] / 307
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	OSTEOARTHRITIS
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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 7[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左膝変形性関節症の悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，変形性関節症，乾癬性関節炎，潜伏結核，ベーカー嚢腫，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左膝変形性関節症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左膝変形性関節症の悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は重度の左膝痛による人工左膝関節全置換術のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，膝関節全置換術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，arcoxia（exinef），dolorol forte，クレキサン，sovenor patch，イグザレルト，ドルミカム，カイトリル（グラニセトロン），dexona，rayzon，perfalgan，cyclokapron，イメンド，alzam 及びセファゾリンであった。

The patient's past medications include:

TRAMACET for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

VIMOVO for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

FOLIC ACID for MTX TOXICITY ([redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted])

LYRICA for PSORIATIC ARTHRITIS PAIN

Causality for UPADACITINIB (Blinded)

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1) Osteoarthritis aggravated (10031162) (Osteoarthritis (10031161)) [v.23.0] [10031162]

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 OSTEOARTHRITIS LEFT KNEE

- Investigator: Total knee replacement

- AbbVie: event is more likely related to pre-existing osteoarthritis.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は南アフリカの 7[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右膝変形性関節症の悪化の事象を発現した。併用療法として 20[redacted] 年 [redacted] 月 [redacted] 日に人工右膝関節全置換術が行われた。

Event 2 の臨床経過：

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右膝変形性関節症の悪化を発現した。

この入院の前の 20[redacted] 年に，20[redacted] 年に診断された両膝関節の変形性関節症が悪化しており，両膝関節の人工置換術が必要と判断され，2[redacted]0 年に手術が行われることとなった。1 回目の膝関節（左）の人工置換術は 20[redacted] 年 [redacted] 月に完了した（AER #20P-143-3302864-00 において報告済み）。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，20[redacted] 年以降に右膝関節の変形性関節症の悪化と診断されていた右膝関節痛のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，人工右膝関節全置換術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院し，外来理学療法を受けることとなった。

The patient's past medications include:
TRAMACET for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - 14 [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

LYRICA for PSORIATIC ARTHRITIS PAIN [redacted] [redacted] 20[redacted] - 20[redacted]) OXFLAM for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)
---
1) Osteoarthritis aggravated (10031162) (Osteoarthritis (10031161)) [v.23.0] [10031162]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OSTEOARTHRITIS RIGHT KNEE

- **Investigator:** Osteoarthritis

- **AbbVie:** Event more likely related to pre-existing degenerative osteoarthritis, pre-existing obesity (screening BMI was 32.8), and advanced age.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
筋酵素上昇	X			
腎仙痛	X			

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

Medical History	Onset Year
OTHER: AMPUTATED RIGHT 5TH FINGER	19[redacted]
OTHER: HEMATURIA	19[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
HYPERTENSION	20[redacted]
OTHER: SINUS BRADYCARDIA	20[redacted]
OTHER: DIVERTICULOSIS	20[redacted]
OTHER: NON-SPECIFIC MUSCLE DISCOMFORT	20[redacted]
OTHER: RENAL STONE	20[redacted]
OTHER: DEGENERATIVE FACET ARTHOPAHTY	20[redacted]
OTHER: INCREASED BODY MASS INDEX	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: BOSNIAK TYPE 1 CYST (LATERAL MID POLE CORTEX OF RIGHT KIDNEY)	20[redacted]

Prior Procedures	Procedure Year
INCREASED CREATINE PHOSPHOKINASE: MUSCLE BIOPSY	NOT REPORTED
SURGERY: VASECTOMY	19[redacted]
SURGERY: ARTHROSCOPY RIGHT KNEE	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	9	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 MG	ORAL	QD	[redacted] / 1	[redacted] / 168	168
ABT-494	15 MG	ORAL	QD	[redacted] / 169	[redacted] / 393	225
ABT-494	15 MG	ORAL	QD	[redacted] / 394		

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-M: 19[redacted]
LOSARTAN	100 mg	QD	Y-M: 20[redacted]
RAMIPRIL	1 OTHER: TAB	QD	Y-M: 20[redacted]
VERAPAMIL	240 mg	QD	Y-M: 20[redacted]
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -311
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -298
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -280
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -235
VIMOVO	1 OTHER: TAB	BID	Y-M: 20[redacted] / -235
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted] / -224
TRAMADOL	100 mg	OTHER: STAT	Y-M: 20[redacted] / -112
PNEUMOCOCCAL VACCINE	0.5 mL	OTHER: STAT	Y-M: 20[redacted] / -28

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LOSARTAN	100 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 81
VERAPAMIL	240 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 141
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -311	Y-M: 20[redacted] / 415
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -298	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -280	Y-M: 20[redacted] / 254
ACETYLCYSTEINE	1 OTHER: TAB	OTHER: 8 HOURLY	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 32
BENZYDAMINE	1 OTHER: SPRAY	OTHER: 8 HOURLY PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 32
METRONIDAZOLE	1 OTHER: APPLICATION	OTHER: 12 HOURLY	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 32
HYZAAR	100/25 mg	QD	Y-M: 20[redacted] / 82	NOT REPORTED
DEXAMETHASONE	2 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
FENTANYL	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
KETOROLAC	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149

ONDANSETRON	2 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
OXYCODONE	5 mg	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
PARACETAMOL	1 g	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
PHENYLEPHRINE	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
PROPOFOL	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
SEVOFLURANE	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
TAMSULOSIN	1 OTHER: TAB	OTHER: STAT	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
MYPRODOL	2 OTHER: TABS	QD	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 152
AUGMENTIN SR	1000 mg	BID	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 168
AUGMENTIN	1 g	BID	Y-M: 20[redacted] / 186	Y-M: 20[redacted] / 190
ENTIRO	1 OTHER: TAB	QD	Y-M: 20[redacted] / 200	NOT REPORTED
MOVICOL	1 OTHER: SATCHET	OTHER: BD PRN	Y-M: 20[redacted] / 200	NOT REPORTED
FLEBOBAG RING LACT	1000 mL	OTHER: STAT	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
HYOSCINE	20 mg	OTHER: STAT	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
LORNOXICAM	16 mg	OTHER: STAT	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
MORPHINE	2 mg	OTHER: STAT	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
MORPHINE	3 mg	OTHER: STAT	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
ONDANSETRON	4 mg	OTHER: STAT	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
PARACETAMOL	1 g	OTHER: STAT	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 254
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 459
PYRIDOXINE	25 mg	QD	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 459
AMITRIPTYLINE	25 mg	OTHER: NOCTE	Y-M: 20[redacted] / 407	NOT REPORTED
ACICLOVIR	800 mg	OTHER: 5 TIMES DAILY	Y-M: 20[redacted] / 407	Y-M: 20[redacted] / 414
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 415	Y-M: 20[redacted] / 419

ETORICOXIB	120 mg	QD	Y-M: 20[redacted] / 416	Y-M: 20[redacted] / 420
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / 421	NOT REPORTED
ISONIAZID	150 mg	QD	Y-M: 20[redacted] / 480	ONGOING
PYRIDOXINE	25 mg	QD	Y-M: 20[redacted] / 480	ONGOING

Event #1: Serious Adverse Event

Event Description	RAISED MUSCLE ENZYMES
Preferred term	筋酵素上昇
AE Onset Date / Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 129): Creatine Kinase: 210 [NOT REPORTED - 172] IU/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 149): MUSCLE BIOPSY: FEATURES CONSISTENT WITH NEUROPATHIC COMPONENT. MILD ASSOCIATED MYOPATHIC FEATURES WITH EVIDENCE OF MITOCHONDRIAL DYSFUNCTION. POSSIBLE DRUG RELATE. NO EVIDENCE OF AN INFLAMMATORY MYOPATHY. DISCUSSED WITH SPECIALIST- NOT INDICATIVE OF ANY SPECIFIC PATHOLOGY; [redacted]20[redacted] (RX DAY 169): STRESS ECG: SINUS BRADYCARDIA.

