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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 15 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: INSOMNIA	20[redacted]
HYPERTENSION	20[redacted]
OTHER: COLITIS	20[redacted]
DEPRESSION: UNKNOWN	20[redacted]
OTHER: CHRONIC BILATERAL SHOULDER PAIN	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	19[redacted]
SURGERY: RIGHT HIP REPLACEMENT	20[redacted]
SURGERY: RIGHT KNEE REPLACEMENT	20[redacted]
SURGERY: LEFT KNEE REPLACEMENT	20[redacted]
SURGERY: OSTEOPENIA	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] / 173	173
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 174		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
LORAZEPAM	1 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	2000 OTHER: UNITS	QD	Y-M: 20[redacted]
LISINOPRIL	20 mg	QD	Y-M: 20[redacted]
CITALOPRAM	40 mg	QD	Y-M: 20[redacted]
IBUPROFEN	600 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -204
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -204
PREDNISONE	10 mg	QD	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
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED
LORAZEPAM	1 mg	QD	Y-M: 20[redacted]	NOT REPORTED
ERGOCALCIFEROL	2000 OTHER: UNITS	QD	Y-M: 20[redacted]	NOT REPORTED
LISINOPRIL	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED
CITALOPRAM	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
IBUPROFEN	600 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -204	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -204	NOT REPORTED
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -204	NOT REPORTED
AZTREONAM	1 g	QD	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 234
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 237
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 237
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 237
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 237
CIPROFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 235
VICODIN	1 OTHER: PILL	PRN	Y-M: 20[redacted] / 235	Y-M: 20[redacted] / 237
LOPERAMIDE	4 mg	QD	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 236
DIPHENHYDRAMINE	25 mg	PRN	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 237
LACTOBACILLUS ACIDOPHILUS	2 OTHER: PILLS	QD	Y-M: 20[redacted] / 237	NOT REPORTED
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 244
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 247

Event #1: Serious Adverse Event

Event Description	WORSENING OF MEDICAL CONDITION (COLITIS)
Preferred term	大腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 231
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 234): Alanine Aminotransferase: 15 [0 - 40] U/L; Aspartate Aminotransferase: 18 [0 - 37] U/L; Blood Urea Nitrogen: 16.8 [2.9 - 7.1] MMOL/L; Creatinine: 186 [44 - 106] UMOL/L; Leukocytes: 15.1 [4.8 - 10.8]

TH/CMM; Sodium: 128 [135 - 145] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 234): BLOOD NPTST084-BLOOD CULTURE OF LEFT ARM: Negative; BLOOD NPTST085-BLOOD CULTURE OF RIGHT ARM: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 234): CT SCAN ABDOMEN/PELVIS: 1.DIFFUSE THICKENING OF THE WALL THE COLON WHICH WAS NONSPECIFIC HOWEVER MAY REPRESENT COLITIS. 2. HIATAL HERNIA

AE Stopped Rx Day	237
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	WORSENING OF MEDICAL CONDITION (COLITIS)
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。本被験者は米国の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，医学的状態の悪化（大腸炎）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，大腸炎，高血圧，うつ病，局面型乾癬，乾癬性関節炎，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。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，被験者は医学的状態の悪化（大腸炎）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，医学的状態の悪化（大腸炎）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，3 日間に及ぶ重度の鋭い非放射状の左下腹部痛（疼痛スケール [redacted]）のため入院した。被験者は悪心，嘔吐，悪寒及び血性下痢も発現していた。被験者に

よれば，発熱は見られなかった。被験者は，これは過去の大腸炎発作に似ていると述べた。抗生物質及び鎮痛薬の静脈内投与並びに水分補給が行われた。被験者は経口抗生物質に切り替えられた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，アズトレオナム，norco，imodium，モルヒネ，protonix，CIPRO，フラジール，lactobacillus 及び zofran であった。

Causality for UPADACITINIB (Blinded)

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1) Colitis aggravated (10009890) (Colitis (10009887)) [v.22.1] [10009890]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF MEDICAL CONDITION (COLITIS)

- Investigator: WORSENING OF MEDICAL CONDITION (COLITIS)

- AbbVie: Event is more likely related to pre-existing history of colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINOTRANSFERASE:** 15 U/L (normal 0 to 40)

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 18 U/L (normal 0 to 37)

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

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

[redacted] **20[redacted] BUN:** 47 mg/dL (normal 8 to 20)

[redacted] **20**[redacted] **CREATININE:** 2.1 mg/dL (normal 0.5 to 1.2)

[redacted] **20**[redacted] **SODIUM:** 128 MMOL/L (normal 135 to 145)

[redacted] **20**[redacted] **WBC:** 15.1 TH/CMM (normal 4.8 to 10.8)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ブドウ球菌感染	X			X

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

Medical History	Onset Year
HEPATITIS: HEPATITIS C	19[redacted]
OTHER: CHRONIC　NECK PAIN	20[redacted]
OTHER: CHRONIC BACK PAIN	20[redacted]
OTHER: POST MENOPAUSAL	20[redacted]
HYPOTHYROIDISM	20[redacted]
KIDNEY DISORDER: CHRONIC KIDNEY DISEASE	20[redacted]
OBESITY	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	CURRENT	0.2 PACK	5[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] / 70	70

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LEVOTHYROXINE	300 ug	QD	Y-M: 20[redacted]

IBUPROFEN	800 mg	TID	Y-M: 20[redacted] / -251
APREMILAST	30 mg	QD	Y-M: 20[redacted] / -134

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
LEVOTHYROXINE	300 ug	QD	Y-M: 20[redacted]	ONGOING
IBUPROFEN	800 mg	TID	Y-M: 20[redacted] / -251	ONGOING
APREMILAST	30 mg	QD	Y-M: 20[redacted] / -134	ONGOING

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

Event Description	POSSIBLE STAPH INFECTION
Preferred term	ブドウ球菌感染
AE Onset Date / Rx Day	[redacted] / 33 (17 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Unknown
Relation to Study Drug by Investigator	Unknown
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。本被験者は米国の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，ブドウ球菌感染の可能性の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，C 型肝炎，甲状腺機能低下症，慢性腎臓病，肥満，局面型乾癬，乾癬性関節炎，紙巻タバコ喫煙者（1 日 0.2 箱を 50 年間）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，被験者はブドウ球菌感染の可能性を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，この被験者の治験薬の投与は完全に中止された。本報告時点でその他の詳細は提供されなかった。

Causality for ABT-494 (Blinded)

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1) Staphylococcal infection (10058080) (Staphylococcal infection (10058080)) [v.21.1] [10058080]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of POSSIBLE STAPH INFECTION

- Investigator: Not reported

- AbbVie: Risk factors include obesity, chronic kidney disease and current tobacco use.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] **20[redacted] BODY WEIGHT:** 56.1 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
虫垂炎	X			X

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

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: HYPERLIPIDEMIA	20[redacted]
OTHER: GALLSTONES	20[redacted]
OTHER: DRUG RELATED HAIR LOSS	20[redacted]
OTHER: TROCHANTERIC BURSITIS LEFT HIP	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CHOLECYSTECTOMY	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		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]-
HYDROXYCHLOROQUINE	200 mg	BID	Y-M: 20[redacted]-

MELOXICAM	15 mg	QD	Y-M: 20[redacted]
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]
FOLINIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -336

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	1 mg	QD	Y-M: 20[redacted]	NOT REPORTED
MELOXICAM	15 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 113
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
FOLINIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / -336	ONGOING
PIP/TAZO	UNKNOWN OTHER: UNKNOWN	OTHER: ONE TIME	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 21
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 22	ONGOING
PARACETAMOL	325 mg	PRN	Y-M: 20[redacted] / 22	ONGOING

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

Event Description	ACUTE APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 21
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 21): CT ABDOMEN/PELVIS WITH IV CONTRAST: MM DILATED APPENDIX WITH SURROUNDING INFLAMMATORY CHANGES SUSPICIOUS FOR ACUTE APPENDICITIS; [redacted]20[redacted] (RX DAY 22): LAPAROSCOPIC APPENDECTOMY: APPENDIX REMOVED	
AE Stopped Rx Day	22
Duration of AE	2 DAYS
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, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

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

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性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，乾癬性関節炎，高脂血症，非喫煙者及び飲酒者（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。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，被験者は急性虫垂炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性虫垂炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右下腹部に放射状に拡がる臍周囲痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腹痛のため入院した。CT スキャンで虫垂炎が明らかとなり，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に腹腔鏡下虫垂切除術を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，ゾシン，zofran 及びタイレノールであった。

Causality for UPADACITINIB (Blinded)

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1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.22.0] [10000677]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE APPENDICITIS

- Investigator: Not applicable

- AbbVie: Event is common in the general population.Relevant Laboratory & Other Diagnostic Tests

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[redacted] **20[redacted] CT ABDOMEN/PELVIS WITH IV CONTRAST:** MM DILATED APPENDIX WITH SURROUNDING INFLAMMATORY CHANGES SUSPICIOUS FOR ACUTE APPENDICITIS

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
複視	X			

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

Medical History	Onset Year
OTHER: FRACTURE RIGHT ANKLE	19[redacted]
OTHER: FATTY TUMOR ON RING FINGER RIGHT HAND	19
MYOCARDIAL INFARCTION	20
OTHER: CARPAL TUNNEL LEFT WRIST	20
CORONARY ARTERY DISEASE: STABLE	20
DIABETES MELLITUS: TYPE II	20
HYPERLIPIDEMIA: STABLE	20
HYPERTENSION	20
OTHER: COLON POLYPS	20
OTHER: PLAQUE PSORIASIS	20
PSORIATIC ARTHRITIS	20

Prior Procedures	Procedure Year
INCREASED CREATINE PHOSPHOKINASE: FRACTIONATED LAB TEST	NOT REPORTED
SURGERY: FRACTURE RIGHT ANKLE REPAIR	19
SURGERY: FATTY TUMOR ON RING FINGER RIGHT HAND REMOVED	19
SURGERY: CARPAL TUNNEL LEFT WRIST SURGERY	20
SURGERY: COLON POLYPS REMOVED	20
SURGERY: CARPAL TUNNEL SURGERY LEFT WRIST	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	20	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	Last Dose	Duration

				Date/Day	Date/Day	(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] / 397	228
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 398		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
NAPROXEN	220 mg	PRN	Y-M: 20[redacted]
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted]
METOPROLOL	25 mg	BID	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METFORMIN	1000 mg	QD	Y-M: 20[redacted]
METFORMIN	1500 mg	QD	Y-M: 20[redacted]
CALCIPOTRIOL	0.005 %	QD	Y-M: 20[redacted]
CLOBETASOL	0.05 %	BID	Y-M: 20[redacted]
LOTRISONE	1/0.05 %	BID	Y-M: 20[redacted] / -359
APREMILAST	30 mg	BID	Y-M: 20[redacted] / -206
EZETIMIBE	10 mg	QD	Y-M: 20[redacted] / -116
ROSUVASTATIN	40 mg	QD	Y-M: 20[redacted] / -116

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
NAPROXEN	220 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
METOPROLOL	25 mg	BID	Y-M: 20[redacted]	NOT REPORTED
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 167
METFORMIN	1000 mg	QD	Y-M: 20[redacted]	NOT REPORTED
METFORMIN	1500 mg	QD	Y-M: 20[redacted]	NOT REPORTED
EZETIMIBE	10 mg	QD	Y-M: 20[redacted] / -116	NOT REPORTED
ROSUVASTATIN	40 mg	QD	Y-M: 20[redacted] / -116	NOT REPORTED
DAPAGLIFLOZIN	5 mg	QD	Y-M: 20[redacted] / 144	NOT REPORTED
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 174	NOT REPORTED
ACETYLSALICYLIC ACID	325 mg	QD	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 174
GADOBUTROL	9 mmol	QD	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 175
INSULIN	3 OTHER: UNITS	PRN	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 177

Event #2: Serious Adverse Event

Event Description DIPLOPIA
Preferred term 複視
AE Onset Date / Rx Day [redacted]20[redacted] / 172
Age at AE Onset 5[redacted]
Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 174): CT HEAD: PROPTOSIS BILATERALLY OF UNCERTAIN CLINICAL SIGNIFICANCE, SMALL FAT-CONTAINING FOCUS IN THE CEREBELLAR CISTERN MEASURING APPROXIMATELY 7 MM WITHOUT MASS EFFECT OR EDEMA WHICH IS COMPLETELY FAT DENSITY; [redacted]20[redacted] (RX DAY 175): ANGIO HEAD WITH CONTRAST MRI: UNREMARKABLE MR ANGIOGRAM HEAD; CAROTID ULTRASOUND: ATHEROSCLEROTIC IRREGULARITY THE RIGHT AND LEFT INTERAL CAROTID ARTERY WITHOUT EVIDENCE FOR LUMINAL STENOSIS; OCCUPATIONAL THERAPY EVALUATION: COMPLETED; PHYSICAL THERAPY EVALUATION: COMPLETED

AE Stopped Rx Day	177
Duration of AE	6 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CORONARY ARTERY 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。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，複視の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，元喫煙者（1 日 1 箱を 20 年間），冠動脈疾患，心筋梗塞，2 型糖尿病，高脂血症，高血圧，局面型乾癬，乾癬性関節炎，現飲酒者（1 日 2 杯未満）及び心臓発作（兄弟が 50 歳の時）の家族歴であった。心筋梗塞の家族歴もあった。

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，被験者は複視を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，複視は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は悪心，嘔吐，後頭部痛，複視及び回転性めまいを発現した。治験責任医師によると，被験者は，視線が右側に偏っており，複数回の嘔吐と，歩行時の右方向への傾きも見られたと報告した。治験責任医師によると，被験者の妻は，被験者には右側顔面下垂が見られたが，喚語困難は見られなかったと報告した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院

し，複数の画像検査が行われた。また，理学療法及び作業療法による評価も行われた。また治験責任医師からは，被験者は本事象発現時にプラビックスを服用していなかったと報告された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，アスピリン，クロピドグレル及びインスリンであった。

Causality for UPADACITINIB (Blinded)

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1) Diplopia (10013036) (Diplopia (10013036)) [v.22.1] [10013036]

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 DIPLOPIA

- Investigator: CORONARY ARTERY DISEASE

- AbbVie: risk factors include pre-existing hypertension and diabetes mellitus.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANGIO HEAD WITHOUT CONTRAST MRI:** UNREMARKABLE MR ANGIOGRAM HEAD

[redacted] **20[redacted] CAROTID ULTRASOUND:** ATHEROSCLEROTIC IRREGULARITY THE RIGHT AND LEFT INTERAL CAROTID ARTERY WITHOUT EVIDENCE FOR LUMINAL STENOSIS

[redacted] **20[redacted] CT HEAD:** PROPTOSIS BILATERALLY OF UNCERTAIN CLINICAL SIGNIFICANCE, SMALL FAT-CONTAINING FOCUS IN THE CEREBELLAR CISTERN MEASURING APPROXIMATELY 7 MM WITHOUT MASS EFFECT OR EDEMA WHICH IS COMPLETELY FAT DENSITY

[redacted] **20[redacted] ECG:** Abnormal. T wave abnormality. Short QT interval

Unknown date ECHOCARDIOGRAM: Results not reported

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腰部脊柱管狭窄症	X	X		

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

Medical History	Onset Year
OTHER: CHICKEN POX	19[redacted]
OTHER: LEFT SPASTIC HEMIPARESIS	19
OTHER: TRAMATIC BRAIN INJURY	19
DEPRESSION: STABLE	20
OTHER: PLAQUE PSORASIS	20
CHOLELITHIASIS: CHOLECYSTITIS	20
OTHER: APPENDICITIS	20
OTHER: IRON DEFICIENCY ANEMIA	20
OTHER: BILATERAL CARPAL SYNDROME	20
DEGENERATIVE DISC DISEASE: LUMBAR SPINE	20
OTHER: LUMBOSACRAL SPINAL STENOSIS	20
PSORIATIC ARTHRITIS	20

Prior Procedures	Procedure Year
SURGERY: LEFT VALGUS MALALIGNMENT	20[redacted]
SURGERY: TIBIAL OSTEOTOMY	20
SURGERY: APPENDECTOMY	20
SURGERY: BILATERAL TUBAL LIGATION	20
SURGERY: CHOLECYSTECTOMY	20
SURGERY: BILATERAL CARPAL SYNDROME SURGERY	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.05 PACK	2[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] / 172	172
ABT-494	15 MG	ORAL	QD	[redacted] / 173	[redacted] / 395	223
ABT-494	15 MG	ORAL	QD	[redacted] / 396	[redacted] / 563	168

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUPROPION	150 mg	QD	Y-M: 20[redacted]
SERTRALINE	100 mg	QD	Y-M: 20[redacted]
BACLOFEN	10 mg	TID	Y-M: 20[redacted]
TIZANIDINE	8 mg	QD	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
TRAMADOL	50 mg	QD	Y-M: 20[redacted]
GABAPENTIN	300 mg	TID	Y-M: 20[redacted]
IBUPROFEN	400 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -116
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -116

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
BUPROPION	150 mg	QD	Y-M: 20[redacted]	ONGOING
SERTRALINE	100 mg	QD	Y-M: 20[redacted]	ONGOING
BACLOFEN	10 mg	TID	Y-M: 20[redacted]	ONGOING
TIZANIDINE	8 mg	QD	Y-M: 20[redacted]	ONGOING
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
TRAMADOL	50 mg	QD	Y-M: 20[redacted]	ONGOING
GABAPENTIN	300 mg	TID	Y-M: 20[redacted]	ONGOING
IBUPROFEN	400 mg	QD	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -116	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -116	ONGOING
DOCUSATE	100 mg	BID	Y-M: 20[redacted] / 565	ONGOING
PARACETAMOL	975 mg	QID	Y-M: 20[redacted] / 565	ONGOING
CEFAZOLIN	2 g	QD	Y-M: 20[redacted] / 565	Y-M: 20[redacted] / 567
MORPHINE	2 mg	QD	Y-M: 20[redacted] / 565	Y-M: 20[redacted] / 567
ONDANSETRON	4 mg	QD	Y-M: 20[redacted] / 565	Y-M: 20[redacted] / 567
SODIUM CHLORIDE	0.9 %	QD	Y-M: 20[redacted] / 565	Y-M: 20[redacted] / 567
OXYCODONE	5 mg	TID	Y-M: 20[redacted] / 567	ONGOING
SENNA ALEXANDRINA	17.2 mg	OTHER: QHS	Y-M: 20[redacted] / 567	ONGOING

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

Event Description	WORSENING OF LUMBOSACRAL SPINAL STENOSIS

Preferred term	腰部脊柱管狭窄症
AE Onset Date / Rx Day	[redacted]20[redacted] / 531
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 567): Calcium: 2.25 [2.17 - 2.67] MMOL/L; Creatinine: 38 [44 - 106] UMOL/L; Glucose: 8.4 [3.9 - 5.5] MMOL/L; Hematocrit: 0.38 [0.31 - 0.46] FRACTION OF 1; Hemoglobin: 129 [117 - 155] G/L; Leukocytes: 10.6 [4.3 - 10.8] 10^9/L; NPTST111-CARBON DIOXIDE: 28 [24 - 32] MMOL/L; NPTST182-EGFR: 90 [89 - 90] (ML/MIN/BSA); NPTST319-MCV (MEAN CORPUSCULAR VOLUME): 91.4 [80 - 100] FL; Platelets: 168 [140 - 440] 10^9/L; Potassium: 3.5 [3.5 - 5.3] MMOL/L; Sodium: 140 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 564): X-RAY LUMBOSACRAL SPINE: WORSENING OF LUMBOSACRAL SPINAL STENOSIS STENOSIS; [redacted]20[redacted] (RX DAY 565): BILATERAL L4/S1 LAMINECTOMIES: SUCCESSFUL; RIGHT SIDED L5/S1 DISCECTOMY: SUCCESSFUL

AE Stopped Rx Day	568 (5 DAYS AFTER LAST TREATMENT)
Duration of AE	38 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	LUMBAR-RADICULOPATHY DUE TO H/O OF LUMBAR SACRAL SPINAL STENOSIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT

Generated: [redacted]
Program Source [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，腰仙部脊柱管狭窄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，左痙性不全片麻痺，外傷性脳損傷，局面型乾癬，鉄欠乏性貧血，腰椎椎間板変性疾患，腰仙部脊柱管狭窄症，現喫煙者（1 日 0.05 箱 29 年間）及び現飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腰仙部脊柱管狭窄症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，腰仙部脊柱管狭窄症の悪化は消失した。

本治験への組入れ前において，被験者には 20[redacted] 年 [redacted] 月より腰仙部脊柱管狭窄症の病歴があった。

腰仙部脊柱管狭窄症が悪化し，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に入院した。徴候・症状は右下肢錯感覚及び背部痛であった。同日，被験者は両側 L4～L5 の椎弓切除術及び右側 L5～S1 の椎間板切除術を受けた。手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。本事象により治験薬の投与は完全に中止された。

治験責任医師によると，この被験者における本事象の危険因子は背部痛であった。

投与された薬剤は塩化ナトリウムであった。

Causality for UPADACITINIB (Blinded)

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1) Lumbosacral spinal stenosis (10081628) (Lumbar spinal stenosis (10025005)) [v.22.1] [10081628]

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 OF LUMBOSACRAL SPINAL STENOSIS

- Investigator: Lumbar radiculopathy due to history of lumbar sacral spinal stenosis

- AbbVie: event is more likely related to pre-existing lumbosacral spinal stenosis. Pre-existing psoriatic arthritis is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CREATININE:** 0.43 mg/dL (normal 0.50 to 1.20)

[redacted] **20[redacted] GLUCOSE:** 152 mg/dL (normal 70 to 99)

[redacted] **20[redacted] X-RAY LUMBOSACRAL SPINE:** WORSENING OF LUMBOSACRAL SPINAL STENOSIS 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
肺炎	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: RESTLESS LEG SYNDROME	19[redacted]
OTHER: CHICKEN POX	19
OTHER: CLAVICLE FRACTURE	19
OTHER: EXCESSIVE FATIGUE	20
OTHER: INSOMNIA	20
DIABETES MELLITUS	20
OTHER: PLAQUE PSORIASIS	20
HYPOTHYROIDISM	20
OTHER: CARPAL TUNNEL	20
HYPERTENSION	20
OTHER: DEGENERATIVE JOINT DISEASE	20
PSORIATIC ARTHRITIS	20
OTHER: RIGHT PINKY FRACTURE	20
OTHER: LEFT SHOULDER PAIN	20
OTHER: LEFT SHOULDER STEROID SHOT	20

Prior Procedures	Procedure Year
SURGERY: LEFT ELBOW ARTHROSCOPY	20[redacted]
SURGERY: LEFT KNEE ARTHROSCOPY	20
SURGERY: CARPEL TUNNEL SURGERY ON LEFT HAND	20
SURGERY: CHOLECYSTECTOMY	20
SURGERY: GALL BLADDER SURGERY	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] / 1	[redacted] / 168	168
ABT-494	15 MG	ORAL	QD	[redacted] / 169	[redacted] / 399	231
ABT-494	15 MG	ORAL	QD	[redacted] / 400		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PRAMIPEXOLE	1 mg	BID	Y-M: 19[redacted]
CYANOCOBALAMIN	1 OTHER: TABLET	QD	Y-M: 19[redacted]
MINERALS NOS W/VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 19[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
INDOMETACIN	75 mg	PRN	Y-M: 20[redacted]
LEVOTHYROXINE	100 OTHER: MCG	PRN	Y-M: 20[redacted]
TRAMADOL	50 mg	QD	Y-M: 20[redacted]
HYDROCHLOROTHIAZIDE	25 mg	PRN	Y-M: 20[redacted]
METFORMIN	500 mg	PRN	Y-M: 20[redacted]
LOSARTAN	25 mg	PRN	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -322
FOLIC ACID	800 OTHER: MCG	QD	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
PRAMIPEXOLE	1 mg	BID	Y-M: 19[redacted]	NOT REPORTED
CYANOCOBALAMIN	1 OTHER: TABLET	QD	Y-M: 19[redacted]	NOT REPORTED
MINERALS NOS W/VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 19[redacted]	NOT REPORTED
INDOMETACIN	75 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
LEVOTHYROXINE	100 OTHER: MCG	PRN	Y-M: 20[redacted]	NOT REPORTED
TRAMADOL	50 mg	QD	Y-M: 20[redacted]	NOT REPORTED
HYDROCHLOROTHIAZIDE	25 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
METFORMIN	500 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
LOSARTAN	25 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -322	NOT REPORTED

FOLIC ACID	800 OTHER: MCG	QD	Y-M: 20[redacted] / - 105	NOT REPORTED
PIPERACILLIN W/TAZOBACTAM	3.375 G / 15 ML OTHER: G/ML	QD	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 81
LEVOFLOXACIN	750 MG / 150 ML OTHER: MG/ML	QD	Y-M: 20[redacted] / 80	Y-M: 20[redacted] / 80
VANCOMYCIN	1500 MG / 250 ML OTHER: MG/ML	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 81

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 77
Age at AE Onset	6[redacted]
Laboratory Testing	

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 77): BLOOD NPTST081-BLOOD CULTURE: Negative-NO GROWTH AT 5 DAYS;
20[redacted] (RX DAY 79): URINE NPTST491-URINE CULTURE: Negative-NO GROWTH <1000 ORGANISMS/ML

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 78): CHEST X RAY: INTERVAL INCREASE IN SIZE OF RIGHT MIDDLE LOBE PNEUMONIA; CT CHEST WITH CONTRAST: RIGHT MIDDLE LOBE PNEUMONIA; [redacted]20[redacted] (RX DAY 80): CHEST X-RAY: STABLE RIGHT MIDDLE LOBE PNEUMONIA

AE Stopped Rx Day	81
Duration of AE	5 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	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。本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，糖尿病，局面型乾癬，甲状腺機能低下症，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。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，被験者は肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 5 日間に及ぶ症状の悪化による発熱及び全身の脱力に伴う非湿性咳嗽で救急治療室を受診した。同日，被験者は退院した。咳嗽及び発熱の悪化は持続した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はさらなる管理のため ER を受診することにした。胸部 CT スキャン検査が行われ，右肺中葉肺炎の徴候が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。治療が行われ，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。

投与された薬剤は，バンコマイシン，levaquin 及びゾシンであった。

Causality for ABT-494 (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.21.0] [10035664]

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 ABT-494 (Blinded)

Event of PNEUMONIA

- Investigator: Not applicable

- AbbVie: Risk factors include age and diabetes mellitus (Marrie, TJ. epidemiology, pathogenesis and microbiology of community acquired pneumonia in adults in uptodate, post TW (ED), uptodate, Waltham, MA)

Relevant Laboratory & Other Diagnostic Tests

Unknown date BLOOD CULTURE: Negative

[redacted] **CHEST X RAY:** Interval increase in size of right middle lobe pneumonia.