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Mild
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: Serious Adverse Event

Event Description	RIGHT RENAL COLIC
Preferred term	腎仙痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 254
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 254): Albumin: 37 [35 - 52] G/L; Bicarbonate: 28 [21 - 31] MMOL/L; Calcium: 2.3 [2.1 - 2.55] MMOL/L; Chloride: 99 [101 - 109] MMOL/L; Creatinine: 90 [59 - 104] UMOL/L; Erythrocytes: 4.1 [4.5 - 5.9] 10^12/L; Hematocrit: 0.41 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 141 [125 - 173] G/L; Leukocytes: 7.1 [4 - 11] 10^9/L; NPTST044-ANION GAP: 11 [3 - 15] MMOL/L; NPTST129-C-REACTIVE PROTEIN: 0.9 [NOT REPORTED - 5] mg/L; NPTST248-EPI GFR: 82 [90 - NOT REPORTED] mL/min/1.73m2; NPTST429-MCV: 100 [81 - 95] FL; NPTST497-PARATHYROID HORMONE: 69.5 [15.2 - 65.7] PG/ML; NPTST497-PARATHYROID HORMONE: 7.3 [1.6 - 6.9] PMOL/L; NPTST661-URATE: 0.4 [0.21 - 0.43] MMOL/L; NPTST662-UREA: 6 [2.1 - 7.1] MMOL/L; Platelets: 247 [140 - 420] 10^9/L; Potassium: 3.6 [3.4 - 4.5] MMOL/L; Sodium: 138 [136 - 146] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 254): CT SCAN: SPECIFICALLY NO SIGNS OF ANY RENAL, URETERIC, VESICOURETERIC OR BLADDER CALCULI SEEN.

AE Stopped Rx Day	254
Duration of AE	1 DAY
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SUSPECTED RENAL STONES. CONFIRMED THROUGH SCAN, NO STONES
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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，筋原性酵素上昇の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元紙巻タバコ喫煙者（1 日 1 箱を 9 年間），血尿，局面型乾癬，高血圧，洞性徐脈，非特異的筋不快感，腎結石，変性椎間関節症，乾癬性関節炎及び少量の現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は筋原性酵素上昇を発現した。

本事象発現前，20[redacted] 年，被験者は筋不快感が出現した。被験者は神経学医を受診した。結果は正常であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は筋不快感及び CK 上昇を発現した。被験者は酒さ皮膚炎（非重篤な事象），上気道感染（非重篤な事象）及び嗜眠（非重篤な事象）を発現した。非重篤な事象はすべて消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は筋生検のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験

者は退院した。

The patient's past medications include:

PNEUMOVAX 23 for VACCINATION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Muscle enzyme increased (10057945) (Muscle enzyme increased (10057945)) [v.21.1] [10057945]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of RAISED MUSCLE ENZYMES

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CREATINE KINASE:** 241 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 287 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 589 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 452 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 625 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 846 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 1454 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 346 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATINE KINASE:** 210 IU/L (normal 0 to 172)

[redacted] **20[redacted] CREATINE KINASE:** 540 U/L (normal 39 to 308)

[redacted] **20[redacted] CREATININE:** 0.9 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] CREATININE:** 0.8 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] CREATININE:** 1 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] CREATININE:** 1 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] CREATININE:** 0.9 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] CREATININE:** 0.9 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] CREATININE:** 1.1 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] CREATININE:** 0.9 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] CREATININE:** 0.9 mg/dL (normal 0.5 to 1.3)

[redacted] **20[redacted] LIMITED MRI BRAIN:** Normal study

[redacted] **20[redacted] LIMITED MRI SPINAL COLUMN:** No abnormality of the spinal cord and spinal canal. Degenerative facet arthropathy and disc disease at L3-4 and L4-5

[redacted] **20[redacted] MRI CERVICAL SPINE:** NO SPINAL CORD ABNORMALITY. Multilevel degenerative disc and facet disease in C3-4

[redacted] **20[redacted] MUSCLE BIOPSY:** Features consistent with neuropathic component, mild association myopathic features with evidence of mitochondrial dysfunction. Possible drug related. No evidence of an inflammatory myopathy.
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は南アフリカの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右腎仙痛の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，元紙巻タバコ喫煙者（1 日 1 箱を 9 年間，1989 年に禁煙），腎結石，ボディ・マス・インデックス増加，乾癬性関節炎，BOSNIAK 分類 1 型の嚢胞（右腎の lateral mid pole cortex）及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右腎仙痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右腎仙痛は消失した。

被験者は夜中の 24 時 00 分に非常に激しい右側腹部痛を来した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はさらなる検査及び疼痛管理のため入院した。CT スキャン検査で腎結石の徴候は認められず，右側腹部痛の原因は不明であった。右側腹部痛は 2～3 時間後に治まった。

投与された薬剤は，アセトアミノフェン，トラマドール，ringers lactate，flomax，xefo，モルヒネ及び hyospasmol であった。

The patient's past medications include:

VIMOVO for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Renal colic (10038419) (Renal colic (10038419)) [v.22.1] [10038419]

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 RIGHT RENAL COLIC

- Investigator: SUSPECTED RENAL STONES. CONFIRMED THROUGH SCAN, NO STONES

- AbbVie: More likely related to pre-existing renal stones and underlying obesity.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 37 G/L (normal 35 to 52)

[redacted] **20[redacted] ANION GAP:** 11 MMOL/L (normal 3 to 15)

[redacted] **20[redacted] BICARBONATE:** 28.0 MMOL/L (normal 21.0 to 31.0)

Unknown date BMI: 35.80247 no units

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 0.9 MG/L (normal <5.0)

[redacted] **20[redacted] CALCIUM:** 2.30 MMOL/L (normal 2.10 to 2.55)

[redacted] **20[redacted] CHLORIDE:** 99 MMOL/L (normal 101 to 109)

[redacted] **20[redacted] CREATININE:** 90 no units (normal 59 to 104)

[redacted] **20[redacted] CT SCAN:** Specifically no signs of any renal, ureteric, vesicoureteric or bladder calculi seen.

[redacted] **20[redacted] GFR:** 82 ML/Min (normal >90)

[redacted] **20[redacted] HEMATOCRIT:** 0.41 L (normal 0.40 to 0.50)

[redacted] **20[redacted] HEMOGLOBIN:** 14.1 G/DL (normal 12.5 to 17.3)

[redacted] **20[redacted] MCV:** 100 FL (normal 81 to 95)

[redacted] **20[redacted] PARATHYROID HORMONE:** 7.3 pmol/L (1.6-6.9)

[redacted] **20[redacted] PARATHYROID HORMONE:** 69.5 pg/mL(15.2-65.7)

[redacted] **20[redacted] PLATELET COUNT:** 247 X10**9/L (normal 140 to 420)

[redacted] **20[redacted] POTASSIUM:** 3.6 MMOL/L (normal 3.4 to 4.5)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.06 X10**12/L (normal 4.5 to 5.9)

[redacted] **20[redacted] SODIUM:** 138 MMOL/L (normal 136 to 146)

[redacted] **20[redacted] URATE:** 0.40 MMOL/L (normal 0.21 to 0.43)

[redacted] **20[redacted] UREA:** 6.0 MMOL/L (normal 2.1 to 7.1)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.1 X10**9/L (normal 4.0 to 11.0)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
頚髄神経根障害	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	4[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: HYPERURICEMIA	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	23	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 391	222
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 392		

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]
DAIVOBET	1 OTHER: APP	QD	Y-M: 20[redacted]

METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -27
VERAPAMIL	1 OTHER: TAB	QD	Y-M: 20[redacted] / -27
PNEUMOCOCCAL VACCINE	0.5 mL	OTHER: STAT	Y-M: 20[redacted] / -24

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
DAIVOBET	1 OTHER: APP	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / -24
ETORICOXIB	90 mg	QD	Y-M: 20[redacted] / -27	NOT REPORTED
VERAPAMIL	1 OTHER: TAB	QD	Y-M: 20[redacted] / -27	NOT REPORTED
PNEUMOCOCCAL VACCINE	0.5 mL	OTHER: STAT	Y-M: 20[redacted] / -24	Y-M: 20[redacted] / -24
HETASTARCH	1500 mL	QD	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 3
RINGER-LACTATE	1 L	OTHER: 8 HOURLY	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 3
DIAZEPAM	10 mg	OTHER: NOCTE	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 6
MORPHINE	10 mg	PRN	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 6
PARECOXIB	40 mg	BID	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 7
PARACETAMOL	1 g	QD	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 9
BISACODYL	5 mg	OTHER: NOCTE	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 6
PREGABALIN	150 mg	BID	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 8
MIDAZOLAM	7.5 mg	QD	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 7
PHENYLEPHRINE	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 7
PROPOFOL	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 7
REMIFENTANIL	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 7
RINGER-LACTATE	1 L	OTHER: 8 HOURLY	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 7
SEVOFLURANE	1 OTHER: DOSE	OTHER: STAT	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 7
CEFAZOLIN	2 g	OTHER: 6 HOURLY	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 8
OXYCODONE	10 mg	OTHER: 4-6 HOURLY/PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 10
TARGIN	10 mg	OTHER: BID/PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 28
STILPANE	2 OTHER: TABS	PRN	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 21
ALLOPURINOL	100 mg	QD	Y-M: 20[redacted] / 29	NOT REPORTED
AUGMENTIN SR	1 g	BID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 36
ENTIRO	1 OTHER: TAB	BID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 36

Event #1: Serious Adverse Event

Event Description	C7 RADICULOPATHY
Preferred term	頚髄神経根障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 3
Age at AE Onset	4[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 4): MRI CERVICAL SPINE: CERVICAL SPONDYLOSIS AT THE C5-6 AND C6-7 LEVELS. MODERATE LEFT AND SEVERE RIGHT C5-6, AND SEVERE LEFT C6-7 NEURAL FORAMINAL STENOSIS; [redacted]20[redacted] (RX DAY 7): ANTERIOR CERVICAL DISECTOMY AND FUSION C5-6 AND C6-7: CORRECTIVE SURGERY

AE Stopped Rx Day	49
Duration of AE	47 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SHOULDER PAIN
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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，C7 神経根障害の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，高血圧，乾癬性関節炎，喫煙者（1 日 1 箱を 23 年間）及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は C7 神経根障害を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，C7 神経根障害は消失した。

被験者はザリガニ釣りに出かけたが，激しい肩痛に見舞われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左肩痛のため入院した。診察の結果，左肩痛は皮膚分節 T1/C6～C7 に見られ，三頭筋反射低下が認められた。被験者は関節炎を有していたため，肩痛が生じやすい素因を持っていた。MRI 検査が行われ，C7 神経根障害が確認された。20[redacted] 年 [redacted] 月 [redacted] 日，C5～C7 の前方頚椎椎間板切除

融合術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，perfalgan，rayzon，ボルベン，セファゾリン，oxynorm，targinact，stilpane，モルヒネ，ジアゼパム及びリリカであった。

The patient's past medications include:

DOVOBET for PSORIASIS (20[redacted] - [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Cervical radiculopathy (10050217) (Cervical radiculopathy (10050217)) [v.22.1] [10050217]

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 C7 RADICULOPATHY

- Investigator: Shoulder pain

- AbbVie: Event is not consistent with study drug's mechanism of action. Pre-existing psoriatic arthritis is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** Screening chest x-ray: incidental T10 wedge compression fracture

[redacted] **20[redacted] MRI CERVICAL SPINE:** Cervical spondylosis at the C5-6 and C6-7 levels. Moderate left and severe right C5-6, and severe left C6-7 neural foraminal stenosis

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 30 mg QD	3[redacted]	FEMALE	MULTIPLE

Medical History	Onset Year
OTHER: VAGINAL THRUSH	20[redacted]
OTHER: INSOMNIA	20
OTHER: RECURRENT URINARY TRACT INFECTION	20
HYPERTENSION	20
OTHER: HIATUS HERNIA	20
OTHER: LOW VITAMIN D LEVELS	20
OTHER: NON-ALCOHOLIC FATTY LIVER DISEASE	20
OTHER: OSTEOPENIA	20
OTHER: PLAGUE PSORIASIS	20
PSORIATIC ARTHRITIS	20
OTHER: L5 DISC TEAR	20
OTHER: MECHANICAL BACKPAIN	20

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	6	20[redacted]
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] / 166	166
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 167	[redacted]20[redacted] / 385	219

ABT-494 30 MG ORAL QD 27JUN2019 / 386

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMITRIPTYLINE	25 mg	OTHER: NOCTE	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
CHLOROQUINE	1 OTHER: TABLET	OTHER: MONDAY TO FRIDAY	Y-M: 20[redacted]
FLUCONAZOLE	150 mg	OTHER: MONTHLY	Y-M: 20[redacted]
ZOLPIDEM	1 OTHER: TABLET	PRN	Y-M: 20[redacted]
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	TID	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
DICLOFENAC	50 mg	BID	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
STILPANE	2 OTHER: TABLET	BID	Y-M: 20[redacted]
ERGOCALCIFEROL	50000 ug	EVERY WEEK	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
NATTO K2 OSTEO	1 OTHER: TABLET	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
DICLOFENAC	1 OTHER: TABLET	PRN	Y-M: 20[redacted]
LORNOXICAM	8 mg	BID	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	1 g	BID	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
TARGIN	10 mg	BID	Y-M: 20[redacted]
XAMIOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
BISOPROLOL	5 mg	QD	Y-M: 20[redacted] / -157
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / -58