[redacted] **CHEST X-RAY:** Stable right middle lobe pneumonia.

[redacted] **CT CHEST WITH CONTRAST:** Right Middle Lobe Pneumonia

Unknown date URINE CULTURE: 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
乳房蜂巣炎	X	X		X

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 15 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: CHICKEN POX	19[redacted]
OTHER: MUMPS	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO AMINOGLYCOSIDE	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO PENICILLIN	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO SULFA DRUGS	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO BIAXIN	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO DOXYCICLINE	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO KEFLEX	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO LEVAQUIN	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO MAXROBID	19
OTHER: ALLERGIC RHINITIS	19
OTHER: FATTY LIVER	19
OTHER: CHOLELITHIASIS	19
HYPERTENSION	19
OTHER: HYPERLIPIDEMIA	20
OTHER: DEPRESSION	20
OTHER: CHRONIC GENERALIZED PAIN	20
OTHER: ACID REFLUX	20
PSORIATIC ARTHRITIS	20
OTHER: NAUSEA	20
OTHER: SUPERFICIAL AND DEEP PERIVASCULAR AND PERIFOLLICULAR LYMPHOCYTIC DERMATITIS	20[redacted]
OTHER: ATYPICAL NEVUS	20
OTHER: BENIGN NEOPLASM OF SKIN	20
OTHER: COMPOUND NEVUS WITH ATYPICAL MELANOCYTIC HYPERPLASIA	20
OTHER: FIBROUS PAPULE	20
OTHER: OPEN COMEDONE	20
OTHER: SKIN TAG	20
OTHER: DERMAL HYPERSENSITIVITY REACTION	20
OTHER: PALMOPLANTAR PUSTULOSIS	20
OTHER: ANAL FISSURE	20
OTHER: DERMATITIS	20
OTHER: MYOCARDIAL BRIDGE	20
OTHER: IRRITATED SEBORRHOIC KERATITIS	20[redacted]

OTHER: BOIL	20
OTHER: ABNORMAL LIVER FUNCTION TEST	20
OTHER: ANXIETY	20
OTHER: PLAQUE PSORIASIS	20
OTHER: PSORIATIC SPONDYLITIS	20
OTHER: GENITAL HERPES	20
OTHER: LICHEN SCLEROSUS	20
OTHER: ACUTE BRONCHITIS	20

Prior Procedures	Procedure Year
SURGERY: CHOLECYSTECTOMY	19
SURGERY: HYSTERECTOMY	19

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	48.5	
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)
PLACEBO		ORAL	QD	20 / 1	20 / 77	77

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ESOMEPRAZOLE	40 mg	QD	Y-M: 20
METOPROLOL	25 mg	QD	Y-M: 20
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20
AMLODIPINE	5 mg	QD	Y-M: 20
ERGOCALCIFEROL	400 OTHER: UNITS/ML	QD	Y-M: 20
PANADEINE CO	300/30 mg	PRN	Y-M: 20
PREGABALIN	75 mg	QD	Y-M: 20
PROMETHAZINE	25 mg	PRN	Y-M: 20
SERTRALINE	50 mg	QD	Y-M: 20
CLOBETASOL	0.05 %	PRN	Y-M: 20
APREMILAST	30 mg	QD	Y-M: 20
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20
MUPIROCIN	2 %	PRN	Y-M: 20
VALACICLOVIR	500 mg	QD	Y-M: 20 / -80

LOCAL ANESTHETICS	0.3 %	PRN	Y-M: 20[redacted] / -28
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / -16

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]	ONGOING
METOPROLOL	25 mg	QD	Y-M: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
AMLODIPINE	5 mg	QD	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	400 OTHER: UNITS/ML	QD	Y-M: 20[redacted]	ONGOING
PANADEINE CO	300/30 mg	PRN	Y-M: 20[redacted]	ONGOING
PREGABALIN	75 mg	QD	Y-M: 20[redacted]	ONGOING
PROMETHAZINE	25 mg	PRN	Y-M: 20[redacted]	ONGOING
SERTRALINE	50 mg	QD	Y-M: 20[redacted]	ONGOING
APREMILAST	30 mg	QD	Y-M: 20[redacted]	ONGOING
MUPIROCIN	2 %	PRN	Y-M: 20[redacted]	ONGOING
VALACICLOVIR	500 mg	QD	Y-M: 20[redacted] / -80	ONGOING
LOCAL ANESTHETICS	0.3 %	PRN	Y-M: 20[redacted] / -28	ONGOING
DOCUSATE	100 mg	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 87
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 73	Y-M: 20[redacted] / 77
LEVETIRACETAM	500 mg	QD	Y-M: 20[redacted] / 73	Y-M: 20[redacted] / 77
VANCOMYCIN	750 mg/kg	OTHER: Q12H	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 82
MORPHINE	2 mg	OTHER: Q4H PRN	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 88
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 91
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 79	ONGOING
DIPHENHYDRAMINE	25 mg	BID	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 79
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 83
CLONIDINE	0.1 mg	OTHER: Q4H PRN	Y-M: 20[redacted] / 91	ONGOING
PITAVASTATIN	2 mg	QD	Y-M: 20[redacted] / 91	ONGOING
DAPTOMYCIN	450 mg	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 99

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

Event Description	LEFT BREAST CELLULITIS
Preferred term	乳房蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 73
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 47): Hematocrit: 0.43 [0.36 - 0.46] FRACTION OF 1; [redacted]20[redacted] (RX DAY 78): Basophils/Leukocytes: 0.6 [0.2 - 1] %; Creatinine: 85 [53 - 115] UMOL/L; Eosinophils/Leukocytes: 1.5 [0.9 - 2.9] %; Erythrocytes: 5.1 [4.2 - 5.4] 10^12/L; Hemoglobin: 132 [120 - 160] G/L; Ketones: NEGATIVE [NOT REPORTED - NOT REPORTED] NEGATIVE; Leukocytes: 6.7 [3 - 12] 10^9/L; Lymphocytes/Leukocytes: 35.5 [20.5 - 45.5] %; Monocytes/Leukocytes: 5.3 [5.5 - 11.7] %; Neutrophils/Leukocytes: 56.8 [43 - 65] %; Platelets: 274 [130 - 400] 10^9/L; Specific Gravity: 1.020 [1 - 1.03] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 78): WOUND NPTST504-WOUND CULTURE: Positive-WOUND CULTURE SHOWS THAT PATIENT HAS ABSCESS GRAM STAIN: 1. RARE WBC'S/RARE GRAM POSITIVE COCCI/ NO EPITHELIAL CELLS 2. CORYNEBACTERIUM SPECIES RARE/DIPHTHEROIDS NO FURTHER WORKUP; [redacted]20[redacted] (RX DAY 83): WOUND NPTST505-WOUND CULTURE (GRAM STAIN FINAL: Positive-RARE WBC'S RARE GRAM POSITIVE COCCI, NO EPITHELIAL CELLS; [redacted]20[redacted] (RX DAY 86): WOUND NPTST160-CULTURE WOUND FINAL: Positive-CORYNEBACTERIUM SPECIES RARE/DIPHTHEROIDS NO FURTHER WORKUP; [redacted]20[redacted] (RX DAY 90): BLOOD NPTST081-BLOOD CULTURE: Negative-NO GROWTH AFTER 5 DAYS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 78): CHEST X-RAY, 1 VIEW: MINIMAL SCARRING OR ATELECTASIS IN THE LINGULA BUT OTHERWISE NORMAL CHEST, THE CARDIOVASCULAR SILHOUETTE IS NORMAL.; CXR 2 VIEWS: HISTORY PROVIDED: LEFT BREAST CELLULITIS FINDINGS: THERE IS NO INFILTRATE OR ATELECTASIS. THE HEART SIZE IS NORMAL. THERE IS NO VASCULAR CONGESTION. THERE IS NO PLEURAL EFFUSION. CONCLUSION: NORMALEXAM; [redacted]20[redacted] (RX DAY 80): ULTRA SOUND BREAST W AX LTD UNI LT: INDICATION: MASTOIDITIS VERSUS ABSCESS LEFT BREAST FINDINGS: 4.4 X 1.8 X 0.5 CM HYPOECHOIC AREA WITHIN THE DERMIS COMPATIBLE WITH PHLEGMONOUS CELLULITIS. NO AXILLARY ADENOPATHY. IMPRESSIONS: INFLAMMATORY LESION OF THE SKIN. ASSESSMENT: ACR BI-RADS CATEOGRY 2 - BENIGN; [redacted]20[redacted] (RX DAY 82): INCISION AND DRAINAGE OF LEFT BREAST ABSCESS: REMOVED THE BREAST TISSUE AND WOUND CULTURES

AE Stopped Rx Day	112 (35 DAYS AFTER LAST TREATMENT)
Duration of AE	40 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。本被験者は米国の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左乳房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，乾癬性関節炎，表在型・深部型の血管周囲性・毛包周囲性リンパ球性皮膚炎，皮膚過敏症反応，皮膚炎，刺激反応性の脂漏性角化症，局面型乾癬，硬化性苔癬，喫煙者（1 日 1 箱を 48.5 年間）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，被験者は左乳房蜂巣炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左乳房蜂巣炎は消失した。

入院前に，左乳房乳頭周囲の下側に水疱が出現し悪化した。被験者はかかりつけ医を受診した。ドキシサイクリンの投与が開始されたが，被験者はこの薬剤に忍容性が認められなかった。水疱は改善せず，乳房が赤くなって炎症を起こした。被験者は専門医を受診し，炎症を伴う左乳房水疱，倦怠感，発汗，体の疼き及び痛みなどの症状のため 20[redacted] 年 [redacted] 月 [redacted] 日に入院した。感染症及び一般外科手術のための診察が開始された。また，抗生物質の静脈内投与及び温湿布による治療も開始されたが，膿瘍が出現した。20[redacted] 年 [redacted] 月 [redacted] 日，左乳房膿瘍の切開及びドレナージが行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，ジフェンヒドラミン，ゾルピデム酒石酸塩，プレガバリン，モルヒネ，ケプラ，ドキシサイクリン，バンコマイシン及びダプトマイシンであった。

The patient's past medications include:

DOXYCYCLINE for UNKNOWN INDICATION

MAXROBID for UNKNOWN INDICATION

LEVAQUIN for UNKNOWN INDICATION

KEFLEX for UNKNOWN INDICATION

BIAXIN for UNKNOWN INDICATION

AMINOGLYCOSIDE for UNKNOWN INDICATION

PENICILLIN for UNKNOWN INDICATION

SULFA for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) Cellulitis breast (10007903) (Breast cellulitis (10006217)) [v.21.1] [10007903]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of LEFT BREAST CELLULITIS

- Investigator: Not applicable

-AbbVie: Risk factors include obesity (BMI 37.9 at screening), advanced age and current smoker.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] CHEST X-RAY, 1 VIEW:** MINIMAL SCARRING OR ATELECTASIS IN THE LINGULA BUT OTHERWISE NORMAL CHEST, THE CARDIOVASCULAR SILHOUETTE IS NORMAL.

[redacted] **20[redacted] CXR 2 VIEWS:** HISTORY PROVIDED: LEFT BREAST CELLULITIS FINDINGS: THERE IS NO INFILTRATE OR ATELECTASIS. THE HEART SIZE IS NORMAL. THERE IS NO VASCULAR CONGESTION. THERE IS NO PLEURAL EFFUSION. CONCLUSION: NORMAL EXAM

[redacted] **20[redacted] ULTRASOUND BREAST WITH AX LTD UNI LT:** INDICATION: MASTOIDITIS VERSUS ABSCESS LEFT BREAST FINDINGS: 4.4 X 1.8 X 0.5 CM HYPOECHOIC AREA WITHIN THE DERMIS COMPATIBLE WITH PHLEGMONOUS CELLULITIS. NO AXILLARY ADENOPATHY. IMPRESSIONS: INFLAMMATORY LESION OF THE SKIN. ASSESSMENT: ACR BI-RADS CATEOGRY 2 - BENIGN

[redacted] **20[redacted] WOUND CULTURE:** Positive. wound culture shows that patient has abscess. 1. Rare WBC's/rare gram positive cocci/no epithelial cells. 2. Corynebacterium species rare/diphtheroids. No further workup.

[redacted] **20[redacted] WOUND CULTURE (GRAM STAIN FINAL):** positive. Rare WBC's. Rare gram positive cocci, no epithelial cells.

[redacted] **20[redacted] WOUND CULTURE FINAL:** Positive. Corynebacterium species rare/diphtheroids. No further workup.

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: ALLERGY TO PENECILLIN	19[redacted]
HEPATITIS: NOT SURE WHICH	19[redacted]
HYPERTENSION	19[redacted]
OBESITY	19[redacted]
OTHER: BENIGN TUMOR STATUS POST SURGERY.	19[redacted]
SEIZURE DISORDER/CONVULSIONS: SEIZURES	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
SLEEP APNEA	19[redacted]
OTHER: POST MENOPAUSAL	19[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: GERD	19[redacted]
OTHER: FOOT FRACTURE (RIGHT)	20[redacted]
OTHER: IRRITABLE BOWEL SYNDROME	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO CODEINE	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO DULOXETINE	20[redacted]
OSTEOARTHRITIS: AFFECTING MULTIPLE JOINTS	20[redacted]
OTHER: MERALGIA PARESTHETICA	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
DEPRESSION: CHRONIC	20[redacted]

Prior Procedures	Procedure Year
SURGERY: GALL BLADDER REMOVAL SURGERY	19[redacted]
SURGERY: BRAIN SURGERY FOR BENIGN BRAIN TUMOR	19[redacted]
SURGERY: SURGERY FOR REPAIR OF DETACHED RETINA RIGHT EYE.	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] / 1	[redacted] / 168	168
ABT-494	15 MG	ORAL	QD	[redacted] / 169	[redacted] / 392	224
ABT-494	15 MG	ORAL	QD	[redacted] / 393		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
OMEPRAZOLE	20 mg	QD	Y-M: 19[redacted]
HYOSCYAMINE	0.375 mg	BID	Y-M: 20[redacted]
AZILSARTAN	40 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
LEVETIRACETAM	750 mg	QD	Y-M: 20[redacted] / -338
CITALOPRAM	40 mg	QD	Y-M: 20[redacted] / -247
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -193

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
OMEPRAZOLE	20 mg	QD	Y-M: 19[redacted]	NOT REPORTED
AZILSARTAN	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	NOT REPORTED
LEVETIRACETAM	750 mg	QD	Y-M: 20[redacted] / -338	NOT REPORTED
CITALOPRAM	40 mg	QD	Y-M: 20[redacted] / -247	NOT REPORTED
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -193	Y-M: 20[redacted] / 281
DICYCLOVERINE	10 mg	PRN	Y-M: 20[redacted] / 29	NOT REPORTED
VALACICLOVIR	800 mg	TID	Y-M: 20[redacted] / 281	Y-M: 20[redacted] / 299

Event #1: Serious Adverse Event

Event Description GASTRIC INDIGESTION

Preferred term 消化不良

AE Onset Date / Rx Day [redacted] / 79

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted] (RX DAY 79): Blood Urea Nitrogen: 9.3 [1.4 - 7.5] MMOL/L; Chloride: 109 [95 - 108] MMOL/L; Erythrocytes: 3.9 [4.2 - 5.4] 10^12/L; NPTST316-MCH: 33 [27 - 31] PG; NPTST333-MPV: 8.6 [9.4 - 12.4] FL; NPTST472-TROPONIN I: 0.05 [0 - 0.05] NG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted] (RX DAY 80): CARDIAC CATHETERIZATION: NEGATIVE FINDINGS.

AE Stopped Rx Day 80

Duration of AE 2 DAYS

Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SUBJECT HAD EATEN HEAVY MEAL CONSISTING OF PIZZA AND THEREAFTER COMPLAINED OF LEFT LOWER CHEST PAIN.
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。本被験者は米国の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，胃消化障害の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，高血圧，良性腫瘍術後の痙攣発作，睡眠時無呼吸，胃食道逆流性疾患，乾癬性関節炎及び非喫煙者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃消化障害を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胃消化障害は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左側胸痛を訴えた。被験者は救急治療室を受診し，評価のため一晩入院した。心臓に原因は見当たらなかった。20[redacted] 年 [redacted] 月 [redacted] 日，心カテーテル検査が行われたが，異常所見は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

Causality for ABT-494 (Blinded)

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1) Indigestion (10021706) (Dyspepsia (10013946)) [v.21.0] [10021706]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of GASTRIC INDIGESTION

- Investigator: SUBJECT HAD EATEN HEAVY MEAL CONSISTING OF PIZZA AND THEREAFTER COMPLAINED OF LEFT LOWER CHEST PAIN.

- AbbVie: event is more likely related to pre-existing gastro esophageal reflux disease.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CARDIAC CATHETERIZATION:** Negative findings

[redacted] **20[redacted] MPV:** 8.6 FL (normal <12.4)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.85 10^6/mm3 (normal 4.20 to 5.40)

[redacted] **20[redacted] TROPONIN:** <0.050 ng/ml

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

Reason for Narrative

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

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

Medical History	Onset Year
HYPERTENSION	19[redacted]
HYPOTHYROIDISM	19
HYPERLIPIDEMIA	19
OSTEOARTHRITIS	20
DIABETES MELLITUS	20
OTHER: PLAQUE PSORIASIS	20
PSORIATIC ARTHRITIS	20

Prior Procedures	Procedure Year
SURGERY: TONSILECTOMY	19[redacted]
SURGERY: VASECTOMY	19
SURGERY: RIGHT WRIST REPAIR	20
SURGERY: RIGHT SHOULDER REPAIR	20
SURGERY: RIGHT SHOULDER LIGAMENT RETRACTION REPAIR	20
SURGERY: RIGHT WRIST CARPAL TUNNEL RELEASE	20
SURGERY: RIGHT WRIST FUSION	20

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1[redacted]	20[redacted] / 61	61

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DILTIAZEM	240 mg	QD	Y-M: 19[redacted]
ENALAPRIL	10 mg	QD	Y-M: 19[redacted]
LEVOTHYROXINE	275 ug	QD	Y-M: 19[redacted]
LOVASTATIN	20 mg	QD	Y-M: 19[redacted]
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 19[redacted]
OXYCOCET	75 mg	BID	Y-M: 20[redacted]
PARACETAMOL	325 mg	BID	Y-M: 20[redacted]
GLIPIZIDE	10 mg	QD	Y-M: 20[redacted]
METFORMIN	1000 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -292
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -292

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
DILTIAZEM	240 mg	QD	Y-M: 19[redacted]	Y-M: 20[redacted] / 62
ENALAPRIL	10 mg	QD	Y-M: 19[redacted]	Y-M: 20[redacted] / 62
LEVOTHYROXINE	275 ug	QD	Y-M: 19[redacted]	Y-M: 20[redacted] / 62
LOVASTATIN	20 mg	QD	Y-M: 19[redacted]	Y-M: 20[redacted] / 62
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 19[redacted]	Y-M: 20[redacted] / 62
GLIPIZIDE	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 62
METFORMIN	1000 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 62
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -292	Y-M: 20[redacted] / 62
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -292	Y-M: 20[redacted] / 62

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

Event Description	CARDIAC ARREST
Preferred term	心停止
AE Onset Date / Rx Day	[redacted]20[redacted] / 62 (6 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	62 (6 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAY
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	DIABETES, HYPERLIPIDEMIA, HYPERTENSION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	RESULTS IN DEATH

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。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，致死的な心停止の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，高血圧，甲状腺機能低下症，高脂血症，糖尿病，乾癬性関節炎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。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，被験者は心停止を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死因は心停止と報告された。剖検は実施されなかった。

被験者は運転中に詳細不明の緊急事態に陥り，死亡した。治験責任医師による追加情報の入手は不可である。

死亡診断書は入手されなかった。

Causality for ABT-494 (Blinded)

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1) Cardiac arrest (10007515) (Cardiac arrest (10007515)) [v.21.1] [10007515]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of CARDIAC ARREST

- Investigator: Diabetes, hyperlipidemia, and hypertension.