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
AMITRIPTYLINE	25 mg	OTHER: NOCTE	Y-M: 20[redacted]	NOT REPORTED
FLUCONAZOLE	150 mg	OTHER: MONTHLY	Y-M: 20[redacted]	NOT REPORTED
ZOLPIDEM	1 OTHER: TABLET	PRN	Y-M: 20[redacted]	NOT REPORTED
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED
DICLOFENAC	50 mg	BID	Y-M: 20[redacted]	NOT REPORTED
STILPANE	2 OTHER: TABLET	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 776
ERGOCALCIFEROL	50000 ug	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
NATTO K2 OSTEO	1 OTHER: TABLET	QD	Y-M: 20[redacted]	NOT REPORTED
PREDNISONE	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 96
SULFASALAZINE	1 g	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 750
BISOPROLOL	5 mg	QD	Y-M: 20[redacted] / -157	NOT REPORTED
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / -58	NOT REPORTED
PREDNISOLONE	1 OTHER: DROP	QID	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 107
CYANOCOBALAMIN	1 mL	OTHER: MONTHLY	Y-M: 20[redacted] / 253	NOT REPORTED
ESCITALOPRAM	10 mg	QD	Y-M: 20[redacted] / 271	NOT REPORTED
ALPRAZOLAM	1 mg	QD	Y-M: 20[redacted] / 271	Y-M: 20[redacted] / 379
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 305
AMOXICILLIN	500 mg	TID	Y-M: 20[redacted] / 362	Y-M: 20[redacted] / 366
ALPRAZOLAM	0.5 mg	TID	Y-M: 20[redacted] / 380	NOT REPORTED
ULTRACET	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 451
FOSFOMYCIN	1 OTHER: SACHET	OTHER: ONCE	Y-M: 20[redacted] / 388	Y-M: 20[redacted] / 388
AUGMENTIN	1 g	BID	Y-M: 20[redacted] / 399	NOT REPORTED
LORNOXICAM	8 mg	OTHER: ONCE	Y-M: 20[redacted] / 415	Y-M: 20[redacted] / 415
ETONOGESTREL	68 mg	OTHER: ONCE	Y-M: 20[redacted] / 428	NOT REPORTED
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 446	Y-M: 20[redacted] / 448
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 448	Y-M: 20[redacted] / 466
METHYLPREDNISOLONE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 460
PARECOXIB	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 460
ACICLOVIR	800 mg	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 460	Y-M: 20[redacted] / 464

CELESTONA BIFAS	1 mL	OTHER: ONCE	Y-M: 20[redacted] / 537	Y-M: 20[redacted] / 537
LIDOCAINE	1 mL	OTHER: ONCE	Y-M: 20[redacted] / 537	Y-M: 20[redacted] / 537
CLOXACILLIN	100 mg	TID	Y-M: 20[redacted] / 626	Y-M: 20[redacted] / 630
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / 750	NOT REPORTED
ULTRACET	2 OTHER: TABLETS	BID	Y-M: 20[redacted] / 777	NOT REPORTED

Event #2: Serious Adverse Event

Event Description	WORSENING OF VERICOSE VEINS BOTH LEGS
Preferred term	静脈瘤
AE Onset Date / Rx Day	[redacted]20[redacted] / 526
Age at AE Onset	3[redacted]

Laboratory Testing
NOT REPORTED

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 526): RIGHT BELOW KNEE GREAT SAPHENOUS VEIN FOAN SCLEROTHERAPY: SUCCESSFUL; RIGHT ACCESSORY SAPHENOUS VEIN RADIOFREQUENCY ABLATION FOAN SCLEROTHERAPY: SUCCESSFUL; BILATERLA LOWER LIMB VARICOSITY AVULSIONS: SUCCESSFUL; LEFT CALF PERFORATOR LIGATION: SUCCESSFUL; LEFT GREAT SAPHENOUS VEIN RADIOFREQUENCY ABLATION: NO PERI OPERATIVE PROBLEMS AND SHE WAS DISCHARGED THE SAME DAY

AE Stopped Rx Day	532
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SHE IS A NURSE AND STANDS A LOT
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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，両脚静脈瘤の悪化の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，関節炎，元喫煙者（1 日 1 箱を 6 年間），高血圧，低ビタミン D 値，非アルコール性脂肪肝疾患，骨減少症，局面型乾癬，乾癬性関節炎及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両脚静脈瘤の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，両脚静脈瘤の悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は両脚静脈瘤の悪化のため入院した。被験者は，職業が看護師であり，長時間立ちっぱなしで脚が疲れると話した。同日，左大伏在静脈のラジオ波焼灼療法，右副伏在静脈のラジオ波焼灼療法及びフォーム硬化療法，右膝関節直下大伏在静脈のフォーム硬化療法，左腓腹部の穿通枝結紮術並びに両側下腿静脈瘤切除術が行われた。合併症はなく，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に退院した。

The patient's past medications include:

AZATHIOPRINE for ARTHRITIS (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CHLOROQUINE for ARTHRITIS (20[redacted] - [redacted] 20[redacted])

LENOVATE OINTMENT for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for PSORIATIC ARTHRITIS and PSORIATIC ARTHRITIS FLARE HANDS, KNEES, FEET ([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])

METHOTREXATE for PSORIASIS and PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ADVANTAN MILK for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VOLTAREN SUPPOSITORY for PSORIATIC ARTHRITIS and PSORIATIC ARTHRITIS FLARE HANDS, KNEES, FEET ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

XEFO for PSORIATIC ARTHRITIS and WORSENING OF BACKPAIN DUE TO L5 TEAR ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

DOVATE OINTMENT for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

TARGINACT for PSORIATIC ARTHRITIS ([redacted])

XAMIOL GEL for PSORIASIS ([redacted])

PRED FORTE for UVEITIS ([redacted])

ACYCLOVIR for COLD SORES ([redacted])

RAYZON for PSORIATIC ARTHRITIS FLARE HANDS, KNEES, FEET ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Varicose veins of lower extremities (10047013) (Varicose vein (10046996)) [v.22.1] [10047013]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF VERICOSE VEINS BOTH LEGS

- Investigator: She is a nurse and stands a lot.

- AbbVie: Event is more likely related to standing a lot due to work. Additional risk factors include female gender and obesity.

Relevant Laboratory & Other Diagnostic Tests

Unknown date BMI: 32.1 no units

[redacted] **WEIGHT:** 85.3 KG

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	5[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
PSORIATIC ARTHRITIS	19[redacted]
OTHER: MECHANICAL BACKPAIN	19[redacted]
DIABETES MELLITUS: TYPE 2	20[redacted]
HYPERTENSION	20[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): NON-ALCOHOLIC FATTY LIVER DISEASE	20[redacted]
TUBERCULOSIS: LATENT	20[redacted]

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	FORMER	2 - 4 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 163	163
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 164	[redacted]20[redacted] / 393	230
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 394		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	7,5 mg	EVERY WEEK	Y-M: 19
METFORMIN	1000 mg	BID	Y-M: 20
METHOTREXATE	7,5 mg	EVERY WEEK	Y-M: 20
ENALAPRIL	20 mg	QD	Y-M: 20
CELECOXIB	200 mg	PRN	Y-M: 20
FOLIC ACID	5 mg	QD	Y-M: 20
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20
DIOVAN AMLO	1 OTHER: TABLET	QD	Y-M: 20
APREMILAST	30 mg	QD	Y-M: 20
VALSARTAN	160 mg	QD	Y-M: 20 / -192
ISONIAZID	300 mg	QD	Y-M: 20 / -23
PYRIDOXINE	25 mg	QD	Y-M: 20 / -23