- AbbVie: Event is more likely related to preexisting diabetes mellitus, hypertension, hyperlipidemia and obesity

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
虚血性脳卒中	X			X
気管支炎	X			X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
TUBERCULOSIS: LATENT TB	19[redacted]
CORONARY ARTERY DISEASE	19
HYPERTENSION	19
DIABETES MELLITUS	20
OTHER: JOINTS PAIN/ARTHRITIS	20
HYPERLIPIDEMIA: HIGH CHOLESTEROL	20
BENIGN PROSTATIC HYPERPLASIA: PROSTATIC HYPERTROPHY	20
OTHER: PLAQUE PSORIASIS	20
PSORIATIC ARTHRITIS	20
OTHER: RIGHT AND LEFT EYE GLAUCOMA	20
OTHER: URINARY RETENTION	20

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY	19[redacted]
SURGERY: APPENDECTOMY	19
SURGERY: CORONARY BYPASS	19
SURGERY: RENAL ARTERY STENT	20
SURGERY: LEG VEIN ABLATION	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1.5 PACK	25	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	[redacted] / 682	289

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 19[redacted]
ALLOPURINOL	300 mg	QD	Y-M: 20[redacted]
CHONDROITIN	300 mg	QD	Y-M: 20[redacted]
GLUCOSAMINE	300 mg	QD	Y-M: 20[redacted]
METFORMIN	500 mg	QD	Y-M: 20[redacted]
AMLODIPINE	5 mg	QD	Y-M: 20[redacted]
ATORVASTATIN	80 mg	QD	Y-M: 20[redacted]
CARVEDILOL	12.5 mg	BID	Y-M: 20[redacted]
ISOSORBIDE MONONITRATE	30 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	QD	Y-M: 20[redacted]
LOSARTAN	25 mg	QD	Y-M: 20[redacted]
TAMSULOSIN	4 mg	QD	Y-M: 20[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
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 19[redacted]	ONGOING
ALLOPURINOL	300 mg	QD	Y-M: 20[redacted]	ONGOING
CHONDROITIN	300 mg	QD	Y-M: 20[redacted]	ONGOING
GLUCOSAMINE	300 mg	QD	Y-M: 20[redacted]	ONGOING
METFORMIN	500 mg	QD	Y-M: 20[redacted]	ONGOING
AMLODIPINE	5 mg	QD	Y-M: 20[redacted]	ONGOING
ATORVASTATIN	80 mg	QD	Y-M: 20[redacted]	ONGOING
CARVEDILOL	12.5 mg	BID	Y-M: 20[redacted]	ONGOING
ISOSORBIDE MONONITRATE	30 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 454
LOSARTAN	25 mg	QD	Y-M: 20[redacted]	ONGOING
TAMSULOSIN	4 mg	QD	Y-M: 20[redacted] / -233	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 309	ONGOING
IRON	324 mg	QD	Y-M: 20[redacted] / 310	ONGOING
SALBUTAMOL	90 OTHER: MCG	PRN	Y-M: 20[redacted] / 462	ONGOING
CEFALEXIN	1 g	QD	Y-M: 20[redacted] / 462	Y-M: 20[redacted] / 464
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 474	Y-M: 20[redacted] / 481

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

Event Description	ISCHEMIC CEREBRAL VASCULAR ACCIDENT
Preferred term	虚血性脳卒中
AE Onset Date / Rx Day	[redacted]20[redacted] / 306
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 306): Basophils: 0.02 [0 - 0.1] 10^9/L; Eosinophils: 0.03 [0.04 - 0.35] 10^9/L; Erythrocytes: 3.7 [4.4 - 5.6] 10^12/L; Hematocrit: 0.38 [0.4 - 0.5] FRACTION OF 1; Leukocytes: 4.9 [4.5 - 10] 10^9/L; Monocytes: 0.58 [0.2 - 1] 10^9/L; NPTST241-HEMOGLOBIN: 11.9 [13 - 17] G/DL; [redacted]20[redacted] (RX DAY 671): Lymphocytes: 0.82 [0.9 - 5] 10^9/L; Neutrophils: 3.35 [1.8 - 7.7] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 306): MRI BRAIN: ISCHEMIC CVA; [redacted]20[redacted] (RX DAY 308): MRI OF THE BRAIN: HIGH GRADE RIGHT VERTEBRAL ARTERY STENOSIS,LEFT HEMISPHERIC STROKE, MODERATE CAROTID STENOSIS; TRANSTHORACIC ECHO: MITRAL VALVE SCLEROSIS, MILD-MODERATE MITRAL REGURGITATION,TRICAFLCT AORTIC VLAVE WITH SCLEROSIS, TRACE PULMONARY VALVE REGURGITATION; [redacted]20[redacted] (RX DAY 309): CT ANGIOGRAM OF HEAD AND NECK: CT ANGIOGRAM OF THE HEAD AND NECK REVEALED FOCAL STENOSIS OF THE RIGHT VERTEBRAL ARTERYOF 80% AND 60% NARROWING OF LEFT INTERNAL CAROTID ARTERY.; CT BRAIN: CT SCAN OF BRAIN WAS PERFORMED AND WAS NEGATIVE.; [redacted]20[redacted] (RX DAY 344): CT SCAN HEAD: MILD TO MODERATE GENERALIZED VOLUME LOSS AND MILD CHRONIC WHITE MATTER ISCHEMIA

AE Stopped Rx Day	344
Duration of AE	39 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	CORONARY ARTERY DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	BRONCHITIS
Preferred term	気管支炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 460
Age at AE Onset	7[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	481
Duration of AE	22 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SUBJECT WAS OUT OF THE COUNTRY AND BY AGE HE WAS MAY LIABLE TO DIFFERENT TYPES OF BACTERIAL 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。本被験者は米国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，虚血性脳血管発作の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元喫煙者（1 日 1.5 箱を 25 年間），冠動脈疾患，高血圧，冠動脈バイパス，腎動脈ステント，糖尿病，コレステロール高値，乾癬性関節炎及び現飲酒者（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。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，被験者は虚血性脳血管発作を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，虚血性脳血管発作は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右側の脱力及び顔面・腕のしびれ感で入院した。被験者は意識清明で，人・場所・時間の見当識障害はなく，発話・言語・理解力も正常であった。右上肢にごくわずかな脱力があり，靴下・手袋型分布における軽度の感覚低下を伴っていた。振戦は見られなかった。被験者は右側の顔面・腕の運動／感覚消失を呈していた。被験者によると，失語症，嚥下障害，構語障害，回転性めまい，霧視，運動失調，眼振，複視，錯乱，意識消失／低下及び四肢の運動／感覚消失はなかった。脳 MRI 検査及び頭部 CT 検査の結果，虚血性脳血管発作と診断された。被験者は，障害や長期に及ぶ後遺症なく回復した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

医療記録によると，被験者は，前の週に出現した 1 日間の右側しびれ感のため，20[redacted] 年 [redacted] 月 [redacted] 日に脳 MRI 検査，20[redacted] 年 [redacted] 月 [redacted] 日に腰椎 MRI 検査を受けた。脳 MRI 検査の結果，急性梗塞，頭蓋内出血及び腫瘤の影響は認められず，軽度から中等度の脳全体の容積減少及び軽度の慢性白質虚血が認められた。腰椎所見は，軽度の脊椎症性変形，局所的な椎間板ヘルニア及び

狭窄なし，真性神経根圧迫なしであった。

投与された薬剤は，硫酸鉄，プラビックス及びアスピリンであった。

Causality for UPADACITINIB (Blinded)

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1) Ischaemic stroke (10061256) (Ischaemic stroke (10061256)) [v.22.1] [10061256]

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 ISCHEMIC CEREBRAL VASCULAR ACCIDENT

- Investigator: CORONARY ARTERY DISEASE

- AbbVie: EVENT IS MORE LIKELY RELATED TO ADVANCED AGE, PRE-EXISTING DIABETES MELLITUS, HYPERTENSION AND HIGH CHOLESTEROL.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ANGIOGRAM:** CT ANGIOGRAM OF HEAD AND NECK: Significant focal stenosis of the right vertebral artery of 80% and 60%narrowing of the left internal carotid artery.

[redacted] **BLOOD PRESSURE:** 176/62 mmHg

[redacted] **BODY TEMPERATURE:** 37.9 Degrees C

[redacted] **CT BRAIN:** ischemic CVA

[redacted] **CT HEAD:** ischemic CVA

[redacted] **CT HEAD:** Mild to moderate generalized volume loss and mild chronic white matter ischemia

[redacted] 20[redacted] **HBA1C:** 6.1

[redacted] 20[redacted] **HEART RATE:** 64 /min

[redacted] 20[redacted] **LDL:** 37 mg/dL

[redacted] 20[redacted] **MRI BRAIN:** ischemic CVA

[redacted] 20[redacted] **MRI BRAIN:** high grade rightvertebral artery stenosis, left hemispheric stroke, moderate carotid stenosis

[redacted] 20[redacted] **MRI BRAIN WITHOUT CONTRAST:** IMPRESSION: No acute infarct, intracranial hemorrhage or mass effect. Mild to moderate generalized volume loss and mild chronic white matter ischemia.

[redacted] 20[redacted] **MRI LUMBAR SPINE WITHOUT CONTRAST:** IMPRESSION: Mild spondylotic changes. No focal disc herniation or stenosis. No frank nerve root compression.

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

[redacted] 20[redacted] **TRIGLYCERIDES:** 322 mg/dL

[redacted] 20[redacted] **TTE:** IMPRESSION: Lumason was used; NO PERICARDIAL EFFUSION; LEFT VENTRICLE EF is estimated at 50% to 55%; MITRAL VALVE sclerosis, mild-moderate regurgitation; TRILEAFLET AORTIC VALVE with sclerosis, no regurgitation; RIGHT ATRIUM mildly increased right atrial size; RIGHT VENTRICLE mildly increased size with systolic pressure of 24.9mmHg; TRICUSPID VALVE trace to mild regurgitation; PULMONARY VALVE trace regurgitation; INTER-ATRIAL SHUNTING
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，気管支炎の事象を発現した。

Event 3 の臨床経過：

関連する病歴は，結核（非活動性結核），元喫煙者（1 日 1.5 箱を 25 年間），高血圧，糖尿病，局面型乾癬，乾癬性関節炎及び現飲酒者（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。

本事象発現前，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は慢性腎臓病（非重篤な事象）を発現し，治験薬の投与が休止された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は咳嗽及び発熱で入院した。治験責任医師によると，本事象に関連する危険因子は被験者の年齢であった。投与された薬剤は抗生物質であり，20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，セファレキシン，ドキシサイクリン及び pro-air であった。

Causality for ABT-494 (Blinded)

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

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of BRONCHITIS

- Investigator: Unknown

- AbbVie: Event iscommon in the general population.

Relevant Laboratory & Other Diagnostic Tests

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

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

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
尿管結石症	X			

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

Medical History	Onset Year
OTHER: TB VACCINE	19[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO PENICILLIN	19
OTHER: PLAQUE PSORIASIS	19
HYPERTENSION	20
OTHER: VERTIGO	20
PSORIATIC ARTHRITIS	20
OTHER: ELEVATED URIC ACID	20
CLOTTING/BLEEDING PROBLEMS: DEEP VEIN THOMBOSIS	20
DIABETES MELLITUS	20
OTHER: LATENT TB	20

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 161	161
ADA	40MG	SC	EOW	[redacted]20[redacted] / 162		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]
FEBUXOSTAT	40 mg	QD	Y-M: 20[redacted]
VALSARTAN	160/12.5 mg	QD	Y-M: 20[redacted]
GLIPIZIDE	2.5 mg	BID	Y-M: 20[redacted]
MECLOZINE	25 mg	PRN	Y-M: 20[redacted]
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -280
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -236
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -236
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -18
PYRIDOXINE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -18

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED
APREMILAST	30 mg	BID	Y-M: 20[redacted]	NOT REPORTED
FEBUXOSTAT	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
VALSARTAN	160/12.5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
GLIPIZIDE	2.5 mg	BID	Y-M: 20[redacted]	NOT REPORTED
MECLOZINE	25 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / -280	NOT REPORTED
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -236	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -236	NOT REPORTED
PYRIDOXINE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -18	NOT REPORTED
KETOROLAC	30 mg	OTHER: ONCE	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 64
MORPHINE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 64

Event #1: Serious Adverse Event

Event Description 3MM URETERAL CALCULUS
Preferred term 尿管結石症
AE Onset Date / Rx Day [redacted]20[redacted] / 64
Age at AE Onset 5[redacted]
Laboratory Testing
NOT REPORTED
Microbiology
[redacted]20[redacted] (RX DAY 65): URINE NPTST491-URINE CULTURE: Negative-GRAM NEGATIVE BACILLI, <10,000 CFU/ML
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 64): CT ABDOMEN AND PELVIS, WITHOUT CONTRAST: 3MM OBSTRUCTING STONE IN DISTAL URETER; [redacted]20[redacted] (RX DAY 65): CYSTOSCOPY, LEFT URETEROSCOPY, STONE EXTRACTION AND LEFT URETERAL STENT REPLACEMENT: STONE EXTRACTED AND STENT PLACED; XR UROGRAM RETROGRADE INTRAOP: FLUOROSCOPY FOR LEFT RETROGRADE UROGRAM AND STENT PLACEMENT

AE Stopped Rx Day	66
Duration of AE	3 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	UNKNOWN AT PRESENT
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。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，3 mm の尿管結石の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，高血圧，尿酸上昇，糖尿病，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 3 mm の尿管結石を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，3 mm の尿管結石は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，鼡径部に放射状に拡がる左側腹部痛のため救急治療室を受診した。腹部・骨盤 CT スキャン検査で 3 mm の左尿管結石が見つかった。Dilaudid の静脈内投与が開始された。左側腹部痛は鎮痛薬でコントロールすることができず，被験者はその後入院した。膀胱鏡検査時に結石除去が行われ，ステント留置が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，ketorolac，モルヒネ及び dilaudid であった。

The patient's past medications include:

INH for LATENT TB ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

PENICILLIN for UNKNOWN INDICATION

Causality for ABT-494 (Blinded)

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1) Ureteral calculus (10046383) (Ureterolithiasis (10077989)) [v.22.0] [10046383]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reactiondid not recur

Alternative Etiology for ABT-494 (Blinded)

Event of 3MM URETERAL CALCULUS

- Investigator: HYPERCALCIUREA

- AbbVie: More likely related to underlying risk factors of elevated uric acid, diabetes and obesity.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT ABDOMEN AND PELVIS WITHOUT CONTRAST:** 3MM OBSTRUCTING STONE IN DISTAL URETER

[redacted] **20[redacted] CYSTOSCOPY:** STONE EXTRACTED AND STENT PLACED

[redacted] **20[redacted] LEFT URETEROSCOPY:** STONE EXTRACTED AND STENT PLACED

[redacted] **20[redacted] URINE CULTURE:** Gram negative bacilli <10,000 CFU/ML

[redacted] **20[redacted] X-RAY, UROGRAPHY RETROGRADE INTRAOP:** FLUOROSCOPY FOR LEFT RETROGRADE UROGRAM AND STENT PLACEMENT

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
呼吸窮迫	X			

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
DEPRESSION	20[redacted]
HYPERTENSION	20
OSTEOARTHRITIS	20
GASTROESOPHAGEAL REFLUX DISEASE	20
OTHER: NARROW ESOPHAGUS	20
OTHER: CERVICAL SPONDYLOSIS	20
OTHER: LEFT SIDE MUXCLE WEAKNESS	20
TRANSIENT ISCHEMIC ATTACK: TIA	20
OTHER: SLEEP APNEA	20
OTHER: ARTHRALGIA RIGHT KNEE	20
DIABETES MELLITUS	20
OTHER: PLAQUE PSORIASIS	20
PSORIATIC ARTHRITIS	20

Prior Procedures	Procedure Year
SURGERY: FRACTURED RIGHT ANKLE	19[redacted]
SURGERY: L SPINE DISKECTOMY	19
SURGERY: C-SPINE FUSION	20

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

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

Study Drug Administration

Study Drug	Dose/Units	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		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ALPRAZOLAM	1.0 mg	TID	Y-M: [redacted]
AMLODIPINE	5.0 mg	QD	Y-M: [redacted]
PARACETAMOL	325.00 mg	PRN	Y-M: [redacted]
PANTOPRAZOLE	40.0 mg	QD	Y-M: [redacted]
ACETYLSALICYLIC ACID	81.0 mg	QD	Y-M: [redacted]
METFORMIN	250.00 mg	QD	Y-M: [redacted]
FOLIC ACID	1.00 mg	QD	Y-M: [redacted]
METHOTREXATE	20.00 mg	EVERY WEEK	Y-M: [redacted]
HYDROXYCHLOROQUINE	200.00 mg	BID	Y-M: [redacted] / -292

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
ALPRAZOLAM	1.0 mg	TID	Y-M: [redacted]	NOT REPORTED
AMLODIPINE	5.0 mg	QD	Y-M: [redacted]	NOT REPORTED
PARACETAMOL	325.00 mg	PRN	Y-M: [redacted]	NOT REPORTED
PANTOPRAZOLE	40.0 mg	QD	Y-M: [redacted]	NOT REPORTED
ACETYLSALICYLIC ACID	81.0 mg	QD	Y-M: [redacted]	NOT REPORTED
FOLIC ACID	1.00 mg	QD	Y-M: [redacted]	NOT REPORTED
HYDROXYCHLOROQUINE	200.00 mg	BID	Y-M: [redacted] / -292	NOT REPORTED
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: [redacted] / 62	NOT REPORTED
GUAIFENESIN	1 OTHER: TABLET	BID	Y-M: [redacted] / 143	Y-M: [redacted] / 158
MEDINITE	2 OTHER: CAPSULES	QD	Y-M: [redacted] / 143	Y-M: [redacted] / 158
VICKS FORMULA 44M	2 OTHER: CAPSULES	BID	Y-M: [redacted] / 143	Y-M: [redacted] / 158
AZITHROMYCIN	500.00 mg	OTHER: ONCE	Y-M: [redacted] / 186	Y-M: [redacted] / 186
CEFTRIAXONE	1000.00 mL	OTHER: ONCE	Y-M: [redacted] / 186	Y-M: [redacted] / 186
METHYLPREDNISOLONE	125.00 mg	OTHER: ONCE	Y-M: [redacted] / 186	Y-M: [redacted] / 186
SALBUTAMOL	3.00 mL	OTHER: ONCE	Y-M: [redacted] / 186	Y-M: [redacted] / 187
SODIUM CHLORIDE	0.9 %	QD	Y-M: [redacted] / 186	Y-M: [redacted] / 188
ALPRAZOLAM	1.00 mg	TID	Y-M: [redacted] / 188	NOT REPORTED

FLUTICASONE	250.00 OTHER: MCG	BID	Y-M: 20[redacted] / 188	NOT REPORTED
SALBUTAMOL	90.00 OTHER: MCG	QID	Y-M: 20[redacted] / 188	NOT REPORTED
TIOTROPIUM	18.00 mg	QD	Y-M: 20[redacted] / 188	NOT REPORTED
AZITHROMYCIN	250.00 mg	QD	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 192
PREDNISONE	40.00 mg	QD	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 202

Event #1: Serious Adverse Event

Event Description	UPPER RESPIRATORY DISTRESS
Preferred term	呼吸窮迫
AE Onset Date / Rx Day	[redacted]20[redacted] / 186
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 186): Glucose: 6.5 [3.9 - 5.5] MMOL/L; NPTST034-ANION GAP: 14 [3 - 11] UNSPECIFIED; NPTST352-O2SAT ART: 93.1 [96 - 97] %; NPTST385-PO2ART: 57.5 [80 - 100] MMHG; [redacted]20[redacted] (RX DAY 187): Glucose: 9.3 [3.9 - 5.5] MMOL/L; Leukocytes: 9.9 [4 - 11] 10^9/L; Lymphocytes/Leukocytes: 0.9 [1 - 1.4] %; NPTST034-ANION GAP: 17 [3 - 11] UNSPECIFIED; Neutrophils/Leukocytes: 80.6 [40 - 78] %

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 186): CHEST RADIOGRAPHS: NO ACUTE PULMONARY OR PLEURAL ABNORMALITY; ELECTROCARDIOGRAM: WITHIN NORMAL LIMITS

AE Stopped Rx Day	194 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	9 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。本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，上気道呼吸窮迫の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，元喫煙者（1 日 1 箱を 20 年間），高血圧，胃食道逆流性疾患，食道狭窄，頚椎融合，頚椎症，左側筋力低下，一過性脳虚血発作，睡眠時無呼吸，糖尿病，乾癬性関節炎

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，被験者は上気道呼吸窮迫を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，上気道呼吸窮迫は消失した。

本事象発現前，20[redacted] 年 [redacted] 月，被験者は上気道呼吸器感染（非重篤）を発現した。上気道呼吸器感染（非重篤）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は上気道呼吸窮迫で入院した。臨床検査及び診断検査が行われた。検査項目は，PO2 ART（検査値：57.5 mmHG）及び O2SAT ART（検査値：93.1%）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，スピリーバ，albuterol，メチルプレドニゾロン，塩化ナトリウム，アジスロマイシン，アルプラゾラム，フルチカゾン，prednisone 及びセフトリアキソンであった。

Causality for UPADACITINIB (Blinded)

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1) Respiratory distress (10038687) (Respiratory distress (10038687)) [v.22.1] [10038687]

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 UPPER RESPIRATORY DISTRESS

- Investigator: Not applicable

- AbbVie: event is more likely related to recent upper respiratory infection. Additional risk factors include significant past smoking history of 1 PPD for 20 years and pre-existing sleep apnea.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANION GAP:** 14.0 Unspecified (normal 3.0 to 11.0)

[redacted] **20[redacted] ANION GAP:** 17.0 Unspecified (normal 3.0 to 11.0)

[redacted] **20[redacted] CHEST RADIOGRAPHS:** No acute pulmonary or pleural abnormality.

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Within normal limits.

[redacted] **20[redacted] GLUCOSE:** 117 mg/dL (normal 70.0 to 99.0)

[redacted] **20[redacted] GLUCOSE:** 167 mg/dL (normal 70.0 to 99.0)

[redacted] **20[redacted] LYMPHOCYTES %:** 0.9 % (normal 1.0 to 1.4)

[redacted] **20[redacted] NEUTROPHILS %:** 80.6 % (normal 40.0 to 78.0)

[redacted] **20[redacted] O2SAT ART:** 93.1 % (normal 96.0 to 97.0)

[redacted] **20[redacted] PO2ART:** 57.5 mmHg (normal 80 to 100)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.9 10^3/uL (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
肺塞栓症	X	X		X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
MIGRAINE HEADACHE	19
ASTHMA	19
PSORIATIC ARTHRITIS	19
OTHER: ANXIETY	19
OTHER: OCCASIONAL HEADACHE	20
OTHER: SEASONAL ALLERGIES	20
DEPRESSION	20
OBESITY	20
OTHER: VITAMIN D DEFICIENCY	20
OTHER: OSTEOARTHRITIC NODULES OF THE DISTAL IP JOINTS	20
OTHER: INSOMNIA	20
OSTEOARTHRITIS	20
OTHER: ITCHING	20

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	19[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	3[redacted]	20[redacted]
CIGARS	FORMER			
E-CIGARETTES	NEVER			
PIPES	FORMER			

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	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169

ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / [redacted]20[redacted] / 385	216
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 386[redacted]20[redacted] / 812	427

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Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
IBUPROFEN	400 mg	TID	Y-M: 19[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 19[redacted]
VACCINIUM MACROCARPON	1 OTHER: TABLET	QD	Y-M: 19[redacted]
OCUVITE	1 OTHER: TABLET	QD	Y-M: 20[redacted]
UBIDECARENONE	10 mg	QD	Y-M: 20[redacted]
CITALOPRAM	40 mg	QD	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
OXYCODONE	1 OTHER: TABLET	BID	Y-M: 20[redacted] / -329
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -140
ZOLPIDEM	5 mg	QD	Y-M: 20[redacted] / -42
DESONIDE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -14
VICODIN	1 OTHER: TABLET	BID	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
IBUPROFEN	400 mg	TID	Y-M: 19[redacted]	NOT REPORTED
OCUVITE	1 OTHER: TABLET	QD	Y-M: 20[redacted]	NOT REPORTED
CITALOPRAM	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
APREMILAST	30 mg	BID	Y-M: 20[redacted]	NOT REPORTED
VICODIN	1 OTHER: TABLET	BID	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 809
DIPHENHYDRAMINE	50 mg	BID	Y-M: 20[redacted] / 2	NOT REPORTED
RETINOL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 111	NOT REPORTED
DIPHENHYDRAMINE	25 mg	QD	Y-M: 20[redacted] / 607	NOT REPORTED
MELATONIN	3 mg	QD	Y-M: 20[redacted] / 795	NOT REPORTED
ALTEPLASE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 808	Y-M: 20[redacted] / 808
ALTEPLASE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 808	Y-M: 20[redacted] / 808
SODIUM CHLORIDE	25 mL	OTHER: HR	Y-M: 20[redacted] / 808	Y-M: 20[redacted] / 808
HEPARIN	11 OTHER: UNITS/KG	OTHER: HR	Y-M: 20[redacted] / 808	Y-M: 20[redacted] / 810
SODIUM CHLORIDE	2 mL	BID	Y-M: 20[redacted] / 808	Y-M: 20[redacted] / 819
POTASSIUM	20 mEq	PRN	Y-M: 20[redacted] / 809	Y-M: 20[redacted] / 811
VICODIN	2 OTHER: TABLETS	PRN	Y-M: 20[redacted] / 809	Y-M: 20[redacted] / 818

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Cardiovascular Events

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Rx Day	[redacted]20[redacted] / 808
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 808): Basophils: 0.0 [0 - 0.3] 099,K/MCL; Basophils/Leukocytes: 0 [0 - 2] %; Calcium: 1.06 [1.15 - 1.29] MMOL/L; Chloride: 109 [98 - 107] MMOL/L; Eosinophils: 0.0 [0.1 - 0.5] 099,K/MCL; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 4.02 [4 - 5.2] 099,MIL/MCL; Glucose: 7.8 [3.9 - 5.5] MMOL/L; Hematocrit: 0.39 [0.36 - 0.47] FRACTION OF 1; Hemoglobin: 123 [120 - 155] G/L; Leukocytes: 13.6 [4.2 - 11] 099,K/MCL; Lymphocytes: 1.2 [1 - 4] 099,K/MCL; Lymphocytes/Leukocytes: 9 [20 - 44] %; Monocytes: 0.8 [0.3 - 0.9] 099,K/MCL; Monocytes/Leukocytes: 6 [2 - 9] %; NPTST095-BUN: 27 [6 - 20] MG/DL; NPTST132-CO2 TOTAL: 23 [19 - 24] MMOL/L; NPTST316-MCH: 30.6 [26 - 34] PG; NPTST317-MCHC: 31.4 [32 - 36.5] G/DL; NPTST318-MCV: 97.5 [78 - 100] FL; NPTST374-PERCENT IMMATUREGRANULACTYES: 1 [NOT REPORTED - NOT REPORTED] %; NPTST415-RDW-CV: 12.7 [11 - 15] %; NPTST470-TROPONIN: 0.81 [NOT REPORTED - 0.1] ng/mL; NPTST472-TROPONIN I: 1.10 [NOT REPORTED - 0.05] ng/mL; NPTST472-TROPONIN I: 1.00 [NOT REPORTED - 0.05] ng/mL; Neutrophils: 11.5 [1.8 - 7.7] 099,K/MCL; Neutrophils/Leukocytes: 84 [50 - 70] %; Platelets: 115 [140 - 450] 099,K/MCL; Potassium: 4 [3.4 - 5.1] MMOL/L; Sodium: 141 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 808): CHEST CT: POSITIVE FOR PE, LARGE CLOT BURDEN. NEGATIVE FOR INFECTION. SEVERAL PULMONARY NODULES.; CHEST X-RAY: NO ACUTE PULMONARY PROCESS; ELECTROCARDIOGRAM: RATE: 125, RHYTHM: SINUS TACHYCARDIA, ABNORMALITY: RSR' OR QR PATTERN IN V1 SUGGESTS RIGHT VENTRICULAR CONDUCTION DELAY. MARKED ST ABNORMALITY, POSSIBLE INFERIOR SUBENDOCARDIAL INJURY. COMPARED WITH PRIOR EKG: ST DEPRESSION IN INFERIOR AND LATERAL LEADS; LOWER EXTREMITY ULTRASOUND: ECHOGENIC MATERIAL WITHIN THE VISUALIZED PORTION OF THE LEFT COMMON FEMORAL VEIN, LIKELY PARTIALLY OCLUSIVE THROMBUS. SHORT INTERVAL FOLLOW UP ULTRASOUND COULD BE CONSIDERED. NO ULTRASOUUND EVIDNECEOF DEEP VENOUS THROMBOSIS IN THE RIGHT LOWER EXTREMITY.; [redacted]20[redacted] (RX DAY 809): ECHOCARDIOGRAM: SEVERE RV SYSTOLIC DYSFUNCTION. MILD PULMONARY HYPERTENTION.

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
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]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺塞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，片頭痛，乾癬性関節炎，元喫煙者（1 日 0.5 箱を 33 年間），肥満，変形性関節症，元喫煙者（パイプ及び葉巻），元飲酒者（1 日 2～4 杯），深部静脈血栓症の家族歴，血沈亢進及び麻薬性鎮痛薬の長期使用であった。変形性関節症の家族歴もあった。

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，被験者は救急科を受診し，同日出現した右側胸痛及び息切れを訴えた。胸痛は両肩に放射状に拡がった。被験者は過去にも同様の疼痛及び息切れを慢性的に経験していたが，今回は「死んでしまうのではないか」と感じられるほどのものであった。また，その日の朝，被験者は気絶して転倒した。被験者は右下肢痛及び左下肢腫脹（非重篤な深部静脈血栓症と診断された）も呈していた。

救急治療室にて，被験者は低血圧の状態にあり，収縮期血圧が 80 台であった。またトロポニン増加及び BNP 増加が認められた。CT 検査で，主肺動脈から遠位部にかけて，RV ストレインを伴って，大きな血栓による肺塞栓が認められた。被験者によれば，その他の随伴症状はなかった。被験者は tPA を投与され，同日 CICU に入院した。エコーの再検査で肺高血圧症が認められたため，肺高血圧症チームによる診察が行われた。左下肢の超音波検査で左下肢深部静脈血栓症（非重篤）が認められた。血液疾患・心不全チームによる診察が行われた。

被験者はこれまでに抗凝固薬を使用しておらず，遠距離の旅行歴，入院歴及び手術歴もなかった。深部静脈血栓症や肺塞栓症の病歴もなかった。喫煙歴があったが，2 年前から禁煙していた。

治験責任医師は，肥満及び体を動かすことの少ない生活であることが本事象の危険因子であったと述べた。被験者には深部静脈血栓症の強力な家族歴があり，父親と 2 人の兄弟が長期にわたって抗凝固療法を受けていた。

本事象により治験薬の投与は中止された。

投与された薬剤は，asa，activase，ヘパリン，lovenox，coumadin，酸素，ワルファリン，タイレノール，塩化カリウム，塩化ナトリウム及び porcine-fastact であった。

The patient's past medicaons include:

METHOTREXATE for PSORIATIC ARTHRITIS (19[redacted] - 19[redacted])

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

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

MEDROL DOSEPACK for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for UPADACITINIB (Blinded)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.22.1] [10037377]

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 PULMONARY EMBOLISM

- Investigator: Not applicable

- AbbVie: More likely related to risk factors such as strong family history of DVT (including father and siblings), obesity, pre-existing psoriasis, and age. Patients older than 40 years old are at higher risk of VTE and that risk doubles with each subsequent decade.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **A/G RATIO:** 0.9 no units

[redacted] 20[redacted] **ALBUMIN:** 3.6 no units

[redacted] 20[redacted] **ALK PHOSPHATASE:** 58 no units

[redacted] 20[redacted] **ALK PHOSPOTASE:** 52 no units

[redacted] 20[redacted] **ALT/SGPT:** 44 no units

[redacted] 20[redacted] **ANION GAP:** 14 no units

[redacted] 20[redacted] **AST:** 34 no units

[redacted] 20[redacted] **AST/SGOT:** 34 no units

[redacted] 20[redacted] **BILIRUBIN:** 0.5 no units

[redacted] 20[redacted] **BLOOD PRESSURE:** Hypotensive in the ED with SBP 80's mmHg.

[redacted] 20[redacted] **BLOOD PRESSURE:** 103/66 mmHg

[redacted] 20[redacted] **BMI:** 33.4 No units

[redacted] 20[redacted] **BUN:** 27 mg/dL (normal 6 to 20)

[redacted] 20[redacted] **BUN:** 16 mg/dL

[redacted] 20[redacted] **CAI:** 1.21 no units

[redacted] 20[redacted] **CALCIUM:** 1.06 MMOL/L (normal 1.15 to 1.29)

[redacted] 20[redacted] **CHEST X-RAY:** No acute cardiopulmonary process. Cardiac silhouette and pulmonary vasculature are within normal limits. No pneumothorax, pleural effusion, or focal airspace opacity. No acute bony abnormality. Minimal right hemidiaphragm elevation. Old left rib deformity.

[redacted] 20[redacted] **CHLORIDE:** 109 MMOL/L (normal 98 to 107)

[redacted] 20[redacted] **CO2:** 23 MMOL/L (normal 19 to 24)

[redacted] 20[redacted] **CO2:** 27 MMOL/L

[redacted] 20[redacted] **CREATININE:** 0.90 no units

[redacted] 20[redacted] **CREATININE:** 0.88 no units

[redacted] 20[redacted] **CT ANGIOGRAM CHEST:** Chest: Good opacification of pulmonary arteries. PE Summary: Most proximal PE right: Proximal right pulmonary artery. Most proximal PE left: Proximal left pulmonary artery. Subjective Bilateral PE Burden: Large. Septal Flattening/Bowing: Yes. RV/LV Ratio:1.4. Coronary artery sclerosis. Heart size is not enlarged. No pericardial effusion. Thoracic aorta is grossly unremarkable besides mild atherosclerosis. No suspicious adenopathy. Visualized thyroid gland demonstrates no focal abnormalities. Probably reactive mildly prominent left supraclavicular nodes. Small sliding hiatal hernia. No suspicious intrathoracic adenopathy. Limited evaluation of the upper abdomen. Reflux of contrast into the hepatic veins. probably partial visualization of left renal cyst. Probably nodular lingular atelectasis. Several sub-3mm pulmonary nodules. For example, 0.2 cm left apical nodule and 0.2 cm right midlung nodule.

[redacted] 20[redacted] **CT SCAN:** Positive for PE: large clot burden from main pulmonary arteries into the distal segments with associated right heart strain. Negative for infection within the chest. Several sub +3mm pulmonary nodules. Recommend follow-up per Fleischner Society criteria guidelines.

[redacted] 20[redacted] **ECHO:** Bilateral Pulmonary embolism s/p tPA ([redacted] 20[redacted]). Moderate RV cavity enlargement. Severe RV systolic dysfunction McConnell's sign. Septal flattening consistent with RV volume overload. Mild pulmonary hypertension, RSVP 39 mmHg. Normal LV size and systolic function, LVEF 65%. No significant valvular abnormalities. Small pericardial effusion.

[redacted] 20[redacted] **ECHO:** S/P TPA for Pulmonary embolism: mildly increased right ventricular size with mildly decreased systolic function. Moderate Pulmonary hypertension with RPASP 67 mmHg. Compared to prior echo dated [redacted] 20[redacted], RV size has significantly decreased and function has improved.

[redacted] 20[redacted] **ECHOCARDIOGRAM:** MODERATE PULMONARY, PASP=53 MMhG. MILD INCREASED RV SIZE WITH MILDLY DECREASED SYSTOLIC FUNCTION. AGITATED SALINE WAS INJECTED THROUGH A PERIPHERAL VEIN AND DID NOT SHOW¥ EVIDENCE OF A SHUNT.

[redacted] 20[redacted] **EGFR AFRICAN AMERICAN:** 77 mL/min/1.73m2

[redacted] 20[redacted] **EGFR NON AFRICAN AMERICAN:** 67 mL/min/1.73m2

[redacted] 20[redacted] **EKG:** Rate 125, rhythm sinus tachycardia. RSR or QR pattern in V1 suggests right ventricular conduction delay. Marked ST abnormality, possible inferior subendocardial injury. Compared with prior EKG (date unknown): ST depression in inferior and lateral leads.

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

[redacted] 20[redacted] **GLUCOSE:** 141 mg/dL (normal 70 to 99)

[redacted] 20[redacted] **GLUCOSE:** 93 mg/dL

[redacted] 20[redacted] **GPT:** 42 no units

[redacted] 20[redacted] **HCT:** 39.1 % (normal 36.0 to 46.5)

[redacted] 20[redacted] **HCT:** 30.4 %

[redacted] 20[redacted] **HGB:** 12.3 G/DL (normal 12.0 to 15.5)

[redacted] 20[redacted] **INR:** 1.1 no units

[redacted] 20[redacted] **IONIZED CALCIUM:** 1.06 no units

[redacted] 20[redacted] **LIPASE:** 90 no units

[redacted] 20[redacted] **LYMPH:** 6 no units

[redacted] 20[redacted] **MG:** 2.2 no units

[redacted] 20[redacted] **NEUTROPHIL:** 89 no units

[redacted] 20[redacted] **O2 SATS:** 98 %

[redacted] 20[redacted] **O2 SATS:** 88 %

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

[redacted] 20[redacted] **PLT:** 126 no units

[redacted] 20[redacted] **POTASSIUM:** 4.0 MMOL/L (normal 3.4 to 5.1)

[redacted] 20[redacted] **PRO-BNP:** 1775 No units

[redacted] 20[redacted] **PTT:** 43 no units

[redacted] 20[redacted] **PULSE:** 126 /min

[redacted] 20[redacted] **PULSE:** 133 /min

[redacted] 20[redacted] **RBC:** 4.02 mil/mcl (normal 4.00 to 5.20)

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

[redacted] 20[redacted] **SODIUM:** 141 no units

[redacted] 20[redacted] **SODIUM:** 139 no units

[redacted] 20[redacted] **SYSTOLIC BLOOD PRESSURE:** 80s

[redacted] 20[redacted] **TEMPERATURE:** 97.6 F

[redacted] 20[redacted] **TOTAL BILIRUBIN:** 0.3 no units

[redacted] 20[redacted] **TOTAL PROTEIN:** 7.5 no units

[redacted] 20[redacted] **TROPONIN:** 0.81 NG/ML (normal <0.10)

[redacted] 20[redacted] **TROPONIN I:** 1.10 NG/ML (normal <0.05)

[redacted] 20[redacted] **ULTRASOUND:** Echogenic material within the visualized portion of the left common femoral vein, likely partially occlusive thrombus. Short interval follow-up ultrasound could be considered. No ultrasound evidence of deep vein thrombosis in the right lower extremity. Left popliteal cyst.

[redacted] 20[redacted] **WBC:** 13.6 k/mcl (normal 4.2 to 11.0)

[redacted] 20[redacted] **WBC:** 5.7 k/mcl

[redacted] 20[redacted] **WBC:** 6.6 k/mcl (normal 4.2 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
骨壊死	X			

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

Medical History	Onset Year
OTHER: PANIC DISORDER	19[redacted]
OTHER: SEASONAL ALLERGIES	20
DEPRESSION	20
OTHER: ANXIETY	20
DIABETES MELLITUS	20
OTHER: PLAQUE PSORIASIS	20
OTHER: TACHYCARDIA	20
HYPOTHYROIDISM	20
OTHER: L PROXIMAL HUMERUS FRACTURE	20
OTHER: TROUBLE SLEEPING	20
PSORIATIC ARTHRITIS	20
OTHER: HAIR LOSS	20

Prior Procedures	Procedure Year
SURGERY: PARTIAL HYSTERECTOMY	19[redacted]
SURGERY: SURGICAL REPAIR OF L SHOULDER FRACTURE	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.25 PACK	1	
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] / 169	169

ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / [redacted]20[redacted] / 223 170 392
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
FLUOXETINE	40 mg	QD	Y-M: 20[redacted]
SALBUTAMOL	1 OTHER: PUFF	PRN	Y-M: 20[redacted]
METFORMIN	1000 mg	QD	Y-M: 20[redacted]
METOPROLOL	75 mg	QD	Y-M: 20[redacted]
SERETIDE	1 OTHER: PUFF	PRN	Y-M: 20[redacted]
LEVOTHYROXINE	100 ug	QD	Y-M: 20[redacted]
SITAGLIPTIN	100 mg	QD	Y-M: 20[redacted]
TRAZODONE	50 mg	PRN	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
FOLIC ACID	2 mg	QD	Y-M: 20[redacted] / -259
ALPRAZOLAM	0.25-0.5 mg	PRN	Y-M: 20[redacted] / -247
BUSPIRONE	10 mg	QD	Y-M: 20[redacted] / -247
FOLIC ACID	5 mg	QD	Y-M: 20[redacted] / -222
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -222
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -199

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
FLUOXETINE	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
SALBUTAMOL	1 OTHER: PUFF	PRN	Y-M: 20[redacted]	NOT REPORTED
METFORMIN	1000 mg	QD	Y-M: 20[redacted]	NOT REPORTED
METOPROLOL	75 mg	QD	Y-M: 20[redacted]	NOT REPORTED
SERETIDE	1 OTHER: PUFF	PRN	Y-M: 20[redacted]	NOT REPORTED
LEVOTHYROXINE	100 ug	QD	Y-M: 20[redacted]	NOT REPORTED
SITAGLIPTIN	100 mg	QD	Y-M: 20[redacted]	NOT REPORTED
TRAZODONE	50 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
ALPRAZOLAM	0.25-0.5 mg	PRN	Y-M: 20[redacted] / -247	NOT REPORTED
BUSPIRONE	10 mg	QD	Y-M: 20[redacted] / -247	NOT REPORTED

METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -222	NOT REPORTED
FOLINIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / 31	NOT REPORTED
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / 275	Y-M: 20[redacted] / 298
METHYLPREDNISOLONE	2 mg	QD	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 302
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 310
METHYLPREDNISOLONE	2 mg	QD	Y-M: 20[redacted] / 311	Y-M: 20[redacted] / 368
NITROFURANTOIN	100 mg	BID	Y-M: 20[redacted] / 316	Y-M: 20[redacted] / 321
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 316	Y-M: 20[redacted] / 379
TRAMADOL	50 mg	OTHER: EVERY 6 HRS AS NEEDED	Y-M: 20[redacted] / 369	ONGOING
CEFAZOLIN	UNKNOWN OTHER: UNKNOWN DOSE	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
CHLORHEXIDINE	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
CLONIDINE	25 ug	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
DEXAMETHASONE	8 mg	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
EPHEDRINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
FENTANYL	25 ug	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
FLEBOBAG RING LACT	800 mL	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
GLYCOPYRRONIUM	0.6 mg	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
LIDOCAINE	3 OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
METOPROLOL	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
MIDAZOLAM	1 mg	OTHER: EVERY 5 MIN AS NEEDED	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
NEOSTIGMINE	3 mg	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
PHENYLEPHRINE	3800 ug	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
PROCHLORPERAZINE	5 mg	OTHER: EVERY 30 MIN AS NEEDED	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
PROMETHAZINE	12.5 mg	OTHER: EVERY 30 MIN AS NEEDED	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
PROPOFOL	234.17 mg	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369

PROPOFOL	350 mg	OTHER: ONCE	Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369
ROCURONIUM	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369
ROPIVACAINE	25 mL	OTHER: ONCE	Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369
SODIUM CHLORIDE	112.8 mL	OTHER: ONCE	Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369
TRANEXAMIC ACID	1280 mg	OTHER: ONCE	Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 369
BACITRACIN	50,000 OTHER: UNITS	OTHER: ONCE	Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 370
VANCOMYCIN	1 g	BID	Y-M: 20[redacted] / 369 Y-M: 20[redacted] / 370

Event #1: Serious Adverse Event

Event Description	COLLAPSED AVASCULAR NECROSIS OF THE LEFT HUMERAL HEAD WITHOUT OBVIOUS GLENOID INVOLVEMENT.
Preferred term	骨壊死
AE Onset Date / Rx Day	[redacted]20[redacted] / 313
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 369): Glucose: 6.8 [3.6 - 11] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 369): OTHER JOINT FLUID NPTST092-BODY FLUID CULTURE, AEROBIC AND: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 369): HEMIARTHROPLASTY OF LEFT SHOULDER, REMOVAL OF OLD FIXATION HARDWARE: INTERVAL EXPLANT OF FIXATION HARDWARE AND PLACEMENT OF LEFT SHOULDER RESURFACING ARTHROPLASTY; OXYGEN: USED DURING SURGERY: CONTINUOUS,TITRATE O2 TO KEEP SPO2 GREATER THAN 92%; X-RAY OF LEFT SHOULDER: INTERVAL PLACEMENT OF A RESURFACING LEFT SHOULDER ARTHROPLASTY, NO DISLOCATION, THERE IS NO LOOSENING OR FRACTURE; [redacted]20[redacted] (RX DAY 370): PHYSICAL THERAPY SESSIONS: POST OP PLAN WILL BE THE STANDARD SHOULDER ARTHROPLASTY PHYSICAL THERAPY PROTOCOL BEGINNING ON POST OP DAY 1. PATIENT WILL BEGIN WTIH 30 DEGRESS PASSIVE SUPINE EXTERNAL ROTATION AT THE SIDE AND 130 DEGREES PASSIVE SUPINE FORWARD ELEVATION.