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
METFORMIN	1000 mg	BID	Y-M: 20	NOT REPORTED
FOLIC ACID	5 mg	QD	Y-M: 20	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20	NOT REPORTED
VALSARTAN	160 mg	QD	Y-M: 20 / -192	NOT REPORTED
ISONIAZID	300 mg	QD	Y-M: 20 / -23	Y-M: 20 / 263
PYRIDOXINE	25 mg	QD	Y-M: 20 / -23	Y-M: 20 / 263
AMLODIPINE	10 mg	QD	Y-M: 20 / 113	NOT REPORTED
CLARITHROMYCIN	500 mg	BID	Y-M: 20 / 282	Y-M: 20 / 286
CLOTRIMAZOLE	TOPICAL USE OTHER: TOPICAL	BID	Y-M: 20 / 327	Y-M: 20 / 331
FLUCONAZOLE	200 mg	QD	Y-M: 20 / 327	Y-M: 20 / 362
SIMVASTATIN	10 mg	OTHER: NOCTE	Y-M: 20 / 393	NOT REPORTED

Event #1: Serious Adverse Event

Event Description	ATYPICAL CHEST PAIN
Preferred term	胸痛
AE Onset Date / Rx Day	20 / 233
Age at AE Onset	5

Laboratory Testing

20 (RX DAY 327): Alanine Aminotransferase: 156 [NOT REPORTED - 50] U/L; Aspartate Aminotransferase: 99 [NOT REPORTED - 50] IU/L; NPTST209-CRP: 27.7 [NOT REPORTED - 5] mg/L; NPTST479-NT-PROBNP: 15 [0 - 125] PG/ML; NPTST646-TROPONIN I: 30 [0 - 70] NG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 327): ELECTRO CARDIOGRAM: NORMAL; [redacted]20[redacted] (RX DAY 328): ECHOCARDIOGRAM: NO ABNORMALITIES; STRESS ELECTROCARDIOGRAM: NO PROVOKABLE ISCHAEMIA; ULTRASOUND OF ABDOMEN: FATTY INFILTRATION OF LIVER, NO HEPATOMEGALY

AE Stopped Rx Day	328
Duration of AE	96 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	OCCASIONAL DIZZINESS AND ON ONE OCCASION HAD AN EPISODE OF PRESYNCOPE.
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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，非定型的胸痛の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，高血圧，非アルコール性脂肪肝疾患，潜伏結核，非喫煙者及び元飲酒者（1 日 2～4 杯）であった。

20[redacted] 年 [redacted] 月，被験者は非定型的胸痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，非定型的胸痛は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日より，非重篤な体位性浮動性めまい及び呼吸困難が出現していた。

被験者は疲労を感じていたが，明らかな胸痛はなかった。CK 増加も認められた。被験者は，心臓専門医の見解を得るため，また脂肪肝疾患の検査のため，20[redacted] 年 [redacted] 月 [redacted] 日に入院した。疲労，過去の体位性浮動性めまい及び労作時呼吸困難は別として，被験者は肝臓の超音波検査のため入院した。被験者は心臓専門医に紹介された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日付け心臓専門医の記録より：被験者は左側胸痛のため来院した。痛みは側腹部及び背部にもあった。症状は局所圧迫により悪化した。症状は安静時に最も顕著であったが，

労作時も時折増悪した。放散痛はなかった。被験者によれば，これらの症状は 3〜4 ヵ月続いていた。動悸は伴っていなかった。被験者にはクラックコカインの使用歴があった。心電図検査の結果は正常で，急性虚血の徴候は認められなかった。運動負荷試験で異常は認められなかった。併存疾患，とりわけ糖尿病が存在することから，胸部不快感の症状が継続するようであれば，冠動脈血管造影術に耐えられないおそれがある。糖尿病を完全にコントロールする必要がある。

The patient's past medications include:

CELEBREX for PSORIATIC ARTHRITIS ([redacted])

APREMILAST for PSORIATIC ARTHRITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Chest pain (10008479) (Chest pain (10008479)) [v.22.1] [10008479]

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 ATYPICAL CHEST PAIN

- Investigator: occasional dizziness and on one occasion had an episode of presyncope.

- AbbVie: Risk factors include pre-existing diabetes mellitus type 2 and hypertension.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL ULTRASOUND:** Fatty infiltration of liver, no hepatomegaly

[redacted] **ALT:** 156 IU/L (normal <50)

[redacted] **20[redacted] AST:** 99 IU/L (normal <50)

[redacted] **20[redacted] BLOOD PRESSURE:** 140-80

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 27.7 IU/L (normal <5)

Unknown date CK: Elevated

[redacted] **20[redacted] CONJUGATED BILIRUBIN:** 5 MCMOL/L (normal <3.4)

[redacted] **20[redacted] ECHOCARDIOGRAM:** no abnormalities

[redacted] **20[redacted] ECHOCARDIOGRAM:** The left ventricle was not dilated and well contracting with normal systolic function. The left ventricle EF was est at 72%. No regional wall motion abnormalities. Left atrium not dialted. Left ventricle hypertrophy and diastolic dysfunction was noted. Mitral vale was morphologically normal with no stenosis or regurgitation.No aortic stenosis or regurgitation. Right side heart not dilated and no tricuspid regurgitation noted. No pericardial effusion. No intra cardiac thrombus or valvular vegitations noted. No abnormalities.

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Not clinically significant

[redacted] **20[redacted] HBA1C:** 6.8 % (normal 3.9 to 6.1)

[redacted] **20[redacted] HEART RATE:** 74 BPM

[redacted] **20[redacted] HEMATOCRIT:** 0.37 L/L (normal 0.4 to 0.5)

[redacted] **20[redacted] HEMOGLOBIN:** 12.3 G/DL (normal 12.5 to 17.3)

[redacted] **20[redacted] LYMPHOCYTES:** 0.8 X10**9/L (normal 1 to 4)

[redacted] **20[redacted] NT-PROBNP:** 15 PG/ML (normal 0 to 125)

[redacted] **20[redacted] RDW:** 16.4 % (normal 10 to 15)

[redacted] **20[redacted] RED CELL COUNT:** 4.28 X10**12/L (normal 4.5 to 5.9)

[redacted] **20[redacted] STRESS ELECTROCARDIOGRAM:** no provokable ischaemia

[redacted] **20[redacted] TROPONIN I:** 30 Ng/L (normal 0 to 70)

[redacted] **20[redacted] TSH:** 3.72 mIU/L (normal 0.38 to 5.33)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
裂孔ヘルニア	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	2[redacted]	FEMALE	MULTIPLE

Medical History	Onset Year
OTHER: PLAGUE PSORIASIS	20[redacted]
OTHER: SCOLIOSIS	20
ANEMIA: IRON DEFICIENCY ANAEMIA	20
OTHER: HYPERMOBILITY SYNDROME	20
MIGRAINE HEADACHE: MIGRAINES	20
PEPTIC ULCER DISEASE: ON TREATMENT	20
OTHER: GASTRIC OESOPHAGEAL REFLUX DISORDER	20
OTHER: LOW VIT D	20
OTHER: METHOTREXATE INDUCED NAUSEA	20
PSORIATIC ARTHRITIS	20

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY AND ADENOIDECTOMY	20
SURGERY: TYMPANOPLASTY	20
SURGERY: APPENDICECTOMY	20
SURGERY: 4 WISDOM TEETH REMOVED	20