AE Stopped Rx Day	369
Duration of AE	57 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	HEMIARTHROPLASTY OF L SHOULDER
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。本被験者は米国の 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，圧迫による上腕骨頭無腐性壊死（明らかな関節窩への拡がりなし）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，糖尿病，左近位上腕骨骨折，乾癬性関節炎，喫煙者（1 日 0.25 箱を 1 年間）及び元飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は圧迫による上腕骨頭無腐性壊死（明らかな関節窩への拡がりなし）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，圧迫による上腕骨頭無腐性壊死（明らかな関節窩への拡がりなし）は消失した。

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，持続する痛みと左肩関節機能障害に対する半関節形成術のため入院した。被験者は，近位上腕骨骨折に対する観血的整復と内固定を受けた後であった。術後経過は良好で，痛みはコントロールすることができた。術後 1 日目，経口鎮痛薬に切り替えられ，十分な効果が認められた。被験者は運動及びモビライゼーションのために理学療法を開始した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，リドカイン，セファゾリン，アセトアミノフェン，アスピリン 81，ヒドロモルフォン，ポリエチレングリコール，senna docusate，メドロール，バンコマイシン，トラマドール，プロクロルペラジン，プロメタジン，バシトラシン，lactated ringers，クロルヘキシジン，フェンタニル，エフェドリン，塩化ナトリウム，フェニレフリン，トラネキサム酸，glycopyrrolate，ネオスチグミン，デキサメタゾン，ミダゾラム，ロクロニウム，プロポフォール，ロピバカイン，クロニジン，メドロール及びオンダンセトロンであった。

Causality for ABT-494 (Blinded)

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1) Aseptic necrosis of head of humerus (10003464) (Osteonecrosis (10031264)) [v.21.1] [10003464]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of COLLAPSED AVASCULAR NECROSIS OF THE HUMERAL HEAD WITHOUT OBVIOUS GLENOID INVOLVEMENT

- Investigator: Hemiarthroplasty of left shoulder

- AbbVie: Risk factors include pre-existing history of L. proximal humerus fracture and subsequent open reduction internal fixation, and chronic concomitant therapy with methylprednisolone.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY FLUID CULTURE, AEROBIC AND ANAEROBIC:** Negative

[redacted] **20[redacted] GLUCOSE:** 122 mg/dL

[redacted] **20[redacted] X-RAY OF LEFT SHOULDER:** Interval placement of resurfacing left shoulder arthroplasty, no dislocation. There is no loosening or fracture

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
脊柱管狭窄症	X			
腎結石症	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 30 mg QD	7[redacted]	FEMALE	WHITE

Medical History	Onset Year
DEPRESSION	19[redacted]
NEPHROLITHIASIS	19
OTHER: ANXIETY	19
MIGRAINE HEADACHE	19
OTHER: PRE-DIABETES	20
GASTROESOPHAGEAL REFLUX DISEASE: DUE TO HIATAL HERNIA	20
OTHER: HIATAL HERNIA	20
OTHER: PLAQUE PSORIASIS	20
OTHER: LICHEN SCLEROSIS	20
OTHER: INSOMNIA	20
OTHER: SLEEP APNEA	20
OSTEOARTHRITIS	20
OTHER: ELEVATED CK	20
OTHER: REACTIVE AIRWAY	20
OTHER: TRIGGER FINGER RELEASE, BILATERAL 3RD FINGER	20
OTHER: DRY EYES	20
OTHER: CONSTIPATION	20
PSORIATIC ARTHRITIS	20
OTHER: SPINAL STENOSIS	20
HYPERLIPIDEMIA: ELEVATED CHOLESTEROL LEVELS	20
HYPERTENSION	20
OTHER: SEASONAL ALLERGIES	20
OTHER: STRESS INCONTINENCE	20
OTHER: BAKER'S CYST R KNEE	20
OTHER: URINARY TRACT INFECTION	20

Prior Procedures	Procedure Year
SURGERY: L4-L5 FUSION	19[redacted]
SURGERY: BILATERAL CORN AND BUNIONECTOMY	20
SURGERY: R HIP REPLACEMENT	20
SURGERY: BLADDER SLING PLACEMENT	20
SURGERY: L KNEE REPLACEMENT	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	4	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	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] / 386	218
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 387		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ESCITALOPRAM	20 mg	QD	Y-M: 20[redacted]
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MELATONIN	5 mg	QD	Y-M: 20[redacted]
RANITIDINE	150 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 2015-[redacted]
CALCIUM	1 OTHER: PACKET	QD	Y-M: 20[redacted]
LOSARTAN	50 mg	QD	Y-M: 20[redacted]
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]
PRAVASTATIN	10 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 2016-[redacted]
BUPROPION	300 mg	QD	Y-M: 2016-[redacted]
AMOXICILLIN	2000 mg	PRN	Y-M: 20[redacted]
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]
FLUTICASONE	1 OTHER: SPRAY	PRN	Y-M: 20[redacted]
GABAPENTIN	600 mg	QD	Y-M: 20[redacted]
IPRATROPIUM	0.03 %	PRN	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -45

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
ESCITALOPRAM	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED

MELATONIN	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
RANITIDINE	150 mg	QD	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 253
LOSARTAN	50 mg	QD	Y-M: 20[redacted]	NOT REPORTED
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PRAVASTATIN	10 mg	QD	Y-M: 20[redacted]	NOT REPORTED
CALCIUM	1 OTHER: PACKET	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 444
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 169
BUPROPION	300 mg	QD	Y-M: 20[redacted]	NOT REPORTED
AMOXICILLIN	2000 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
FLUTICASONE	1 OTHER: SPRAY	PRN	Y-M: 20[redacted]	NOT REPORTED
GABAPENTIN	600 mg	QD	Y-M: 20[redacted]	NOT REPORTED
IPRATROPIUM	0.03 %	PRN	Y-M: 20[redacted]	NOT REPORTED
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -45	NOT REPORTED
VACCINIUM MACROCARPON	500 mg	QD	Y-M: 20[redacted] / 16	NOT REPORTED
ESTRADIOL	2 g	OTHER: TWICE PER WEEK	Y-M: 20[redacted] / 22	NOT REPORTED
PROPRANOLOL	10 mg	PRN	Y-M: 20[redacted] / 44	NOT REPORTED
DIPHENHYDRAMINE	50 mg	PRN	Y-M: 20[redacted] / 58	NOT REPORTED
CHLORHEXIDINE	15 mL	BID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 87
HYDROCORTISONE	1 OTHER: LIGHT APPLICATION	BID	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 129
LIDOCAINE	5 %	QD	Y-M: 20[redacted] / 155	Y-M: 20[redacted] / 185
LOTRISONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 169	Y-M: 20[redacted] / 235
OXYCODONE	5 mg	BID	Y-M: 20[redacted] / 187	Y-M: 20[redacted] / 208
PARACETAMOL	500-1000 mg	OTHER: EVERY 4-6 HRS PRN	Y-M: 20[redacted] / 187	Y-M: 20[redacted] / 208
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / 199	Y-M: 20[redacted] / 305

PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 209	NOT REPORTED
FOLIC ACID	3 mg	QD	Y-M: 20[redacted] / 254	NOT REPORTED
IBUPROFEN	600 mg	TID	Y-M: 20[redacted] / 254	NOT REPORTED
LEVOFLOXACIN	250 mg	QD	Y-M: 20[redacted] / 284	Y-M: 20[redacted] / 294
METHENAMINE	1000 mg	QID	Y-M: 20[redacted] / 302	ONGOING
METRONIDAZOLE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 309	NOT REPORTED
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / 312	NOT REPORTED
KETOROLAC	10 mg	QID	Y-M: 20[redacted] / 320	Y-M: 20[redacted] / 320
KETOROLAC	30 mg	OTHER: ONCE	Y-M: 20[redacted] / 320	Y-M: 20[redacted] / 320
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 320	Y-M: 20[redacted] / 320
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 320	Y-M: 20[redacted] / 320
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / 320	Y-M: 20[redacted] / 327
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 320	Y-M: 20[redacted] / 332
VICODIN	5/325 mg	PRN	Y-M: 20[redacted] / 320	Y-M: 20[redacted] / 333
ATROPINE	0.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 322
CEFTRIAXONE	1 g	OTHER: ONCE	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 322
FLEBOBAG RING LACT	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 322
HYDROCORTISONE	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 322
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 322
ONDANSETRON	8 mg	OTHER: ONCE	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 322
AMOXICILLIN	500 mg	TID	Y-M: 20[redacted] / 325	Y-M: 20[redacted] / 327

Event #1: Serious Adverse Event

Event Description	WORSENING OF PRE-EXISTING SPINAL STENOSIS
Preferred term	脊柱管狭窄症
AE Onset Date / Rx Day	[redacted]20[redacted] / 107
Age at AE Onset	7[redacted]

Laboratory Testing
NOT REPORTED
Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 114): MRI OF LUMBAR SPINE: NO ACUTE FRACTURE OR SUBLUXATION. THAT IS POST LUMBAR FUSION FROM L4 THROUGH S1 WITH LAMINECTOMY CHANGES AT L4 AND L5. WHEN COMPARED TO THE PREVIOUS EXAMINATION, DISC DISEASE FROM L1-L2 THROUGH L5-S1REMAIN STABLE. THERE IS A SLIGHT PROGRESSION OF DISC DISEASE AT T9-T10, T10-T11 AND T11-T12. CENTRAL STENOSIS AT L3-L4 BEING STABLE. FORAMINAL ENCROACHMENT WITH IMPINGEMENT OF THE EXITING RIGHT L3 TO AND L3 NERVE ROOTS REMAIN UNCHANGED.; [redacted]20[redacted] (RX DAY 187): LAMINECTOMY: STABLE STATUS POST LUMBAR LAMINECTOMY L1-L4 WITH EXCISION SYNOVIAL CYST AT L3-4.; XR OF LUMBAR SPINE: INTRAOPERATIVE VIEW DEMONSTRATING REMOTE POSTERIOR FUSION FROM L3 THROUGH S1. SURGICAL RETRACTOR IS IN PLACE POSTERIORLY. THERE ARE 2 METALLIC SURGICAL PROBES. THE MOST INFERIORLY DIRECTED PROBE TIPPROJECTS POSTERIOR TO THE L3 VERTEBRAL BODY NEAR THE INFERIOR ENDPLATE. SUPERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L1 VERTEBRAL BODY NEAR ITS INFERIOR ENDPLATE.; XR OF LUMBAR SPINE: AS BEFORE THERE IS A REMOTE POSTERIOR FUSION FROM L4 THROUGH S1. POSTERIOR SURGICAL RETRACTOR AND SURGICAL DEFECTS. THE SUPERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L1 VERTEBRAL BODY NEAR THE SUPERIOR ENDPLATE. THE MORE INFERIORLY DIRECTED PROBE TIP NOW PROJECTS POSTERIOR TO THE L4 VERTEBRAL BODY NEAR ITS SUPERIOR ENDPLATE.

AE Stopped Rx Day	187
Duration of AE	81 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	MEDICAL HISTORY OF SPINAL STENOSIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	KIDNEY STONE
Preferred term	腎結石症
AE Onset Date / Rx Day	[redacted]20[redacted] / 320
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 320): Alanine Aminotransferase: 25 [7 - 52] U/L; Albumin: 39 [35 - 50] G/L; Alkaline Phosphatase: 85 [34 - 104] U/L; Aspartate Aminotransferase: 28 [13 - 39] U/L; Basophils: 0.1 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.4 [0.25 - 1] %; Bilirubin: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Bilirubin: 7 [5 - 17] UMOL/L; Blood: 3+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood Urea Nitrogen: 7.1 [2.5 - 8.9] MMOL/L; Calcium: 2.17 [2.15 - 2.57] MMOL/L; Chloride: 107 [98 - 107] MMOL/L; Creatinine: 98 [53 - 106] UMOL/L; Eosinophils: 0.1 [0 - 0.8] 10^9/L; Eosinophils/Leukocytes: 1.3 [0.9 - 2.9] %; Erythrocytes: 10-25 [0 - 2] /HPF; Erythrocytes: 3.8 [4.2 - 5.4] 10^12/L; Glucose: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: 5.6 [4.1 - 6.1] MMOL/L; Hematocrit: 0.36 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 116 [125 - 160] G/L; Ketones: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 0-5 [0 - 5] /HPF; Leukocytes: 8.2 [3.6 - 10.6] 10^9/L; Lymphocytes: 1.4 [1.5 - 3.5] 10^9/L; Lymphocytes/Leukocytes: 16.5 [24 - 44] %; Monocytes: 0.8 [0.1 - 1] 10^9/L; Monocytes/Leukocytes: 9.3 [2.5 - 9] %; NPTST035-ANON GAP: 11 [8 - 17] MEQ/L; NPTST050-APPEARANCE: CLEAR [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST065-BACTERIA: PRESENT [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST131-CO2: 26 [21 - 31] MMOL/L; NPTST135-COLOR: YELLOW [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST150-CREATININE CLEARANCE: 61.77 [NOT REPORTED - NOT REPORTED] ML/MIN; NPTST184-EGFR NON -AA: 48 [60.1 - 100] ML/MIN/1.73M2; NPTST223-GFR AA: 58 [59 - 100] ML/MIN/1.73M2; NPTST272-IG#: 0.06 [0 - 0.1] 10^3/UL; NPTST273-IG%: 0.7 [0 - 3] %; NPTST316-MCH: 30.3 [27 - 32] PG; NPTST317-MCHC: 32.1 [32 - 36] G/DL; NPTST318-MCV: 94.3 [78 - 100] FL; NPTST333-MPV: 8.5 [6 - 11] FL; NPTST345-NRBC %: 0.1 [0 - 0] %; NPTST346-NRBC#: 0.1 [0.03 - 0.12] 10^3/UL; NPTST414-RDW: 16.6 [11.5 - 14] %; NPTST444-SQUAMOUS EPI: 2-5 [0 - 2] /HPF; NPTST502-VOLUME: >7 [NOT REPORTED - NOT REPORTED] ML; Neutrophils: 5.9 [1.3 - 6] 10^9/L; Neutrophils/Leukocytes: 71.8 [36 - 66] %; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT

REPORTED; Platelets: 361 [150 - 450] 10^9/L; Potassium: 3.7 [3.4 - 5.1] MMOL/L; Protein: TRACE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 60 [60 - 83] G/L; Sodium: 140 [136 - 145] MMOL/L; Specific Gravity: 1.020 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Urobilinogen: 0.2 [0.2 - 0.2] UNIT NOT REPORTED; pH: 7.5 [7 - 7] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 321): Basophils: 0.03 [NOT REPORTED - 0.08] 10^3/uL; Basophils/Leukocytes: 0.3 [0 - 2] %; Bilirubin: NEGATIVE [NOT REPORTED - NOT REPORTED] NONE PROVIDED; Creatinine: 162 [45 - 84] UMOL/L; Eosinophils: 0.12 [0.04 - 0.36] 10^9/L; Eosinophils/Leukocytes: 1.3 [1 - 4] %; Erythrocytes: 4.3 [3.9 - 5.2] 10^12/L; Glucose: 50 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hematocrit: 0.41 [0.34 - 0.45] FRACTION OF 1; Hemoglobin: 129 [112 - 157] G/L; Ketones: 5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 9.1 [4 - 10] 10^9/L; Lymphocytes: 1.86 [1.18 - 3.74] 10^9/L; Lymphocytes/Leukocytes: 20.6 [20 - 44] %; Monocytes: 0.63 [0.2 - 0.76] 10^9/L; Monocytes/Leukocytes: 7 [2 - 9] %; NPTST009-ABSOLUTE IMMATURE GRANULOCYTE C: 0.05 [NOT REPORTED - 0.05] X10^3/MCL; NPTST010-ABSOLUTE NRBCS: 0.00 [NOT REPORTED - 0.01] X10^3/MCL; NPTST127-CLARITY: SLIGHTLY CLOUDY [NOT REPORTED - NOT REPORTED] NONE PROVIDED; NPTST135-COLOR: YELLOW [NOT REPORTED - NOT REPORTED] NONE PROVIDED; NPTST182-EGFR: 33 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST185-EGFR NON AFRICAN AMERICAN: 27 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST271-IG AUTO: 0.6 [NOT REPORTED - NOT REPORTED] %; NPTST304-LEUKOCYTS ESTERASE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST316-MCH: 30.4 [25.6 - 32.2] PG; NPTST317-MCHC: 31.5 [31 - 34.6] G/DL; NPTST318-MCV: 96.5 [82 - 100.8] FL; NPTST333-MPV: 8.2 [8.97 - 11.96] FL; NPTST344-NRBC: 0 [0 - 0] /100 WBC; NPTST353-OCCULT BLOOD: SMALL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST414-RDW: 16.7 [11.7 - 14.4] %; Neutrophils: 6.36 [1.56 - 6.13] 10^9/L; Neutrophils/Leukocytes: 70.2 [50 - 70] %; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 391 [139 - 379] 10^9/L; Protein: 100 [NOT REPORTED - NOT REPORTED] mg/dL; Specific Gravity: 1.024 [1.003 - 1.035] UNIT NOT REPORTED; Urobilinogen: <2.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; pH: 5 [5 - 9] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 322): Basophils: <0.03 [NOT REPORTED - 0.08] X10^3/MCL; Basophils/Leukocytes: 0.1 [0 - 2] %; Blood Urea Nitrogen: 6.1 [2.5 - 7.9] MMOL/L; Calcium: 2.1 [2.12 - 2.52] MMOL/L; Chloride: 111 [98 - 107] MMOL/L; Creatinine: 96 [45 - 84] UMOL/L; Eosinophils: 0.03 [0.04 - 0.36] 10^9/L; Eosinophils/Leukocytes: 0 [1 - 4] %; Erythrocytes: 3.7 [3.9 - 5.2] 10^12/L; Glucose: 7.4 [3.9 - 5.5] MMOL/L; Hematocrit: 0.36 [0.34 - 0.45] FRACTION OF 1; Hemoglobin: 114 [112 - 157] G/L; Leukocytes: 7.8 [4 - 10] 10^9/L; Lymphocytes: 0.61 [1.18 - 3.74] 10^9/L; Lymphocytes/Leukocytes: 7.8 [20 - 44] %; Monocytes: 0.26 [0.2 - 0.76] 10^9/L; Monocytes/Leukocytes: 3.3 [2 - 9] %; NPTST009-ABSOLUTE IMMATURE GRANULOCYTE C: <0.03 [NOT REPORTED - 0.05] X10^3/MCL; NPTST010-ABSOLUTE NRBCS: 0.00 [NOT REPORTED - 0.01] X10^3/MCL; NPTST034-ANION GAP: 6.0 [4 - 12] UNIT NOT REPORTED; NPTST096-BUN/CR RATIO: 15.6 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST131-CO2: 24 [21 - 32] MMOL/L; NPTST183-EGFR AFRICAN AMERICAN: 59 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST185-EGFR NON AFRICAN AMERICAN: 49 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST271-IG AUTO: 0.3 [NOT REPORTED - NOT REPORTED] %; NPTST316-MCH: 30.5 [25.6 - 32.2] PG; NPTST317-MCHC: 31.8 [31 - 34.6] G/DL; NPTST318-MCV: 95.7 [NOT REPORTED - 100.8] fL; NPTST333-MPV: 8.6 [8.97 - 11.96] FL; NPTST347-NRBCS: 0.0 [NOT REPORTED - NOT REPORTED] /100 (WBCS); NPTST414-RDW: 16.7 [11.7 - 14.4] %; Neutrophils: 6.93 [1.56 - 6.13] 10^9/L; Neutrophils/Leukocytes: 88.5 [50 - 70] %; Platelets: 350 [139 - 379] 10^9/L; Potassium: 4.5 [3.5 - 5.1] MMOL/L; Sodium: 141 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 337): Bilirubin: SMALL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood: LARGE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Ketones: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: SMALL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST050-APPEARANCE: CLOUDY [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST135-COLOR: RED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 300 OR GREATER [NOT REPORTED - NOT REPORTED] mg/dL; Specific Gravity: 1.020 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Urobilinogen: 1.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; pH: 7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 320): URINE NPTST156-CULTURE: Negative-25,000 COL/ML3 OR MORE COLONY TYPES, NONE IN PREDOMINANCE, SUSPECTED CONTAMINATION, SUGGEST REPEAT SPECIMEN.; [redacted]20[redacted] (RX DAY 321): URINE NPTST156-CULTURE: Negative; [redacted]20[redacted] (RX DAY 325): URINE NPTST156-CULTURE: Negative; [redacted]20[redacted] (RX DAY 345): URINE NPTST156-CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 320): CT SCAN: CT SCAN WITHOUT CONTRAST SHOWS MILD TO MODERATE LEFT HYDRONEPHROSIS WITH OBSTRUCTING 5MM STONE IN THE DISTAL URETER.THERE ARE PUNCTATE 1-2MM NONOBSTRUCTING STONES AT THE UPPER AND LOWER POLE OF THE LEFT KIDNEY; [redacted]20[redacted] (RX

DAY 321): CT SCAN: THERE IS A 3 TO 4MM OBSTRUCTING KIDNEY STONE IDENTIFIED IN THE LEFT URETHRA WITH MODERATE UPSTREAM HYROURETERNEPHROSIS.; CTSCAN: THERE IS A LEFT SIDED DOUBLE J URETERAL STENT IN PLACE. NO LEFT HYDRONEPHROSIS.; LEFT URETHRAL STENT PLACEMENT: STENT PLACED; [redacted] (RX DAY 337): CYSTOSCOPY WITH STENT REMOVAL: SUCCESSFUL URETERAL STENT REMOVAL AFTER SPONTANEOUS PASSAGE OF STONE.; [redacted] (RX DAY 344): RENAL AND BLADDER ULTRASOUND: TRANSCUTANEOUS IMAGINE WAS PERFORMED OF KIDNEYS AND BLADDER AND NO SIGNIFICANT ABNORMALITY WAS FOUND; [redacted] (RX DAY 359): CYSTOSCOPY WITH BILATERAL RETROGRADE PYELOGRAMS: THE URETHRA WAS WITHOUT LESION OR STRICTURES. THE BLADDER WAS WITHOUT ANY EVIDENCE OF TUMORS. THERE ARE NO CALCULI. THERE WAS A STAGE II CYSTOCELE. THE PREVIOUSLY IDENTIFIED ULCERATED OR ERYTHEMA THISLESION WERE NO LONGER IDENTIFIED. THE BLADDER WALL WAS NORMAL. THE TRIGONE WAS NORMAL AND THE URETERAL ORIFICES WERE ORTHOTOPIC. THEY APPEARED NORMAL. CLEAR EFFLUX WAS NOTED BILATERALLY. NO DISTINCTLESIONS WERE IDENTIFIABLE AND THERE WAS NOTHING THAT WARRANTED A BIOPSY ON THIS EXAM.

AE Stopped Rx Day	327
Duration of AE	8 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	NATURALLY PREDISPOSED TO KIDNEY STONE DEVELOPMENT
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。本被験者は米国の 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，既存の脊柱管狭窄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，元喫煙者（1 日 2 箱を 4 年間），L4 及び L5 の融合，変形性関節症，右人工股関節置換，乾癬性関節炎，脊柱管狭窄症，高血圧，膀胱スリング，左膝関節置換及び元飲酒者（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，被験者は既存の脊柱管狭窄症の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，既存の脊柱管狭窄症の悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は椎弓切除術のため入院した。病歴及び身体的診察の結果，重度の L2 と L3 の狭窄で，L3 と L4 の椎間肥大及び滑液嚢腫を伴っていた。被験者は背部痛を伴う神経性跛行症状を呈していた。また，L4 の椎弓根に近い L3 と L4 の間の椎間板腔が狭くなっていた。同日，L1～L4 の開放両側椎弓切除術と，L3 及び L4 の滑液嚢腫切除が行われた。L1～L4 の開放両側椎弓切除術及び L3～L4 の滑液嚢腫切除が終了した。被験者の経過は非常に良好で神経根症状はなく，本人もとても良くなったと述べた。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貼付剤であった。

Causality for ABT-494 (Blinded)

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1) Spinal column stenosis (10041540) (Spinal column stenosis (10041540)) [v.21.1] [10041540]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of WORSENING OF PRE-EXISTING SPINAL STENOSIS

- Investigator: MEDICAL HISTORY OF SPINAL STENOSIS

- AbbVie: EVENT MORE LIKELY RELATED TO PRE-EXISTING SPINAL STENOSIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] MRI OF LUMBAR SPINE:** NO ACUTE FRACTURE OR SUBLUXATION. THAT IS POST LUMBAR FUSION FROM L4 THROUGH S1 WITH LAMINECTOMY CHANGES AT L4 AND L5. WHEN COMPARED TO THE PREVIOUS EXAMINATION, DISC DISEASE FROM L1-L2 THROUGH L5-S1

REMAIN STABLE. THERE IS A SLIGHT PROGRESSION OF DISC DISEASE AT T9-T10, T10-T11 AND T11-T12. CENTRAL STENOSIS AT L3-L4 BEING STABLE. FORAMINAL ENCROACHMENT WITH IMPINGEMENT OF THE EXITING RIGHT L3 TO AND L3 NERVE ROOTS REMAIN UNCHANGED.

[redacted] **20[redacted] XR OF LUMBAR SPINE:** AS BEFORE THERE IS A REMOTE POSTERIOR FUSION FROM L4 THROUGH S1. POSTERIOR SURGICAL RETRACTOR AND SURGICAL DEFECTS. THE SUPERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L1 VERTEBRAL BODY NEAR THE SUPERIOR ENDPLATE. THE MORE INFERIORLY DIRECTED PROBE TIP NOW PROJECTS POSTERIOR TO THE L4 VERTEBRAL BODY NEAR ITS SUPERIOR ENDPLATE.

[redacted] **20[redacted] XR OF LUMBAR SPINE:** INTRAOPERATIVE VIEW DEMONSTRATING REMOTE POSTERIOR FUSION FROM L3 THROUGH S1. SURGICAL RETRACTOR IS IN PLACE POSTERIORLY. THERE ARE 2 METALLIC SURGICAL PROBES. THE MOST INFERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L3 VERTEBRAL BODY NEAR THE INFERIOR ENDPLATE. SUPERIORLY DIRECTED PROBE TIP PROJECTS POSTERIOR TO THE L1 VERTEBRAL BODY NEAR ITS INFERIOR ENDPLATE.
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-572

治験責任医師からの報告。本被験者は米国の 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，腎結石の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，腎結石症，元喫煙者（1 日 2 箱を 4 年間），糖尿病前症，胃食道逆流性疾患，CK 上昇，変形性関節症，便秘，乾癬性関節炎，コレステロール値上昇，高血圧，膀胱スリング設置，腹圧性尿失禁，尿路感染及び元飲酒者（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，被験者は腎結石を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，腎結石は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は病院を受診し，背部痛及び悪心を訴えた。CT スキャン検査で腎結石が見つかった。被験者は麻薬性鎮痛薬を投与されて帰宅した。翌日，被験者は背部痛が悪化したため ED を再受診した。入院となり，CT スキャンの再検査が行われ，鎮痛薬が投与された。腎結石は大きすぎて通過困難と報告された。20[redacted] 年 [redacted] 月 [redacted] 日，左尿道ステントが留置された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，腎結石が自然に通過したため，膀胱鏡下で尿道ステント抜去が行われた。

投与された薬剤は，toradal，zofran，ヒドロコドン・アセトアミノフェン合剤，ketorolac，オンダンセトロン，タムスロシン，生理食塩液，オンダンセトロン，ミダゾラム，セフトリアキソン，アトロピン，シプロフロキサシン及びヒドロコルチゾンであった。

Causality for ABT-494 (Blinded)

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1) Kidney stone (10023436) (Nephrolithiasis (10029148)) [v.22.0] [10023436]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of KIDNEY STONE

- Investigator: Naturally predisposed to kidney stone development.