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

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 188	188

ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / [redacted]20[redacted] / 393 189	205
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 394	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
IRON IN OTHER COMBINATIONS	30 mg	QD	Y-M: 20[redacted]
PREDNISONE	30 mg	PRN	Y-M: 20[redacted]
ULTRACET	2 OTHER: TABLETS	QD	Y-M: 20[redacted]
AMITRIPTYLINE	10 mg	OTHER: NOCTE	Y-M: 20[redacted]
ETORICOXIB	90 mg	QD	Y-M: 20[redacted]
CELECOXIB	200 mg	BID	Y-M: 20[redacted]
ETONOGESTREL	68 mg	OTHER: EVERY 3 YEARS	Y-M: 20[redacted]
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -147
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -147
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -147
ERGOCALCIFEROL	50 000 OTHER: UNITS	OTHER: ALT WEEKS	Y-M: 20[redacted] / -144
TRAMADOL	50 mg	OTHER: STAT	Y-M: 20[redacted] / -98
CELESTONA BIFAS	1 mL	OTHER: STAT	Y-M: 20[redacted] / -21
LIDOCAINE	1 mL	OTHER: STAT	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
IRON IN OTHER COMBINATIONS	30 mg	QD	Y-M: 20[redacted]	NOT REPORTED
ULTRACET	2 OTHER: TABLETS	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 181
AMITRIPTYLINE	10 mg	OTHER: NOCTE	Y-M: 20[redacted]	NOT REPORTED
CELECOXIB	200 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 181
ETONOGESTREL	68 mg	OTHER: EVERY 3 YEARS	Y-M: 20[redacted]-08	NOT REPORTED
ERGOCALCIFEROL	50 000 OTHER: UNITS	OTHER: ALT WEEKS	Y-M: 20[redacted] / -144	NOT REPORTED
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 165
MIDAZOLAM	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 165	NOT REPORTED
ZOLPIDEM	12.5 mg	OTHER: NOCTE	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 184
GRANISETRON	1 g	OTHER: 8HRLY/PRN	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 185
LORNOXICAM	8 mg	OTHER: 8HRLY	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 185
ONDANSETRON	4 mg	OTHER: 6-8HRLY	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 185

PARACETAMOL	1 g	OTHER: 6HRLY	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 185
PETHIDINE	75 mg	OTHER: 8HRLY/PRN	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 185
PROCHLORPERAZINE	12.5 mg	OTHER: 8 HRLY/PRN	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 185
TARGIN	10 mg	OTHER: 12 HRLY	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 185

Event #1: Serious Adverse Event

Event Description	HIATIS HERNIA
Preferred term	裂孔ヘルニア
AE Onset Date / Rx Day	[redacted]20[redacted] / 165
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 182): LAPAROSCOPIC NISSEN FUNDOPLICATION:	
AE Stopped Rx Day	182
Duration of AE	18 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DECREASED TONE OF THE LOWER OESOPHAGEAL SPHINCTER
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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，裂孔ヘルニアの事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，鉄欠乏性貧血，過剰可動性症候群，消化性潰瘍疾患（治療中），胃食道逆流症，メトトレキサート誘発性悪心，乾癬性関節炎，非喫煙者及び現飲酒者（1

日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は裂孔ヘルニアを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，裂孔ヘルニアは消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，胃内視鏡検査が行われ，大きな（非重篤）裂孔ヘルニアが認められ，これが不快感の原因であることが判明した。被験者は，横になると呼吸困難が出現するため，体を起こしたまま寝なければならなかった。20[redacted] 年 [redacted] 月 [redacted] 日，ヘルニア修復のため被験者は入院した。治験実施計画書に従って，手術前に治験薬の投与が中止された。20[redacted] 年 [redacted] 月 [redacted] 日，ヘルニア修復後に本事象は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，targinact，perfalgan，ペチジン及び xefo であった。

The patient's past medications include:

TRUSTAN for PEPTIC ULCER DISEASE ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Hiatal hernia (10020024) (Hiatus hernia (10020028)) [v.22.1] [10020024]

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 HIATIS HERNIA

- Investigator: decreased tone of the lower oesophageal sphincter

- AbbVie: DEVELOPMENT OF THE EVENT IS NOT CONSISTENT WITH THE STUDY DRUG'S MECHANISM OF ACTION. ADDITIONAL RISK FACTORS INCLUDE SUBJECT IS OVERWEIGHT (BMI 27 AT SCREENING) AND PRE-EXISTING HYPERMOBILITY SYNDROME.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **GASTROSCOPY:** Laparoscopic Nissen fundoplication.

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	3[redacted]	FEMALE	MULTIPLE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: IRRITABLE BOWEL SYNDROME	20[redacted]
OTHER: HIATUS HERNIA	20[redacted]
OTHER: LOWER BACKPAIN(MECHANICAL)	20[redacted]
OTHER: ACNE PREVIOUSLY	20[redacted]
OTHER: IRON DEFIECIENCY	20[redacted]
OTHER: LOW VITAMIN D LEVEL	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: ALLERGY TO SULPHURS	20[redacted]
DEPRESSION	20[redacted]
OTHER: ANXIETY	20[redacted]
OTHER: ABNORMAL LFT'S SECONDARY TO LEFLUNOMIDE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TUBAL LIGATION	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)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 393	225

ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 394

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-M: 19[redacted]
COLECALCIFEROL	5000 OTHER: UNITS	QD	Y-M: 20[redacted]
CELESTONA BIFAS	2 mL	OTHER: STAT	Y-M: 20[redacted]
ERGOCALCIFEROL	50000 IU	EVERY WEEK	Y-M: 20[redacted]
FERYWEL	1 OTHER: TABLET	BID	Y-M: 20[redacted]
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
NAPROXEN	500 mg	QD	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
VIMOVO	1 OTHER: TABLET	BID	Y-M: 20[redacted]
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
MESALAZINE	800 mg	BID	Y-M: 20[redacted]
CHLOROQUINE	1 OTHER: TABLET	OTHER: MONDAY TO FRIDAY	Y-M: 20[redacted]
AMITRIPTYLINE	10 mg	OTHER: NOCTE	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
STILPANE	2 OTHER: TABLET	OTHER: 6HOURLY	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
AMITRIPTYLINE	25 mg	OTHER: NOCTE	Y-M: 20[redacted]
DULOXETINE	60 mg	QD	Y-M: 20[redacted]
ETORICOXIB	90 mg	QD	Y-M: 20[redacted]
FOLIC ACID	10 mg	QD	Y-M: 20[redacted]
LEFLUNOMIDE	10 mg	OTHER: 5 DAYS PER WEEK	Y-M: 20[redacted]
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]
ALPRAZOLAM	0.25 mg	OTHER: NOCTE	Y-M: 20[redacted]
AMITRIPTYLINE	50 mg	QD	Y-M: 20[redacted]
DULOXETINE	90 mg	QD	Y-M: 20[redacted]
PARACETAMOL	1000 mg	TID	Y-M: 20[redacted]
TRAMADOL	50 mg	TID	Y-M: 20[redacted]
NORGESIC	2 OTHER: TABLETS	OTHER: PRN	Y-M: 20[redacted]
ALPRAZOLAM	0.25 mg	BID	Y-M: 20[redacted]
DULOXETINE	120 mg	QD	Y-M: 20[redacted]
TRAMADOL	100 mg	TID	Y-M: 20[redacted]
LEFLUNOMIDE	20 mg	OTHER: 5 DAYS PER WEEK	Y-M: 20[redacted]
PROPRANOLOL	10 mg	QD	Y-M: 20[redacted]
PROPRANOLOL	10 mg	BID	Y-M: 20[redacted] / -265
LEFLUNOMIDE	20 mg	OTHER: 3 DAYS PER WEEK	Y-M: 20[redacted] / -193
LEFLUNOMIDE	10 mg	QD	Y-M: 20[redacted] / -111

LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted] / -50
DULOXETINE	90 mg	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
COLECALCIFEROL	5000 OTHER: UNITS	QD	Y-M: 20[redacted]	NOT REPORTED
ERGOCALCIFEROL	50000 IU	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PREDNISONE	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED
VIMOVO	1 OTHER: TABLET	BID	Y-M: 20[redacted]	NOT REPORTED
CHLOROQUINE	1 OTHER: TABLET	OTHER: MONDAY TO FRIDAY	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
AMITRIPTYLINE	50 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PARACETAMOL	1000 mg	TID	Y-M: 20[redacted]	NOT REPORTED
NORGESIC	2 OTHER: TABLETS	OTHER: PRN	Y-M: 20[redacted]	NOT REPORTED
ALPRAZOLAM	0.25 mg	BID	Y-M: 20[redacted]	NOT REPORTED
TRAMADOL	100 mg	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 71
PROPRANOLOL	10 mg	BID	Y-M: 20[redacted] / 265	- NOT REPORTED
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted] / 50	- Y-M: 20[redacted] / 71
DULOXETINE	90 mg	QD	Y-M: 20[redacted] / 15	- NOT REPORTED
BETAHISTINE	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 17	NOT REPORTED
PARACETAMOL	500 mg	BID	Y-M: 20[redacted] / 137	NOT REPORTED
TRAMADOL	50 mg	BID	Y-M: 20[redacted] / 137	NOT REPORTED
METFORMIN	500 mg	BID	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 217
CLOTRIMAZOLE	1 OTHER: PESSERY	OTHER: ONCE	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 228
AUGMENTIN	1 g	BID	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 233
NYSTATIN	1 mL	QID	Y-M: 20[redacted] / 293	Y-M: 20[redacted] / 306
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / 404	NOT REPORTED
CYANOCOBALAMIN	1 mL	EVERY WEEK	Y-M: 20[redacted] / 428	NOT REPORTED
LIDOCAINE	5 mL	OTHER: ONCE	Y-M: 20[redacted] / 428	Y-M: 20[redacted] / 428

METHYLPREDNISOLONE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 428	Y-M: 20[redacted] / 428
ACICLOVIR	800 mg	OTHER: 4 HOURLY	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 431
PROMETHAZINE	25 mg	OTHER: NOCTE	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 447
ACICLOVIR	800 mg	OTHER: 8HRLY	Y-M: 20[redacted] / 431	Y-M: 20[redacted] / 434
ACICLOVIR	800 mg	QID	Y-M: 20[redacted] / 434	Y-M: 20[redacted] / 443
PREGABALIN	75 mg	OTHER: NOCTE	Y-M: 20[redacted] / 434	Y-M: 20[redacted] / 446
CEFUROXIME	500 mg	BID	Y-M: 20[redacted] / 666	NOT REPORTED

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

Event Description	HERPES ZOSTER OF UPPER LEG, BUTTOCK AND LOWER BACK
Preferred term	帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 429
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 431): Hematocrit: 0.36 [0.36 - 0.46] FRACTION OF 1; NPTST209-CRP: 10 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (RX DAY 434): Alanine Aminotransferase: 93 [NOT REPORTED - 35] U/L; Aspartate Aminotransferase: 40 [NOT REPORTED - 35] U/L; NPTST290-GAMMA GT-S: 230 [NOT REPORTED - 38] U/L; Protein: 64 [45 - 84] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	446
Duration of AE	18 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は南アフリカの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，大腿，臀部及び腰部の帯状疱疹の事象を発現した。

Event 4 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，非喫煙者及び非飲酒者であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は大腿，臀部及び腰部の帯状疱疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，大腿，臀部及び腰部の帯状疱疹は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はヘルペスを発症した。ヘルペスは左腰部及び臀部の 2 つの皮膚分節に及んでいた。診断は総合診療医が病歴及び身体的診察の結果に基づき確定した。被験者は痛みに対処することができず，20[redacted] 年 [redacted] 月 [redacted] 日に主治医の指示で静脈内抗ウイルス療法及びヘルペス後神経痛のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者には水疱瘡ワクチン及び帯状疱疹ワクチンの接種歴があった。帯状疱疹の既往歴はなかった。

投与された薬剤は，アシクロビル，リリカ及び phenergan であった。

The patient's past medications include:

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

SALAZOPYRINE EN for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

STILPANE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ARCOXIA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LEFLUNOMIDE for PSORIATIC ARTHRITIS ([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])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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 HERPES ZOSTER OF UPPER LEG, BUTTOCK AND LOWER BACK

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 93 U/L (normal <35)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 40 U/L (normal <35)

[redacted] **20[redacted] CRP:** 10 MG/L (normal <5)

[redacted] **20[redacted] GAMMA GT-S:** 230 U/L (normal <38)

[redacted] **20[redacted] HEMATOCRIT:** 35.8 % (normal 36 to 46)

[redacted] **20[redacted] TOTAL PROTEIN:** 64 G/L (normal 45 to 84)

[redacted] **20[redacted] X-RAY:** No erosion on the hands and feet.

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 30 mg QD	5[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAGUE PSORIASIS	19[redacted]
PSORIATIC ARTHRITIS	19[redacted]
OTHER: HYPERCHOLESTEROLAEMIA	20[redacted]
OTHER: IMPAIRED FASTING GLUCOSE	20[redacted]

Prior Procedures	Procedure Year
SURGERY: LEFT ACL REPAIR	19[redacted]
SURGERY: LEFT SHOULDER ROTATOR CUFF REPAIR	19[redacted]
SURGERY: LEFT KNEE ARTHROSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	30 PACK	35	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 393	224
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 394		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INDOMETACIN	100 mg	QD	Y-M: 20[redacted]
INDOMETACIN	100 mg	QD	Y-M: 20[redacted]
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
DICLOFENAC	100 mg	OTHER: ALT DAYS	Y-M: 20[redacted]
ETORICOXIB	90 mg	OTHER: ALT DAYS	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ETORICOXIB	90 mg	OTHER: ALT DAYS	Y-M: 20[redacted]	NOT REPORTED
CITALOPRAM	20 mg	QD	Y-M: 20[redacted] / 306	NOT REPORTED
METFORMIN	1000 mg	QD	Y-M: 20[redacted] / 537	NOT REPORTED
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 538	NOT REPORTED
ENOXAPARIN	80 mg	BID	Y-M: 20[redacted] / 538	Y-M: 20[redacted] / 542
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 538	Y-M: 20[redacted] / 624
RIVAROXABAN	15 mg	QD	Y-M: 20[redacted] / 542	NOT REPORTED

Event #1: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description PULMONARY EMBOLI

Preferred term 肺塞栓症

AE Onset Date / Rx Day [redacted]20[redacted] / 537

Age at AE Onset 5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 537): Leukocytes: 9.3 [15 - 10] 10^9/L; Monocytes: 0.89 [0 - 0.8] 10^9/L; NPTST221-D DIMER: 342 [500 - NOT REPORTED] ng/mL; NPTST534-PROTHROMBIN: 1.0 [0.9 - NOT REPORTED] 099,NOT APPLICABLE

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 537): CT PULMONARY ANGIOGRAM: SMALL BILATERAL PULMONARY EMBOLI

AE Stopped Rx Day 645

Duration of AE 109 DAYS

Severity Severe

Relation to Study Drug by Investigator No Reasonable Possibility

Investigator Alternative Etiology ACCORDING TO PHYSICIAN LETTER: REFERRED FOR INVESTIGATION OF CHRONIC COUGH EXCESS ETOH IF HE GETS UP OR PERFORMS ANY ACTIVITIES HE DEVELOPS TACHYCARDIA.