- AbbVie: Event is more likely related to pre-existing history of nephrolithiasis. Obesity is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 25 U/L (normal 7 to 52)

[redacted] **20[redacted] ALBUMIN:** 3.9 G/DL (normal 3.5 to 5.0)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 85 U/L (normal 34 to 104)

[redacted] **20[redacted] ANION GAP:** 11 MEQ/L (normal 8 to 17)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 28 U/ML (normal 13 to 39)

[redacted] **20[redacted] BASOPHILS:** 0.40 % (normal 0.25 to 1.00)

[redacted] **20[redacted] BASOPHILS %:** 0.3 %

[redacted] **20[redacted] BASOPHILS ABS:** 0.03 X10**3/MCL (normal <0.08)

[redacted] **20[redacted] BILIRUBIN:** 0.4 mg/dL (normal 0.3 to 1.0)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 20 mg/dL (normal 7 to 25)

Unknown date BMI: 32.88646 mg/m2

[redacted] **20[redacted] BUN:** 17 mg/dL (normal >22)

[redacted] **20[redacted] BUN/CREATININE RATIO:** 15.6 mL/min/1.73m2 (Norml >=60)

[redacted] **20[redacted] CALCIUM:** 8.4 mg/dL (normal 8.5 to 10.1)

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

[redacted] **20[redacted] CHLORIDE:** 111 MMOL/L (normal 98 to 107)

[redacted] **20[redacted] CO2:** 26 MMOL/L (normal 21 to 31)

[redacted] **20[redacted] CREATININE:** 1.11 mg/dL (normal 0.60 to 1.20)

[redacted] **20[redacted] CREATININE:** 1.83 mg/dL (normal 0.51 to 0.95)

[redacted] **20[redacted] CREATININE:** 1.09 mg/dL (normal 0.51 to 0.95)

[redacted] **20[redacted] CREATININE CLEARANCE:** 61.77 ML/Min

[redacted] **20[redacted] CTSCAN:** CT SCAN WITHOUT CONTRAST SHOWS MILD TO MODERATE LEFT HYDRONEPHROSIS WITH OBSTRUCTING 5MM STONE IN THE DISTAL URETER.THERE ARE PUNCTATE 1-2MM NONOBSTRUCTING STONES AT THE UPPER AND LOWER POLE OF THE LEFT KIDNEY

[redacted] **20[redacted] CT SCAN:** THERE IS A 3 TO 4MM OBSTRUCTING KIDNEY STONE IDENTIFIED IN THE LEFT URETER WITH MODERATE UPSTREAM HYROURETERNEPHROSIS.

[redacted] **20[redacted] CT SCAN:** THERE IS A LEFT SIDED DOUBLE J URETERAL STENT IN PLACE. NO LEFT HYDRONEPHROSIS.

[redacted] **20[redacted] CYSTOSCOPY:** SUCCESSFUL URETERAL STENT REMOVAL AFTER SPONTANEOUS PASSAGE OF STONE.

[redacted] **20[redacted] EGFR:** 33 mL/min/1.73m2 (Normal >= 60)

[redacted] **20[redacted] EGFR (NON AFRICAN AMERICAN):** 27 mL/min/1.73m2 (Normal >= 60)

[redacted] **20[redacted] EGFR AFRICAN AMERICAN:** 59 ¥mL/min/1.73m2 (Normal >= 60)

[redacted] **20[redacted] EGFR NON AFRICAN AMERICAN:** 49 mL/min/1.73m2 *Normal >= 60)

[redacted] **20**[redacted] **EOSINOPHILS:** 1.3 % (normal 0.9 to 2.9)

[redacted] **20**[redacted] **EOSINOPHILS %:** 0.0 %

[redacted] **20**[redacted] **GFR AA:** 58 mL/min/1.73m2 (Normal 59 to 100)

[redacted] **20**[redacted] **GLUCOSE:** 101mg/dL (normal 74 to 109)

[redacted] **20**[redacted] **GLUCOSE:** 134 mg/dL (normal 70 to 99)

[redacted] **20**[redacted] **HEMATOCRIT:** 36.1 % (normal 37.0 to 47.0)

[redacted] **20**[redacted] **HEMATOCRIT:** 41.0 % (normal 34.1 to 44.9)

[redacted] **20**[redacted] **HEMOGLOBIN:** 11.6 G/DL (normal 12.5 to 16.0)

[redacted] **20**[redacted] **HEMOGLOBIN:** 12.9 G/DL (normal 11.2 to 15.7)

[redacted] **20**[redacted] **HEMOGLOBIN:** 11.4 G/DL (normal 11.2 to 15.7)

[redacted] **20**[redacted] **LYMPHOCYTES:** 16.5 % (normal 24.0 to 44.0)

[redacted] **20**[redacted] **LYMPHOCYTES ABS:** 1.4 X10**3/MCL (normal 1.5 to 3.5)

[redacted] **20**[redacted] **LYMPHOCYTES ABS:** 186 10^3/uL (normal 1.18 to 3.74)

[redacted] **20**[redacted] **LYMPHOCYTES ABS:** 0.61 X10**3/MCL (normal 1.18 to 3.74)

[redacted] **20**[redacted] **MONOCYTE ABS:** 0.26 X10**3/MCL (normal 0.20 to 0.76)

[redacted] **20**[redacted] **MONOCYTES:** 9.3 % (normal 2.5 to 9.0)

[redacted] **20**[redacted] **NEUTROPHILS:** 71.8 % (normal 36.0 to 66.0)

[redacted] **20**[redacted] **NEUTROPHILS:** 70.2 % (normal 36.0 to 66.0)

[redacted] **20**[redacted] **NEUTROPHILS %:** 88.5 %

[redacted] **20**[redacted] **NEUTROPHILS ABS:** 6.36 X10**3/MCL (normal 1.56 to 6.13)

[redacted] **20**[redacted] **NEUTROPHILS ABS:** 6.93 X10**3/MCL (normal 1.56 to 6.13)

[redacted] **20**[redacted] **PLATELET COUNT:** 361 X10**3/MCL (normal 150 to 450)

[redacted] **20**[redacted] **PLATELET COUNT:** 391 X10**3/MCL (normal 139 to 379)

[redacted] **20**[redacted] **PLATELET COUNT:** 350 X10**3/MM**3 (normal 139 to 379)

[redacted] **20**[redacted] **POTASSIUM:** 3.7 MMOL/L (normal 3.4 to 5.1)

[redacted] **20**[redacted] **POTASSIUM:** 4.5 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] PROTEIN:** 6.0 G/DL (normal 6.0 to 8.3)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.83 X10**6/MCL (normal 4.2 to 5.40)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.25 X10**6/MCL (normal 3.93 to 5.22)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.74 X10**6/MCL (normal 3.93 to 5.22)

[redacted] **20[redacted] RENAL AND BLADDER ULTRASOUND:** TRANSCUTANEOUS IMAGINE WAS PERFORMED OF KIDNEYS AND BLADDER AND NO SIGNIFICANT ABNORMALITY WAS FOUND

[redacted] **20[redacted] SODIUM:** 140 MMOL/L (normal 136 to 145)

[redacted] **20[redacted] SQUAMOUS EPI (URINE):** 2-5 HPF (normal 0-2 /HPF)

[redacted] **20[redacted] URINE APPEARANCE:** Clear

[redacted] **20[redacted] URINE APPEARANCE:** CLOUDY/RED

[redacted] **20[redacted] URINE BACTERIA:** Present

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

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

[redacted] **20[redacted] URINE BILIRUBIN:** SMALL

[redacted] **20[redacted] URINE BLOOD:** 3+ (normal = negative)

[redacted] **20[redacted] URINE BLOOD:** LARGE

[redacted] **20[redacted] URINE CLARITY:** slightly cloudy

[redacted] **20[redacted] URINE COLOR:** Yellow

[redacted] **20[redacted] URINE COLOR:** Yellow

[redacted] **20[redacted] URINE CULTURE:** 25,000 COL/ML3 OR MORE COLONY TYPES, NONE IN PREDOMINANCE, SUSPECTED CONTAMINATION, SUGGEST REPEAT SPECIMEN

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

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

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

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

[redacted] **20[redacted] URINE GLUCOSE:** 50 no unit

[redacted] **20[redacted] URINE GLUCOSE:** NEGATIVE

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

[redacted] **20[redacted] URINE KETONES:** 5 no unit

[redacted] **20[redacted] URINE KETONES:** NEGATIVE

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

[redacted] **20[redacted] URINE LEUKOCYTES ESTERASE:** Negative

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

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

[redacted] **20[redacted] URINE NITRITE:** NEGATIVE

[redacted] **20[redacted] URINE OCCULT BLOOD:** Small (normal = negative)

[redacted] **20[redacted] URINE PH:** 7.5 no units (normal 7.0 to 7.0)

[redacted] **20[redacted] URINE PH:** 5 no units (normal 5 to 9)

[redacted] **20[redacted] URINE PH:** 7 NO UNITS

[redacted] **20[redacted] URINE PROTEIN:** Trace (normal = negative)

[redacted] **20[redacted] URINE PROTEIN:** 100 mg/dL

[redacted] **20[redacted] URINE PROTEIN:** 300MG/DL OR GREATER

[redacted] **20[redacted] URINE RBC:** 10-25 /HPF (normal >=0 to <=2)

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.020 no units (normal 1.003 to 1.035)

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.024 no units (normal 1.003 to 1.035)

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.020 NO UNIT

[redacted] **20[redacted] URINE UROBILINOGRN:** 1.0 NO UNITS

[redacted] **20[redacted] URINE UROBILIRUBIN:** 0.2 no units (normal 0.2 to 0.2)

[redacted] **20[redacted] URINE UROBILIRUBIN:** <2.0 (Normal <= 2.0

[redacted] **20[redacted] URINE VOLUME:** >7 mL

[redacted] **20[redacted] URINE WBC:** 0-5 /HPF (Normal >= 0 to <= 5)

[redacted] **20[redacted] URINE WHITE BLOOD CELLS:** SMALL

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.2 X10**3/MCL (normal 3.6 to 10.6)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.05 X10**3/MCL (normal 3.98 to 10.04)

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
胃腸炎	X			X

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

Medical History	Onset Year
OTHER: PERIODICALLY EXPERIENCES SYMPTOMS OF SCIATICA	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: REACTIVE AIRWAY DISEASE	20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
OTHER: PLANTAR FASCIAL FIBROMATOSIS	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
HYPERTENSION: DIAGNOSIS PRIOR TO 1ST DOSE OF I.P. ICF SIGNED 07SEP2017	20[redacted]
ANGINA: PRINZMETAL'S ANGINA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: NASAL SURGERY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	FORMER			
CIGARETTES	FORMER	0.5 PACK	5	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] / 394	226
ABT-494	30 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
MONTELUKAST	10.00 mg	QD	Y-M: 20[redacted]
PROCATEROL	90 OTHER: MCG	PRN	Y-M: 20[redacted]
SERETIDE	250.0 OTHER: MCG	PRN	Y-M: 20[redacted]
FOLIC ACID	1.00 mg	QD	Y-M: 20[redacted]
METHOTREXATE	25.00 mg	EVERY WEEK	Y-M: 20[redacted] / -116
ACETYLSALICYLIC ACID	81.00 mg	QD	Y-M: 20[redacted] / -11
AMLODIPINE	5.00 mg	QD	Y-M: 20[redacted] / -11
ATORVASTATIN	40.00 mg	QD	Y-M: 20[redacted] / -11
CLOPIDOGREL	75.00 mg	QD	Y-M: 20[redacted] / -11
GLYCERYL TRINITRATE	0.40 mg	QD	Y-M: 20[redacted] / -11

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
MONTELUKAST	10.00 mg	QD	Y-M: 20[redacted]	NOT REPORTED
SERETIDE	250.0 OTHER: MCG	PRN	Y-M: 20[redacted]	NOT REPORTED
FOLIC ACID	1.00 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 606
METHOTREXATE	25.00 mg	EVERY WEEK	Y-M: 20[redacted] / -116	Y-M: 20[redacted] / 606
ACETYLSALICYLIC ACID	81.00 mg	QD	Y-M: 20[redacted] / -11	NOT REPORTED
VERAPAMIL	240.00 mg	QD	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 606
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / 58	NOT REPORTED
ROSUVASTATIN	5.00 mg	OTHER: QOD	Y-M: 20[redacted] / 58	NOT REPORTED
HYDROCHLOROTHIAZIDE	25 mg/m2	QD	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 604
POTASSIUM	20 mg	QD	Y-M: 20[redacted] / 606	Y-M: 20[redacted] / 607
LEVOFLOXACIN	750 mg	QD	Y-M: 20[redacted] / 607	Y-M: 20[redacted] / 612
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 607	Y-M: 20[redacted] / 612

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

Event Description	GASTROENTERITIS
Preferred term	胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 602
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	608
Duration of AE	7 DAYS
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the	NO

Event
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。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，胃腸炎の事象を発現した。

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 0.5 箱を 5 年間），乾癬性関節炎，高血圧，元噛みタバコ使用者及び現飲酒者（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，被験者は胃腸炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，胃腸炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，嘔吐，発熱，難治性下痢及び脱水で来院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，塩化カリウム，メトロニダゾール及びレボフロキサシンであった。

Causality for UPADACITINIB (Blinded)

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1) Gastroenteritis (10017888) (Gastroenteritis (10017888)) [v.22.1] [10017888]

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 GASTROENTERITIS

- Investigator: Not applicable

- AbbVie: Event is common in the general population.

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
椎間板変性症	X			
脊椎後方すべり症	X			

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

Medical History	Onset Year
DEGENERATIVE DISC DISEASE	19[redacted]
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: ANXIETY	20[redacted]
HYPERLIPIDEMIA	20[redacted]
OTHER: HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
OTHER: SLEEP APNEA	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: GASTROESOPHAGEAL REFLUX DISORDER	20[redacted]

Prior Procedures		Procedure Year
SURGERY: LUMBAR SPINE DISCECTOMY	DEGENERATIVE DISC DISEASE	19[redacted]
SURGERY: LEFT ROTATOR CUFF REPAIR		19[redacted]
SURGERY: CERVICAL SPINE FUSION	DEGENERATIVE DISC DISEASE	20[redacted]
SURGERY: INGUINAL HERNIA		20[redacted]
SURGERY: LEFT ROTATOR CUFF REPAIR		20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 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] / 168	168

ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 390 222
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 391	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LORAZEPAM	2 mg	OTHER: QHS	Y-M: 20[redacted]
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]
ENALAPRIL	20 mg	QD	Y-M: 20[redacted]
LEFLUNOMIDE	20 mg	QD	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
VICODIN	7.5 mg	BID	Y-M: 20[redacted] / -298

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
LORAZEPAM	2 mg	OTHER: QHS	Y-M: 20[redacted]	NOT REPORTED
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED
ENALAPRIL	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	NOT REPORTED
VICODIN	7.5 mg	BID	Y-M: 20[redacted] / -298	NOT REPORTED

Event #1: Serious Adverse Event

Event Description	DEGENERATIVE DISC DISEASE WITH RETROLISTHESIS
Preferred term	椎間板変性症
AE Onset Date / Rx Day	[redacted]20[redacted] / 504
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 504): L5-S1 TRANSFORAMINAL LUMBAR INTERBODY FUSION: RESOLVED

AE Stopped Rx Day	507
Duration of AE	4 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	LIFESTYLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	DEGENERATIVE DISC DISEASE WITH RETROLISTHESIS
Preferred term	脊椎後方すべり症
AE Onset Date / Rx Day	[redacted]20[redacted] / 504
Age at AE Onset	5[redacted]

Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 504): L5-S1 TRANSFORAMINAL LUMBAR INTERBODY FUSION: RESOLVED

AE Stopped Rx Day	507
Duration of AE	4 DAYS
Severity	Mild
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	LIFESTYLE
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。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，後方すべり症を伴う椎間板変性疾患の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，椎間板変性疾患に対する腰椎椎間板切除術，元喫煙者（1 日 1 箱を 10 年間），左肩回旋筋腱板修復術，局面型乾癬，椎間板変性疾患に対する頚椎融合術，高血圧，乾癬性関節炎，左肩回旋筋腱板修復術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，被験者は後方すべり症を伴う椎間板変性疾患を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，後方すべり症を伴う椎間板変性疾患は消失した。

被験者は長年にわたって腰椎の痛み及びこわばり感を患っていた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，L5～S1 の経椎間孔的腰椎椎体間固定術を受けた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院

した。医療記録は本報告時点で未入手であった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Spinal retrolisthesis (10081602) (Spinal retrolisthesis (10081602)) [v.22.1] [10081602]

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

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

Dechallenge: Not Applicable

2) Degenerative disc disease (10070241) (Intervertebral disc degeneration (10061246)) [v.22.1] [10070241]

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 DEGENERATIVE DISC DISEASE WITH RETROLISTHESIS

- Investigator: Lifestyle

- AbbVie: Risk factors include prior history of lumbar spine discectomy, pre-existing psoriatic arthritis and obesity.

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
遠隔転移を伴う肺癌	X	X	X	X

Treatment Group	Age at Study Start	Sex	Race
UPA 15 mg QD	7[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	NOT REPORTED
GASTROESOPHAGEAL REFLUX DISEASE	19[redacted]
DIABETES MELLITUS	20[redacted]
OTHER: SEASONAL ALLERGIES	20[redacted]
HYPERLIPIDEMIA	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	FORMER	1 PACK	50	20[redacted]
CIGARS	CURRENT			
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] / 170	170
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 171	[redacted]20[redacted] / 312	142

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted] / -208
METFORMIN	500 mg	BID	Y-M: 20[redacted] / -208
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -208

SULFASALAZINE	500 mg	QD	Y-M: 20[redacted] / -208
VICODIN	5-325 mg	PRN	Y-M: 20[redacted] / -208
FOLIC ACID	2 mg	QD	Y-M: 20[redacted] / -181
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted] / -181
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / -125
MAGNESIUM	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -125

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	10 mg	QD	Y-M: 20[redacted] / -208	ONGOING
METFORMIN	500 mg	BID	Y-M: 20[redacted] / -208	ONGOING
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -208	ONGOING
SULFASALAZINE	500 mg	QD	Y-M: 20[redacted] / -208	ONGOING
VICODIN	5-325 mg	PRN	Y-M: 20[redacted] / -208	ONGOING
FOLIC ACID	2 mg	QD	Y-M: 20[redacted] / -181	ONGOING
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted] / -181	ONGOING
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / -125	ONGOING
MAGNESIUM	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -125	ONGOING

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

Event Description	LUNG CANCER - LEFT KIDNEY & LIVER METASTASIZE
Preferred term	遠隔転移を伴う肺癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 239
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	313 (67 DAYS AFTER LAST TREATMENT)
Duration of AE	75 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, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, RESULTS IN DEATH

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。本被験者は米国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，致死的な肺癌，左腎・肝転移の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，糖尿病，高脂血症，乾癬性関節炎，元喫煙者（1 日 1 箱を 50 年間），局面型乾癬，現飲酒者（1 日 2 杯未満）及び現葉巻喫煙者であった。

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。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，被験者は肺癌，左腎・肝転移を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死因は肺癌，左腎・肝転移と報告された。剖検が実施されたかどうかは不明である。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は息切れを来し，CT スキャン検査及び呼吸器の治療のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，本事象によりこの被験者の治験は中止された。

Causality for UPADACITINIB (Blinded)

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1) Lung cancer metastatic (10050017) (Lung cancer metastatic (10050017)) [v.22.0] [10050017]

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 LUNG CANCER, LEFT KIDNEY AND LIVER METASTASIZE

- Investigator: Not applicable

- AbbVie: Risk factors include smoking history of 1 PPD for 50 years and advanced age.

Relevant Laboratory & Other Diagnostic Tests

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

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

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo to UPA 15 mg QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
SYNCOPE: NEUROCARDIOGENIC SYNCOPE	19[redacted]
OTHER: PLAQUE PSORIASIS	19
MIGRAINE HEADACHE	19
DEPRESSION: BIPOLAR DEPRESSION	19
OBESITY	19
OTHER: ANXIETY	19
GASTROESOPHAGEAL REFLUX DISEASE	19
OTHER: URINARY INCONTINENCE	20
OTHER: CENTRALIZED BODY PAIN	20
OTHER: SYNOVITIS	20
ASTHMA	20
PSORIATIC ARTHRITIS	20
OTHER: UNSPECIFIED NONTOXIC NODULAR GOITER	20
HYPERTENSION	20
OTHER: DEEP VEIN THROMBOSIS	20
OTHER: PRE-DIABETES MELLITUS	20
OTHER: INSOMNIA	20
OTHER: MUSCLE SPASMS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: VERTICAL BANDED GASTROPLASTY	19[redacted]
SURGERY: TUBAL LIGATION	20
SURGERY: C-SECTION	20
SURGERY: TOTAL HYSTERECTOMY	20
SURGERY: RIGHT KNEE MENISCAL REPAIR	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.25 PACK	12	
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] / 179	179
ABT-494	15 MG	ORAL	QD	[redacted] / 180	[redacted] / 395	216
ABT-494	15 MG	ORAL	QD	[redacted] / 396		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
OMEPRAZOLE	20 mg	QD	Y-M: 19[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
OXYBUTYNIN	5 mg	QD	Y-M: 20[redacted]
IBUPROFEN	200 mg	PRN	Y-M: 20[redacted]
SALBUTAMOL	90 ug	PRN	Y-M: 20[redacted]
SULFASALAZINE	1500 mg	TID	Y-M: 20[redacted]
BUSPIRONE	30 mg	QD	Y-M: 20[redacted]
CITALOPRAM	40 mg	QD	Y-M: 20[redacted]
TIZANIDINE	4 mg	OTHER: Q6 HOURS	Y-M: 20[redacted]
TOPIRAMATE	100 mg	QD	Y-M: 20[redacted]
ZOLPIDEM	10 mg	PRN	Y-M: 20[redacted]
VARENICLINE	0.5 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
OMEPRAZOLE	20 mg	QD	Y-M: 19[redacted]	Y-M: 20[redacted] / 120
OXYBUTYNIN	5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 120
IBUPROFEN	200 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
SALBUTAMOL	90 ug	PRN	Y-M: 20[redacted]	NOT REPORTED
BUSPIRONE	30 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 301
CITALOPRAM	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 301
TIZANIDINE	4 mg	OTHER: Q6 HOURS	Y-M: 20[redacted]	NOT REPORTED
ZOLPIDEM	10 mg	PRN	Y-M: 20[redacted]	NOT REPORTED
TOPIRAMATE	100 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 211
VARENICLINE	0.5 mg	QD	Y-M: 20[redacted] / -92	Y-M: 20[redacted] / 362
LEVOFLOXACIN	750 mg	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 63
AZITHROMYCIN	250 mg	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
AZTREONAM	1 g	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
VANCOMYCIN	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
SODIUM CHLORIDE	2 L	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 64
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 70

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 60
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 63): Leukocytes: 6.8 [4 - 10] 10^9/L; NPTST102-C-REACTIVE PROTEIN: 6.4 [0 - 0.6] MG/DL; NPTST387-PROCALCITONIN: 0.04 [0 - 0.25] NG/ML; NPTST421-RESPIRATORY PATHOGEN PANEL: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 64): NPTST063-B-TYPE NATRUIRETIC PEPTIDE: 106 [0 - 100] PG/ML; NPTST302-LEGIONELLA PNEUMOPHILA ANTIGEN: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST448-STEP PNEUMONIA ANTIGEN: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]0[redacted] (RX DAY 65): Leukocytes: 6.3 [4 - 10] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 63): OTHER NASOPHARYNGEAL SWAB NPTST422-RESPIRATORY PCR PANEL: Negative; [redacted]20[redacted] (RX DAY 64): SPUTUM NPTST019-AEROBIC RESPIRATORY CULTURE: Negative; URINE NPTST302-LEGIONELLA PNEUMOPHILA ANTIGEN: Negative; URINE NPTST449-STREP PNEUMONIA ANTIGEN: Negative; [redacted]20[redacted] (RX DAY 65): SPUTUM NPTST420-RESPIRATORY GRAM STAIN CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 63): CHEST XRAY: 1. INTERVAL DEVELOPMENT OF PATCHY AIRSPACE OPACITY IN THE LEFT MIDLUNG THAT MAY BE INFECTIOUS IN ETIOLOGY. 2. NO DISPLACED RIB OR CLAVICULAR FRACTURES. 3. UNREMARKABLE CARDIAC AND MEDIASTINAL CONTOURS. NO PLEURAL EFFUSION OR PNEUMOTHORAX.; CT ANGIO CHEST WITH CONTRAST- PULMONARY EMBOLISM PROTOCOL: 1. NO PULMONARY EMBOLISM. 2. SUPERIOR SEGMENT LEFT LOWER LOBE PNEUMONIA. 3. MOSAIC ATTENUATION OF THE LUNGS, WHICH MAY RELATE TO SMALL AIRWAYS DISEASE.; [redacted]20[redacted] (RX DAY 64): ECHOCARDIOGRAM: NORMAL LEFT VENTRICULAR DIASTOLIC FUNCTION. NO EVIDENCE OF RIGHT-TO-LEFT SHUNT BY IV SALINE CONTRAST STUDY. TECHNICALLY DIFFICULT STUDY DUE TO BODY HABITUS. CONCLUSIONS ---------- NORMAL OVERALL LEFT VENTRICULAR SYSTOLIC FUNCTION. NORMAL OVERALL RIGHT VENTRICULAR SYSTOLIC FUNCTION.