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: M15-572

治験責任医師からの報告。本被験者は南アフリカの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺塞栓症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，局面型乾癬，乾癬性関節炎，元喫煙者（1 年 30 箱を 35 年間），高コレステロール血症及び現飲酒者（1 日 2 杯未満）であった。

本治験において，被験者は，盲検性維持のため，盲検化された経口製剤の連日投与と盲検化された皮下注製剤の 2 週ごとの投与を受ける予定である。報告によれば，本事象発現前において，盲検化された皮下注製剤の最終投与は 20[redacted] 年 [redacted] 月 [redacted] 日であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺塞栓症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺塞栓症は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日に本事象が発現する前，国内線飛行機で 2 時間の移動中に咳嗽及び嘔吐が出現し，ほぼ午前中を通して持続した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は車（12 時間超）で帰宅し，呼吸困難を発現した。被験者は，少し話しては休むという状態であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は酸素が不足しているような感覚を覚えた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，慢性咳嗽，過剰 ETOH，起床後のあらゆる活動に伴う頻脈のため，呼吸器科医を受診した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，過剰な咳嗽，頻脈（労作時のみで安静時にはなし）及び息切れのため入院した。血管造影検査で肺塞栓症と診断された。入院中，O2 飽和度は正常で，発熱も見られなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

治験責任医師によると，被験者にはほかにも肥満や年齢などの危険因子があった。

退院時サマリーより：20[redacted] 年 [redacted] 月 [redacted] 日から [redacted] 月 [redacted] 日にかけて，被験者の徴候・症状は徐々に改善した。発熱はなく，排尿があり，呼吸困難は減少した。20[redacted] 年 [redacted] 月 [redacted] 日，胸部の診察で呼気延長と散発的な断続性ラ音が聴取されたが，粘性の咳嗽は減少していた。

投与された薬剤は，prednisone，pantoloc，クレキサン及びイグザレルトであった。

The patient's past medications include:

ARTHREXIN for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted], 20[redacted] - 20[redacted])

FOLIC ACID for MTX TOXICITY MANAGEMENT ([redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CATAFLAM for PSORIATIC ARTHRITIS (20[redacted] - 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.23.0] [10037377]

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 PULMONARY EMBOLI

- Investigator: According to physician letter - referred for investigation of chronic cough excess ETOH if he gets up or performs any activities he develops tachycardia. No recent travel.

- AbbVie: Risk factors include pre-existing obesity, pre-existing psoriasis and age. According to the American Heart Association: "Patients older than 40 years are at higher risk, and that risk doubles with each subsequent decade."

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] **20[redacted] ANGIOGRAM:** CT Pulmonary: Small focal filling defects noted within the knee a proximal right upper lobe segmental pulmonary arteries, distal right middle lobe segmental pulmonary artery, proximal right lower lobe segmental pulmonary arteries and proximal left upper lobe segmental pulmonary arteries. No abnormal dilatation of the pulmonary arty trunk. No features of right heart strain. no pericardial effusions, no

pleural effusions, no hilar or medialstinal lymphadenopathy. Central airway patent. 5mm right horizontal perifissural nodule. Punctate calcified nodule within the right middle lobe. 1.5 mm calcified nodule within the left lingular segment. No bronchiectasis. Subtle atelectasis/tree in bud nodular pattern within the right lung base anteriorly. Mild bibasal posterior dependent lung changes. Spondylosis. No sinister osseous lesions. Small bilateral pulmonary emboli.

[redacted] **20[redacted] BILI TOTAL:** <34

[redacted] **20[redacted] BLOOD PRESSURE:** 138/75 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 124/70 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 157/86 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 136/75 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 135/87 mmHg

[redacted] **20[redacted] BMI:** 34.4 no units

[redacted] **20[redacted] BODY TEMPERATURE:** 36.5 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 36.2 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 36.4 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 36.5 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 36.4 Degrees C

[redacted] **20[redacted] CHEST CT SCAN:** Small bilateral pulmonary emboli. No features of right heart strain. No features of bronchiectasis. Subtle atelectasis/tree in bud nodular pattern within the right lung base anteriorly. Differential includes ineffective change/endobronchial impaction. Mild bibasal posterior dependent lung changes. Probable small calcified granulomas within the right middle lobe and left lingular segment, with 5 mm right horizontal perifissural nodule.

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

[redacted] **20[redacted] CT PULMONARY ANGIOGRAM:** small bilateral pulmonary emboli

[redacted] **20[redacted] D-DIMER:** 342 NG/ML (normal <500)

[redacted] **20[redacted] DNA QUANT:** Negative

[redacted] **20[redacted] EKG:** sinus bradycardia

[redacted] **20[redacted] IGM:** Negative

[redacted] **20[redacted] MONOCYTES:** 0.89 no units (normal 0.00 to 0.80)

[redacted] **20[redacted] MONOCYTES ABSOLUTE:** 0.89 X10**9/L (normal 0.00 to 0.80)

[redacted] **20[redacted] OXYGEN SATURATION:** 97 %

[redacted] **20[redacted] OXYGEN SATURATION:** 99 %

[redacted] **20[redacted] OXYGEN SATURATION:** 99 %

[redacted] **20[redacted] OXYGEN SATURATION:** 96 %

[redacted] **20[redacted] PROTHROMBIN:** 1.0 no units (normal >0.9)

[redacted] **20[redacted] PULSE RATE:** 65 /min

[redacted] **20[redacted] PULSE RATE:** 57 /min

[redacted] **20[redacted] PULSE RATE:** 80 /min

[redacted] **20[redacted] RESPIRATORY RATE:** 15 no units

[redacted] **20[redacted] RESPIRATORY RATE:** 14 no units

[redacted] **20[redacted] RESPIRATORY RATE:** 15 no units

[redacted] **20[redacted] RESPIRATORY RATE:** 14 no units

[redacted] **20[redacted] RESPIRATORY RATE:** 15 no units

[redacted] **20[redacted] RHESUS:** Negative

[redacted] **20[redacted] SSA52/60:** Negative

[redacted] **20[redacted] URINALYSIS:** Clear/yellow. Amorphous material absent, epithelial cells absent, red blood cells absent, yeast absent, crystals absent casts none, leucocytes 0-5. Bilirubin negative, blood negative glucose 3 plus, ketones negative, leucocyte esterase negative, nitrite negative, protein negative, urobilinogen normal, anitmicrobial substance absent.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.3 X10**9/L (normal 10 to 15)