AE Stopped Rx Day	65
Duration of AE	6 DAYS
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	LIKELY COMMUNITY ACQUIRED PNEUMONIA.
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。本被験者は米国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺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，喘息，乾癬性関節炎，高血圧，肺気腫／慢性閉塞性肺疾患，現喫煙者（1 日 0.25 箱を 12 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，被験者は肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，肺炎は消失した。

被験者は，20[redacted] 年 [redacted] 月 [redacted] 日の起床時，中背部周囲に放射状に拡がる左乳房の痛みを自覚した。起き上がって少し歩いたところで息切れがし，一過性の頭部ふらふら感と疲労が出現した。この痛みは深く息を吸うと悪化した。被験者は乾癬性関節炎のためすでにリウマチ科に予約を入れていた。胸部 X 線検査が行われ，左肺中葉肺炎の可能性が示唆された。Levaquin 750 mg/日 5 日間の投与が開始された。被験者によれば，発熱はなかったが，悪寒があった。20[redacted] 年 [redacted] 月 [redacted] 日，右上唇に熱性疱疹が出現した。疱疹は痂皮化し，時折透明の滲出液が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，1 日 2 回程度の一過性（持続時間 15～20 分）の悪心を伴う右上腹部痛が出現した。また，左腱痛も出現し，動くと悪化したが，うずくような痛みが絶えずあった。被験者によると，姉妹の 1 人が気管支炎を発症していた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は ER を受診し，息切れ，腹痛，疲労増加，頭部ふらふら感及び悪心を訴えた。肺塞栓症が懸念されたため，胸部 CT 検査が行われたが，肺塞栓症は認められなかった。しかし，左肺下葉上区の肺炎が明らかとなった。被験者は ER 受診時に Levaquin を 4 日間服用していたが，これは静注抗生物質に切り替えられた。20[redacted] 年 [redacted] 月 [redacted] 日，息切れのため，被験者は入院し，緊急検査を受けることとなった。治験責任医師によると，喘息，COPD 及び現喫煙者が関連のある危険因子であった。心エコー検査が行われた。結果は，駆出率 70%で異常なし，B 型ナトリウム利尿ペプチド（BNP）がごくわずかに増加していた。プロカルシトニン値は本事象の持続期間を通して正常であった。20[redacted] 年 [redacted] 月 [redacted] 日，白血球増加症は認められず，息切れも消失し，被験者はドキシサイクリン 100 mg bid 5 日間を処方されて退院した。抗生物質の投与期間終了後，被験者より，症状は消失したと報告された。

投与された薬剤は，azithromax，アズトレオナム，バンコマイシン，ドキシサイクリン及び levaquin であった。

Causality for UPADACITINIB (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.22.1] [10035664]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMONIA

- Investigator: Likely community acquired pneumonia.

- AbbVie: Event more likely related to current smoking status and COPD. The investigator reports a risk factor of COPD, which is very likely due to subject's smoking history.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] AEROBIC RESPIRATORY CULTURE (SPUTUM): negative

[redacted] 20[redacted] B-TYPE NATRIURETIC PEPTIDE: 106 PG/ML (normal 0 to 100)

[redacted] 20[redacted] C-REACTIVE PROTEIN: 6.4 mg/dL (normal 0.0 to 0.6)

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

[redacted] 20[redacted] CHEST X-RAY: possible left middle lobe pneumonia

[redacted] 20[redacted] CHEST XRAY: 1. INTERVAL DEVELOPMENT OF PATCHY AIRSPACE OPACITY IN THE LEFT MIDLUNG THAT MAY BE INFECTIOUS IN ETIOLOGY. 2. NO DISPLACED RIB OR CLAVICULAR FRACTURES. 3. UNREMARKABLE CARDIAC AND MEDIASTINAL CONTOURS. NO PLEURAL EFFUSION OR PNEUMOTHORAX.

[redacted] 20[redacted] CT ANGIO CHEST WITH CONTRAST-PULMONARY EMBOLISM PROTOCOL: 1. No pulmonary embolism. 2. Superior segment left lower lobe pneumonia. 3. Mosaic attenuation of the lungs, which may relate to small airways disease

[redacted] 20[redacted] ECHOCARDIOGRAM: Normal left ventricular diastolic function. No evidence of right-to-left shunt by iv saline contrast study. Technically difficult study due to body habitus. Conclusions: Normal overall left ventricular systolic function. Normal overall right ventricular systolic function. Ejection fraction of 70%

[redacted] 20[redacted] LEGIONELLA PNEUMOPHILA ANTIGEN (URINE): negative

[redacted] **20[redacted] PROCALCITONIN:** 0.04 ng/mL (normal 0.00 to 0.25)

[redacted] **20[redacted] RESPIRATORY PATHOGEN PANEL:** NASOPHARYNGEAL SWAB: negative

[redacted] **20[redacted] STREP PNEUMONIA ANTIGEN (URINE):** negative

[redacted] **20[redacted] WBC:** 6.8 K/UL (normal 4.0 to 10.0)

[redacted] **20[redacted] WBC:** 6.3 K/UL (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
肝性脳症	X	X		X

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

Medical History	Onset Year
HEPATITIS: HEPATITIS C WITHOUT COMA,CHRONIC	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
HEPATITIS: CIRRHOSIS OF LIVER	20[redacted]
HYPERTENSION	20[redacted]
OTHER: HYPERTROPHIC CARDIOMYOPTHY	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	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	FORMER	1 PACK	20	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ADA	40MG	SC	EOW	[redacted]20[redacted] / 1	[redacted]20[redacted] / 172	172

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
FISH OIL	1280 mg	QD	Y-M: 20[redacted]

NAPROXEN	440 mg	QD	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
AMINO ACIDS NOS W/CAFFEINE/CITRUS AURANTIUM/G	4 OTHER: TABLETS	QD	Y-M: 20[redacted]
ATENOLOL	50 mg	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	PRN	Y-M: 20[redacted]
TRIAMCINOLONE	1 OTHER: APP	PRN	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -159
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted] / -159
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted] / -62
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -55
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -48

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
FISH OIL	1280 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 93
NAPROXEN	440 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 93
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 93
AMINO ACIDS NOS W/CAFFEINE/CITRUS AURANTIUM/G	4 OTHER: TABLETS	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 93
ATENOLOL	50 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 93
OMEPRAZOLE	20 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 93
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / -159	Y-M: 20[redacted] / 93
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -48	Y-M: 20[redacted] / 88
FOLINIC ACID	5 mg	OTHER: 12HRS POST MTX AND 24 HOURS POST MTX	Y-M: 20[redacted] / 39	Y-M: 20[redacted] / 89
ATENOLOL	50 mg	QD	Y-M: 20[redacted] / 98	NOT REPORTED

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

Event Description	HEPATIC ENCEPHALOPATHY
Preferred term	肝性脳症
AE Onset Date / Rx Day	[redacted]20[redacted] / 94
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 94): Alanine Aminotransferase: 19 [0 - 40] U/L; Albumin: 40 [35 - 50] G/L; Alkaline Phosphatase: 84 [30 - 130] U/L; Aspartate Aminotransferase: INVALID -HEMOLYSIS [0 - 37] U/L; Bilirubin: 34 [0 - 21] UMOL/L; NPTST029-AMMONIA: 135 [0 - 72] UMOL/L; NPTST398-PROTHROMBIN TIME: 12.2 [9.3 - 11.7] SEC; Prothrombin Intl. Normalized Ratio: 1.21 [0.9 - 1.1] RATIO; [redacted]20[redacted] (RX DAY 95): NPTST265-HOMOCYSTEINE: 9.7 [0 - 12.2] UMOL/L; [redacted]20[redacted] (RX DAY 113): NPTST029-AMMONIA: 141 [0 - 72] UMOL/L; NPTST501-VITAMIN B12: 591

[200 - 1100] (PG/MOL); [redacted] (RX DAY 120): NPTST029-AMMONIA: 118 [0 - 72] UMOL/L; [redacted] (RX DAY 148): NPTST029-AMMONIA: 139 [0 - 72] UMOL/L; [redacted] (RX DAY 171): NPTST029-AMMONIA: 132 [0 - 72] UMOL/L; [redacted] (RX DAY 182): NPTST029-AMMONIA: 96 [0 - 72] UMOL/L; [redacted] (RX DAY 196): NPTST029-AMMONIA: 97 [0 - 72] UMOL/L

Microbiology

[redacted] (RX DAY 94): OTHER NASAL SWAB NPTST335-MRSA SURVEILLANCE CULTURE: Negative-NEGATIVE

SAE Supplemental Procedure

[redacted] (RX DAY 94): CT HEAD/BRAIN WITHOUT CONTRAST: NORMAL UNENHANCED CRANIAL CT; MRA ARTERIOGRAM OF THE HEAD AND NECK WITH CONTRAST: NEGATIVE; MRI BRAIN WITH/WITHOUT CONTRAST: NEGATIVE; ULTRASOUND ABDOMEN COMPLETE: UNREMARKABLE SONOGRAM OF THE ABDOMEN; [redacted] (RX DAY 95): 2D ECHOCARDIOGRAM TRANSTHORACIC: LEFT VENTRICLE NORMAL IN SIZE AND SYSTOLIC FUNCTION; NO SIGNIFICANT VALVULAR ABNORMALITIES; DIASTOLIC FUNCTION IS NORMAL; NO EVIDENCE OF VEGETATION OR CARDIAC SOURCE OF EMBOLI; MILD LAE

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Severe
Relation to Study Drug by Investigator	Reasonable Possibility
Investigator Alternative Etiology	METHOTREXATE
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。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肝性脳症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は，C 型肝炎（慢性型，肝性昏睡なし），元喫煙者（1 日 1 箱を 20 年間），局面型乾癬，肝硬変，高血圧，肥大型心筋症，乾癬性関節炎及び元飲酒者（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，被験者は肝性脳症を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者より，前日の夜に「変な」感じがあったと報告された。被験者は，眠ることはできたものの寝過ごし，目覚まし時計の音も聞こえなかった。被験者は出勤したが，プリントしたり，パスワードを入力したりといった単純な作業ができなかった。同日，被験者は，錯乱，記憶障害及び不明瞭発語により，妻に連れられて救急治療室を受診した。被験者は，不明瞭発語，錯乱，そして TIA 又は薬剤の副作用の可能性のため，観察室に入院した。肝パネル検査の結果はビリルビン増加以外は正常で，神経症状と血清アンモニア値に基づき肝性脳症と診断された。血中アンモニアを低下させる目的でラクツロースが投与された。20[redacted] 年 [redacted] 日，腹部超音波検査で肝硬変やその他の急性病変は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は安定状態で退院した。被験者は意識清明で見当識障害はなく，途中で息継ぎをすることなく完全な文章で話すことができた。治験薬及びメトトレキサートの中止後に神経症状は改善したが，ベースラインの状態には戻っていなかった。

治験薬の投与が再開され，血清アンモニア値のモニタリングが行われた。20[redacted] 年 [redacted] 月 [redacted] 日，24 週後の規定来院時において，神経症状が入院時とほぼ同じくらい悪い状態で再発していた。被験者によれば，精神的混濁は治験薬再開後に悪化した。

治験薬の投与は完全に中止された。

投与された薬剤はラクツロースであった。

The patient's past medications include:

TRIAMCINOLONE for PSORIASIS (20[redacted] - [redacted] 20[redacted])

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])

Causality for UPADACITINIB (Blinded)

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1) Hepatic encephalopathy (10019660) (Hepatic encephalopathy (10019660)) [v.22.1] [10019660]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction recurred

Alternative Etiology for UPADACITINIB (Blinded)

Event of HEPATIC ENCEPHALOPATHY

- Investigator: METHOTREXATE

- AbbVie: event is more likely related to pre-existing chronic hepatitis C and cirrhosis of liver.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] 2D ECHOCARDIOGRAM TRANSTHORACIC:** LEFT VENTRICLE NORMAL IN SIZE AND SYSTOLIC FUNCTION; NO SIGNIFICANT VALVULAR ABNORMALITIES; DIASTOLIC FUNCTION IS NORMAL; NO EVIDENCE OF VEGETATION OR CARDIAC SOURCE OF EMBOLI; MILD LAE.

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

[redacted] **20[redacted] ALBUMIN:** 3.7 G/L(normal 3.3 to 4.9)

[redacted] **20[redacted] ALBUMIN:** 4.1 G/L (normal 3.3 to 4.9)

[redacted] **20[redacted] ALBUMIN:** 4.0 G/DL (normal 3.5 to 5.0)

[redacted] **20[redacted] ALBUMIN:** 4.1 G/L (normal 3.3 to 4.9)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 84 U/L (normal 30 to 130)

[redacted] **20[redacted] AMMONIA:** 135 umol/L (normal 0 to 32)

[redacted] **20[redacted] AMMONIA:** 141 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 141 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 118 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 139 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 132 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 96 umol/L (normal 0 to 72)

[redacted] **20[redacted] AMMONIA:** 97 umol/L (normal 0 to 72)

[redacted] **20[redacted] BILIRUBIN:** 2.0 mg/dL (normal 0.0 to 1.2)

[redacted] **20[redacted] CT HEAD/BRAIN WITHOUT CONTRAST:** Normal unenhanced cranial CT.

[redacted] **20[redacted] HOMOCYSTEINE:** 9.7 MMOL/L (normal 0 to 12.2)

[redacted] **20[redacted] INTERNATIONAL NORMALIZED RATIO:** 1.21 ratio (normal 0.9 to 1.1)

2000 LIVER BIOPSY: cirrhosis due to hepatitis C

[redacted] **20[redacted] MRA ARTERIOGRAM OF THE HEADAND NECK WITH CONTRAST:** Negative.

[redacted] **20[redacted] MRI BRAIN WITH/WITHOUT CONTRAST:** Negative

[redacted] **20[redacted] MRSA SURVEILLANCE CULTURE:** Negative

[redacted] **20[redacted] PROTHROMBIN TIME:** 12.2 SEC (normal 9.3 to 11.7)

[redacted] **20[redacted] SGOT:** 32 U/L (normal 11 to 36)

[redacted] **20[redacted] SGOT:** 38 U/L (normal 11 to 36)

[redacted] **20[redacted] SGOT:** 24 U/L (normal 11 to 36)

[redacted] **20[redacted] SGPT:** 20 U/L (normal 6 to 43)

[redacted] **20[redacted] SGPT:** 29 U/L (normal 6 to 43)

[redacted] **20[redacted] SGPT:** 18 U/L (normal 6 to 43)

[redacted] **20[redacted] ULTRASOUND ABDOMEN COMPLETE:** Unremarkable sonogram of the abdomen

[redacted] **20[redacted] VITAMIN B12:** 591 pg/mol (normal 200 to 1100)

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
敗血症	X	X		X

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

Medical History	Onset Year
OTHER: AORTIC STENOSIS, CONGENITAL	19[redacted]
VALVULAR HEART DISEASE: UNICUSPID VALVE	19[redacted]
HEPATITIS: HEPATITIS C	19[redacted]
VALVULAR HEART DISEASE: BICUSPID AORTIC VALVE REPAIR	19[redacted]
VALVULAR HEART DISEASE: BICUSPID AORTIC VALVE REPAIR	20[redacted]
VALVULAR HEART DISEASE: BICUSPID AORTIC VALVE REPLACEMENT	20[redacted]
OTHER: ACTIVE 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	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 63	63

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]-
WARFARIN	7 mg	QD	Y-M: 20[redacted]-

VITAMINS NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted] / -131
PARACETAMOL	625 mg	PRN	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
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
WARFARIN	7 mg	QD	Y-M: 20[redacted]	ONGOING
VITAMINS NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]	ONGOING
APREMILAST	30 mg	BID	Y-M: 20[redacted] / -131	ONGOING
PARACETAMOL	625 mg	PRN	Y-M: 20[redacted] / -124	ONGOING
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 64
CARVEDILOL	6.25 mg	BID	Y-M: 20[redacted] / 77	ONGOING
LISINOPRIL	5 mg	QD	Y-M: 20[redacted] / 77	ONGOING
PARACETAMOL	975 mg	PRN	Y-M: 20[redacted] / 77	ONGOING
SODIUM CHLORIDE	10 mL	OTHER: AS DIRECTED	Y-M: 20[redacted] / 77	ONGOING
SODIUM CHLORIDE	3 L	OTHER: ONCE	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 77
CEFEPIME	NOT REPORTED	OTHER: UNK	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 79
DOXYCYCLINE	NOT REPORTED	OTHER: UNK	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 79
VANCOMYCIN	NOT REPORTED	OTHER: UNK	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 79
HEPARIN	NOT REPORTED	OTHER: UNK	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 84
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 79	ONGOING
GENTAMICIN	100MG/50ML-NACL 0.9% mg	QD	Y-M: 20[redacted] / 79	ONGOING
DICLOFENAC	1.3 %	PRN	Y-M: 20[redacted] / 84	ONGOING
METHOCARBAMOL	750 mg	PRN	Y-M: 20[redacted] / 84	ONGOING

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

Event Description	ACUTE SEPSIS
Preferred term	敗血症
AE Onset Date / Rx Day	[redacted]20[redacted] / 55
Age at AE Onset	5[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 77): Glucose: 7.2 [4.1 - 5.9] MMOL/L; Leukocytes: NORMAL [NOT REPORTED - NOT

REPORTED] UNK; NPTST412-RAPID TROPONIN: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST487-URINALYSIS: UNREMARKABLE [NOT REPORTED - NOT REPORTED] NA; [redacted]20[redacted] (RX DAY 82): NPTST479-TROUGH AND PEAK LEVEL FOR GENTA: UNK [NOT REPORTED - NOT REPORTED] UNK; [redacted]20[redacted] (RX DAY 84): Prothrombin Intl. Normalized Ratio: 3.39 [0.8 - 1.1] RATIO

Microbiology

[redacted]20[redacted] (RX DAY 77): BLOOD NPTST156-CULTURE: Positive-GRAM-POSITIVE COCCI BACTEREMIA

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 77): ECHOCARDIOGRAM: MODERATE TO SEVERE EF (30-35%);DID NOT REVEAL PRESENCE OF VEGETATION; EKG: SINUS TACHYCARDIA, CHRONIC LEFT BUNDLE BRANCH BLOCK; [redacted]20[redacted] (RX DAY 79): TRANSESOPHAGEAL ECHOCARDIOGRAM: LEFT VENTRICLE: THE CAVITY SIZE INCREASED. SYSTOLIC FUNCTION IS MODERATELY TO SEVERELY REDUCED. THE ESTIMATED EJECTION FRACTION IS 35%.TRICUSPID VALVE: MILD REGURGITATION.

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。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急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，大動脈狭窄（先天性），大動脈一尖弁，大動脈二尖弁置換，C 型肝炎，人工心臓弁を用いた大動脈弁置換術，活動性局面型乾癬，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，被験者は急性敗血症を発現した。

被験者は 11 歳時に先天性大動脈二尖弁修復術を受けていたが，大動脈狭窄が進行した。20[redacted] 年，被験者は人工心臓弁置換術を受けた。20[redacted] 年 [redacted] 月，駆出率が 55%であった。

入院前において，被験者の症状は船旅に出る直前の 20[redacted] 年 [redacted] 月 [redacted] 日に出現した。20[redacted] 年 [redacted] 月 [redacted] 日，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，約 3 週間続いている一過性の発熱（104°F）のため ER を受診した。発熱は船旅の 2 日目に出現した。そのほかにも被験者は，悪心，空吐き（嘔吐なし）を伴う食欲喪失，胸部上部不快感及び発熱に伴う寝汗を訴えた。ER で行われた心電図検査で，洞性頻脈及び虚血性変化を伴わない慢性左脚ブロックが認められた。心内膜炎の可能性が疑われた。同日，被験者は入院した。心エコー検査で中等度から重度の駆出率（30%～35%）が認められた。経胸壁心エコー検査及び経食道心エコー検査で大動脈弁疣贅は認められなかったが，血液培養で緑色連鎖球菌が認められた。このような状況において，来院時の推定される人工大動脈弁心内膜炎，先行して行われた歯科治療，既存の人工心臓弁，及び血液培養で特定された病原菌に対する治療が行われた。まず，バンコマイシン，セフェピム及びドキシサイクリンの投与が開始された。血液培養の結果が得られると，セフトリアキソン及びゲンタマイシンの静脈内投与に切り替えられた。20[redacted] 年 [redacted] 月 [redacted] 日，PICC ライン留置術が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者の状態は問題なく，退院した。退院時までに行われた抗生物質療法の期間は計 5 週間であった。

投与された薬剤は，ゲンタマイシン，塩化ナトリウム，リシノプリル，ヘパリン，セフトリアキソン，ドキシサイクリン，タイレノール，バンコマイシン及びセフェピムであった。

Causality for ABT-494 (Blinded)

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1) Sepsis (10040047) (Sepsis (10040047)) [v.22.0] [10040047]

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 ACUTE SEPSIS

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD CULTURE:** Positive (Streptococcus viridans)

Unknown date BODY TEMPERATURE: 104 F

20[redacted] CARDIAC CATHETERIZATION: Normal

[redacted] **20[redacted] ECHOCARDIOGRAM:** Left Ventricle: Moderate to severe reduced EF (30-35%) Aortalve: Mechanical prosthetic valve Mitral Valve: Mild regurgitation Aortic Root: Poorly visualized, moderately dilated

[redacted] **20[redacted] EJECTION FRACTION:** 55%

[redacted] **20[redacted] VITALS:** Discharge vitals: T 36.5C; Tmin 36.3C; Tmax 36.9; HR 72(monitored), RR 18; BP 119/77; SpO2 98%

[redacted] **20[redacted] EKG:** Sinus tachycardia, chronic left bundle branch block

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Occasional supraventricular premature complex, left bundle branch block.

[redacted] **20[redacted] GLUCOSE:** 129

Unknown date HEMOGLOBIN: Normal

[redacted] **20[redacted] INTERNATIONAL NORMALIZED RATIO:** 3.39

Unknown date LACTIC ACID: 2.8 no unit

Unknown date PLATELETS: Normal

[redacted] **20[redacted] TRANSESOPHAGEAL ECHOCARDIOGRAM:** Aortic Valve: No obvious vegetations Mitral Valve: Leaflets are mildly thickened, Mild regurgitation, minute mobile echodensities likely benign fibrinous strands Left ventricle: The cavity size increased. Systolic function is moderately to severely reduced. The estimated ejection fraction is 35%.tricuspid valve: Mild regurgitation. Aorta: ascending aorta is moderately dilated, no atheroma

[redacted] **20[redacted] TROPONIN:** Rapid-negative

[redacted] **20[redacted] URINALYSIS:** Unremarkable

Unknown date WHITE BLOOD CELLS: Normal

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
睡眠時無呼吸症候群	X			
創離開	X			

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

Medical History	Onset Year
OTHER: BELL PARALYSIS	19[redacted]
PSORIATIC ARTHRITIS	19[redacted]
OTHER: BELL PARALYSIS	20[redacted]
OTHER: BILATERAL PLANTAR PSORIASIS PLAQUE	20[redacted]
OTHER: NAIL PSORIASIS ON TOES	20[redacted]
HYPERTENSION	20[redacted]
OTHER: SEROTONIN LEVEL DISORDER	20[redacted]
OTHER: FIRST TOE DACTYLITIS	20[redacted]
OTHER: SYNOVITIS LEFT WRIST , MCP	20[redacted]

Prior Procedures	Procedure Year
SURGERY: VASECTOMY	20[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]

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	FORMER	More than 4 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] / 399	230
ADA	40MG	SC	EOW	[redacted]20[redacted] / 400	[redacted]20[redacted] / 645	246

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
DILTIAZEM	240 mg	QD	Y-M: 20[redacted] / -217
CITALOPRAM	10 mg	QD	Y-M: 20[redacted] / -158

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	25 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
DILTIAZEM	240 mg	QD	Y-M: 20[redacted] / -217	NOT REPORTED
CITALOPRAM	10 mg	QD	Y-M: 20[redacted] / -158	NOT REPORTED
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / 2	NOT REPORTED
ALL OTHER NON-THERAPEUTIC PRODUCTS	NA	OTHER: FACIAL MASK	Y-M: 20[redacted] / 197	NOT REPORTED
MOMETASONE	2 OTHER: VAPORISATIONS	BID	Y-M: 20[redacted] / 301	ONGOING
TRIAMCINOLONE	20 mg	OTHER: ONLY ONCE	Y-M: 20[redacted] / 346	Y-M: 20[redacted] / 346
DEXAMETHASONE	6 mg	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
HYDROMORPHONE	0.5 mg	PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 367
HYDROMORPHONE	1 mg	PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 375
LABETALOL	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 367
DEXAMETHASONE	6 mg	OTHER: ONCE	Y-M: 20[redacted] / 370	Y-M: 20[redacted] / 370
GRANISETRON	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 370	Y-M: 20[redacted] / 370
HYDROMORPHONE	0.5 mg	PRN	Y-M: 20[redacted] / 370	Y-M: 20[redacted] / 370
LABETALOL	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 370	Y-M: 20[redacted] / 370
DEXAMETHASONE	6 mg	BID	Y-M: 20[redacted] / 370	Y-M: 20[redacted] / 372
TRIAMCINOLONE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 508	Y-M: 20[redacted] / 508
TRIAMCINOLONE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 647	Y-M: 20[redacted] / 647

Event #1: Serious Adverse Event

Event Description	OBSTRUCTIVE SLEEP APNEA
Preferred term	睡眠時無呼吸症候群
AE Onset Date / Rx Day	[redacted]20[redacted] / 183
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 366): BILATERAL LOWERING OF LOWER TURBINATES: RECOVERED; BILATERAL TONSILECTOMY: RECOVERED; SEPTOPLASTIA: RECOVERED; UVULO-PALATO PHARNGOPLASTY: RECOVERED	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	Moderate
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	RESPIRATORY TRACT ANATOMIC ABNORMALITIES
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	SURGICAL WOUND OPENING
Preferred term	創離開
AE Onset Date / Rx Day	[redacted]20[redacted] / 369
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 369): LEFT TONSIL HEMOSTASIS REVISION BY CAUTERIZATION: WENT WELL , PATIENT DISCHARGE ON DEC 8TH.	
AE Stopped Rx Day	369
Duration of AE	1 DAY
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	SURGICAL INTERVENTION FOR OBSTRUCTIVE SLEEP APNEA
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 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，閉塞性睡眠時無呼吸及び手術創の開口の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，乾癬性関節炎，元喫煙者（1 日 1 箱を 8 年間），高血圧及び元飲酒者（1 日 4 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，被験者は閉塞性睡眠時無呼吸を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は手術創の開口を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，手術創の開口は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は閉塞性睡眠時無呼吸と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は睡眠時にマスクを使用する持続的気道陽圧法（CPAP）を開始した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は閉塞性睡眠時無呼吸に対する外科的処置のため入院し，同日手術が行われた。これらの手術は，鼻中隔形成術，両側下鼻甲介切除術，両側扁桃摘出術及び口蓋垂口蓋咽頭形成術であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は手術創の開口により再入院した。喉に出血が見られ，再入院を指示された。創傷開口を閉鎖するための手術が行われ，焼灼で左扁桃が止血された。手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，タイレノール，デカドロン及び dilaudid であった。

Causality for UPADACITINIB (Blinded)

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1) Obstructive sleep apnea syndrome (10055577) (Sleep apnoea syndrome (10040979)) [v.22.1] [10055577]

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

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

Dechallenge: No

2) Wound dehiscence (10048031) (Wound dehiscence (10048031)) [v.22.1] [10048031]

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 OBSTRUCTIVE SLEEP APNEA

- Investigator: Respiratory tract anatomic abnormalities

- AbbVie: Etiology of the event is not consistent with the study drug's mechanism of action. Additional risk factors include male gender and subject is overweight.

Event of SURGICAL WOUND OPENING

- Investigator: Surgical intervention for obstructive sleep apnea.

- AbbVie: Event is more likely a complication related to surgical procedure done on [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
帯状疱疹	X			

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

Medical History	Onset Year
OTHER: PSORIASIS	19[redacted]
OTHER: PSORIASIS PLAQUE	19[redacted]
OTHER: SEASONAL ALLERGY	19[redacted]
OTHER: OCCASIONNAL DIARRHEA	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: VASECTOMY	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] / 175	175
ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 176		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
NISITA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
MOMETASONE	0.1 %	PRN	Y-M: 20[redacted]

ERGOCALCIFEROL	10000 OTHER: UNITS	QD	Y-M: 20[redacted] / -172
FISH OIL	1 OTHER: TAB	OTHER: 3 TIMES WEEKS	Y-M: 20[redacted] / -172
FOLIC ACID	5 mg	OTHER: 6 DAYS OVER 7	Y-M: 20[redacted] / -172
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -172
VARICELLA ZOSTER VACCINE	0.5 mL	OTHER: ONCE	Y-M: 20[redacted] / -146
IBUPROFEN	400 mg	BID	Y-M: 20[redacted] / -142
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -105
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -14
VARICELLA ZOSTER VACCINE	0.5 mL	OTHER: ONCE	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
NISITA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]	NOT REPORTED
ERGOCALCIFEROL	10000 OTHER: UNITS	QD	Y-M: 20[redacted] / -172	NOT REPORTED
FISH OIL	1 OTHER: TAB	OTHER: 3 TIMES WEEKS	Y-M: 20[redacted] / -172	NOT REPORTED
FOLIC ACID	5 mg	OTHER: 6 DAYS OVER 7	Y-M: 20[redacted] / -172	NOT REPORTED
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / -172	Y-M: 20[redacted] / 255
IBUPROFEN	400 mg	BID	Y-M: 20[redacted] / -142	NOT REPORTED
HYDROCORTISONE	1 %	PRN	Y-M: 20[redacted] / 15	NOT REPORTED
ACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / 250	Y-M: 20[redacted] / 257
PREGABALIN	50 mg	BID	Y-M: 20[redacted] / 253	NOT REPORTED
ACICLOVIR	800 mg	TID	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 263
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted] / 273	NOT REPORTED

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

Event Description	WORSENING OF HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 257
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day 285

Duration of AE	29 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。本被験者はカナダの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，帯状疱疹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，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，被験者は帯状疱疹の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹の悪化は消失した。

本事象発現前，20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹（非重篤）が出現した。20[redacted] 年 [redacted] 月 [redacted] 日，アシクロビルの投与が開始されたが，改善は見られず，新たな病変が認められた。この時点で治験薬の投与が休止された。

被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に救急治療室に紹介され，入院した。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。帯状疱疹は L1 及び T12 領域の右側の 2 つの皮膚分節に認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

被験者は 20[redacted] 年 [redacted] 月と 20[redacted] 年 [redacted] 月に帯状疱疹ワクチンを受けていた。水疱瘡及び帯状疱疹の病歴はなかった。

投与された薬剤は，アシクロビル及びリリカであった。

The patient's past medications include:

ELOCOM for PSORIASIS (20[redacted] - [redacted] 20[redacted])

SHINGRIX for HERPES ZOSTER PREVENTION ([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: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF HERPES ZOSTER

- Investigator: Not applicabe

- AbbVie: Not applicable

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
心膜炎	X			X

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

Medical History	Onset Year
OTHER: CAT ALLERGY	19[redacted]
OTHER: ENVIRONMENTAL ALLERGIES	19
OTHER: PLAQUE PSORIASIS	20
DEGENERATIVE DISC DISEASE: C4-C6 DEGENERATIVE CHANGES	20
OTHER: DYSPHAGIA	20
PSORIATIC ARTHRITIS	20
OTHER: MENOPAUSE	20

Prior Procedures	Procedure Year
SURGERY: GASTROSCOPY	20[redacted]

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]20[redacted] / 1	[redacted]20[redacted] / 171	171
ADA	40MG	SC	EOW	[redacted]20[redacted] / 172	[redacted]20[redacted] / 392	221
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
NAPHCON-A	2 OTHER: DROPS	PRN	Y-M: 19[redacted]
SALBUTAMOL	100 ug	PRN	Y-M: 19[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
IBUPROFEN	400 mg	PRN	Y-M: 20[redacted]
ARTHROTEC	75/200 OTHER: MG/MCG	BID	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
NAPROXEN	500 mg	PRN	Y-M: 20[redacted]
ARTHROTEC	50/200 OTHER: MG/MCG	BID	Y-M: 20[redacted]
FOLIC ACID	5 mg	OTHER: 6 DAYS PER WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
PANADEINE CO	1 OTHER: TABLET	PRN	Y-M: 20[redacted]
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted] / -312
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted] / -305

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
NAPHCON-A	2 OTHER: DROPS	PRN	Y-M: 19[redacted]	NOT REPORTED
SALBUTAMOL	100 ug	PRN	Y-M: 19[redacted]	Y-M: 20[redacted] / 652
NAPROXEN	500 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 652
FOLIC ACID	5 mg	OTHER: 6 DAYS PER WEEK	Y-M: 20[redacted]	NOT REPORTED
METHOTREXATE	25 mg	EVERY WEEK	Y-M: 20[redacted]	NOT REPORTED
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted] / -305	NOT REPORTED
ACETYLSALICYLIC ACID	162 mg	OTHER: ONCE	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 653
COLCHICINE	1.2 mg	BID	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 653
DIMENHYDRINATE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 653
KETOROLAC	30 mg	OTHER: ONCE	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 653
MAGNESIUM SULFATE	2 g	OTHER: ONCE	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 653
MORPHINE	2.5 mg	BID	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 653

IPRATROPIUM	500 ug	OTHER: Q6H	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 655
SALBUTAMOL	2.5 mg	OTHER: Q6H	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 655
DALTEPARIN	5000 IU	QD	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 656
KETOROLAC	10 mg	QID	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 656
NICOTINE	14 mg	QD	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 708
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / 653	Y-M: 20[redacted] / 753
ULTRACET	2 OTHER: TABLET	OTHER: Q6H	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 655
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 656
COLCHICINE	0.6 mg	BID	Y-M: 20[redacted] / 654	Y-M: 20[redacted] / 753
PANTOPRAZOLE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 656	Y-M: 20[redacted] / 658
AZITHROMYCIN	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 657
FUROSEMIDE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 657
RED BLOOD CELLS	1 OTHER: UNIT	OTHER: ONCE	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 657
HYDROMORPHONE	0.5 mg	OTHER: Q2H	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 658
KETOROLAC	30 mg	OTHER: Q8H	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 658
CEFUROXIME	2 g	QD	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 661
CLARITHROMYCIN	250 mg	QD	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 662
ACETYLSALICYLIC ACID	650 mg	TID	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 753
ULTRACET	2 OTHER: TABLET	PRN	Y-M: 20[redacted] / 658	Y-M: 20[redacted] / 659
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 660	Y-M: 20[redacted] / 798
BENZOCAINE	1 OTHER: SPRAY	OTHER: ONCE	Y-M: 20[redacted] / 661	Y-M: 20[redacted] / 661
FENTANYL	50 ug	OTHER: ONCE	Y-M: 20[redacted] / 661	Y-M: 20[redacted] / 661
MIDAZOLAM	3 mg	OTHER: ONCE	Y-M: 20[redacted] / 661	Y-M: 20[redacted] / 661
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y-M: 20[redacted] / 662	NOT REPORTED
CLONIDINE	0.1 mg	QD	Y-M: 20[redacted] / 713	Y-M: 20[redacted] / 743
GABAPENTIN	100 mg	BID	Y-M: 20[redacted] / 723	Y-M: 20[redacted] / 753

VENLAFAXINE	37.5 mg	QD	Y-M: 20[redacted] / 747	Y-M: 20[redacted] / 760
NAPROXEN	500 mg	BID	Y-M: 20[redacted] / 775	Y-M: 20[redacted] / 804
RABEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 799	NOT REPORTED

Event #2: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular Events

Event Description	PERICARDITIS
Preferred term	心膜炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 653
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 658): Alanine Aminotransferase: 35 [0 - 25] U/L; Albumin: 26 [33 - 45] G/L; Alkaline Phosphatase: 198 [30 - 120] U/L; Basophils: 0.01 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.1 [0 - 1] %; Calcium: 2.31 [2.1 - 2.6] MMOL/L; Chloride: 101 [97 - 106] MMOL/L; Creatinine: 54 [35 - 97] UMOL/L; Eosinophils: 0.2 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 2.6 [0 - 5] %; Erythrocytes: 4 [3.8 - 5.2] 10^12/L; Hematocrit: 0.39 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 127 [120 - 160] G/L; Leukocytes: 7.6 [4.5 - 11] 10^9/L; Lymphocytes: 1.39 [1.3 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 18.3 [22 - 52] %; Monocytes: 1.06 [0.3 - 0.8] 10^9/L; Monocytes/Leukocytes: 13.9 [5 - 12] %; NPTST075-BILIRUBIN DIRECT: 4 [0 - 7] UMOL/L; NPTST076-BILIRUBIN TOTAL: 10 [5 - 21] UMOL/L; NPTST143-CORRECTED CALCIUM: 2.59 [2.1 - 2.6] MMOL/L; NPTST224-GGT: 99 [5 - 29] U/L; NPTST275-IMMATURE GRANS: 0.4 [NOT REPORTED - NOT REPORTED] %; NPTST276-IMMATURE GRANS ABS: 0.03 [NOT REPORTED - NOT REPORTED] 10^9/L; NPTST305-LIPASE: 21 [0 - 60] U/L; NPTST312-MAGNESIUM: 0.82 [0.7 - 0.96] MMOL/L; NPTST316-MCH: 32.1 [26 - 34] PG; NPTST317-MCHC: 326 [320 - 365] G/L; NPTST318-MCV: 98.5 [80 - 98] FL; NPTST333-MPV: 9.8 [9.4 - 12.4] FL; NPTST375-PHOSPHATE: 0.94 [0.81 - 1.45] MMOL/L; NPTST395-PROTEIN TOTAL: 64 [60 - 80] G/L; NPTST414-RDW: 14.6 [11.4 - 14.4] %; NPTST485-UREA: 5.2 [2.8 - 7.1] MMOL/L; Neutrophils: 4.92 [1.8 - 5.4] 10^9/L; Neutrophils/Leukocytes: 64.7 [34 - 68] %; Platelets: 274 [140 - 440] 10^9/L; Potassium: 4.2 [3.5 - 5.1] MMOL/L; Sodium: 142 [135 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 659): Alanine Aminotransferase: 32 [0 - 25] U/L; Albumin: 28 [33 - 45] G/L; Alkaline Phosphatase: 183 [30 - 120] U/L; Basophils: 0.01 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.2 [0 - 1] %; Chloride: 101 [97 - 106] MMOL/L; Creatinine: 53 [35 - 97] UMOL/L; Eosinophils: 0.22 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 3.4 [0 - 5] %; Erythrocytes: 4.3 [3.8 - 5.2] 10^12/L; Hematocrit: 0.15 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 142 [120 - 160] G/L; Leukocytes: 6.4 [4.5 - 11] 10^9/L; Lymphocytes: 1.79 [1.3 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 27.8 [22 - 52] %; Monocytes: 0.61 [0.3 - 0.8] 10^9/L; Monocytes/Leukocytes: 9.5 [5 - 12] %; NPTST075-BILIRUBIN DIRECT: 3 [0 - 7] UMOL/L; NPTST076-BILIRUBIN TOTAL: 5 [5 - 21] UMOL/L; NPTST102-C-REACTIVE PROTEIN: 92 [0 - 5] MG/L; NPTST224-GGT: 91 [5 - 29] U/L; NPTST275-IMMATURE GRANS: 0.2 [NOT REPORTED - NOT REPORTED] %; NPTST275-IMMATURE GRANS: 0.01 [NOT REPORTED - NOT REPORTED] 10^9/L; NPTST305-LIPASE: 23 [0 - 60] U/L; NPTST316-MCH: 33.3 [26 - 34] PG; NPTST317-MCHC: 341 [320 - 365] G/L; NPTST318-MCV: 97.4 [80 - 98] FL; NPTST333-MPV: 9.2 [9.4 - 12.4] FL; NPTST395-PROTEIN TOTAL: 69 [60 - 80] G/L; NPTST414-RDW: 14.2 [11.4 - 14.4] %; NPTST485-UREA: 5 [2.8 - 7.1] MMOL/L; Neutrophils: 3.8 [1.8 - 5.4] 10^9/L; Neutrophils/Leukocytes: 58.9 [34 - 68] %; Platelets: 308 [140 - 440] 10^9/L; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Sodium: 146 [135 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 660): Alanine Aminotransferase: 29 [0 - 25] U/L; Albumin: 28 [33 - 45] G/L; Alkaline Phosphatase: 162 [30 - 120] U/L; Basophils: 0.02 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 1] %; Calcium: 2.35 [2.1 - 2.6] MMOL/L; Chloride: 100 [97 - 106] MMOL/L; Creatinine: 58 [35 - 97] UMOL/L; Eosinophils: 0.24 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 3.8 [0 - 5] %; Erythrocytes: 4.2 [3.8 - 5.2] 10^12/L; Hematocrit: 0.4 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 135 [120 - 160] G/L; Leukocytes: 6.3 [4.5 - 11] 10^9/L; Lymphocytes: 2.02 [1.3 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 32.2 [22 - 52] %; Monocytes: 0.56 [0.3 - 0.8] 10^9/L; Monocytes/Leukocytes: 8.9 [5 - 12] %; NPTST075-BILIRUBIN DIRECT: 2 [0 - 7] UMOL/L; NPTST076-BILIRUBIN TOTAL: 5 [5 - 21] UMOL/L; NPTST102-C-REACTIVE PROTEIN: 57 [0 - 5] MG/L; NPTST143-CORRECTED CALCIUM: 2.59 [2.1 - 2.6] MMOL/L; NPTST224-GGT: 81 [5 - 29] U/L; NPTST305-LIPASE: 21 [0 - 60] U/L; NPTST312-MAGNESIUM: 0.73 [0.7 - 0.96] MMOL/L; NPTST375-PHOSPHATE: 1.07 [0.81 - 1.45] MMOL/L; NPTST395-PROTEIN TOTAL: 67 [60 - 80] G/L; NPTST485-UREA: 4.8 [2.8 - 7.1] MMOL/L; Neutrophils: 3.41 [1.8 - 5.4] 10^9/L; Neutrophils/Leukocytes: 54.5 [34 - 68] %; Platelets: 324 [140 - 440] 10^9/L; Potassium: 4.2 [3.5 - 5.1] MMOL/L; Sodium: 143 [135 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 661): Alanine Aminotransferase: 37 [0 - 25] U/L; Albumin: 30 [33 - 45] G/L; Alkaline Phosphatase: 164 [30 - 120] U/L; Basophils: 0.02 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 1] %; Calcium: 2.36 [2.1 - 2.6] MMOL/L; Chloride: 102 [97 - 106] MMOL/L; Creatinine: 61 [35 - 97] UMOL/L;

Eosinophils: 0.2 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 2.6 [0 - 5] %; Erythrocytes: 4.4 [3.8 - 5.2] 10^12/L; Hematocrit: 0.44 [0.35 - 0.47] FRACTION OF 1; Hemoglobin: 142 [120 - 160] G/L; Leukocytes: 7.6 [4.5 - 11] 10^9/L; Lymphocytes: 1.96 [1.3 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 25.7 [22 - 52] %; Monocytes: 0.64 [0.3 - 0.8] 10^9/L; Monocytes/Leukocytes: 8.4 [5 - 12] %; NPTST077-BILIRUBIN, DIRECT: 2 [0 - 7] UMOL/L; NPTST078-BILIRUBIN,TOTAL: 4 [5 - 21] UMOL/L; NPTST102-C-REACTIVE PROTEIN: 42 [0 - 5] MG/L; NPTST143-CORRECTED CALCIUM: 2.56 [2.1 - 2.6] MMOL/L; NPTST224-GGT: 81 [5 - 29] U/L; NPTST305-LIPASE: 31 [0 - 60] U/L; NPTST312-MAGNESIUM: 0.76 [0.7 - 0.96] MMOL/L; NPTST316-MCH: 32.2 [26 - 34] PG; NPTST317-MCHC: 321 [320 - 365] G/L; NPTST318-MCV: 100.5 [80 - 98] FL; NPTST333-MPV: 9.6 [9.4 - 12.4] FL; NPTST375-PHOSPHATE: 1 [0.81 - 1.45] MMOL/L; NPTST414-RDW: 13.7 [11.4 - 14.4] %; NPTST485-UREA: 5 [2.8 - 7.1] MMOL/L; Neutrophils: 4.8 [1.8 - 5.4] 10^9/L; Neutrophils/Leukocytes: 62.7 [34 - 68] %; Platelets: 353 [140 - 440] 10^9/L; Potassium: 4.1 [3.5 - 5.1] MMOL/L; Protein: 73 [60 - 80] G/L; Sodium: 145 [135 - 147] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 657): BLOOD NPTST083-BLOOD CULTURE LEFT ARM: Negative-NO ORGANISMS FOLLOWING 5 DAYS OF INCUBATION; BLOOD NPTST086-BLOOD CULTURE RIGHT ARM: Negative-NO ORGANISMS FOLLOWING 5 DAYS OF INCUBATION; OTHER PERICARDIAL FLUID NPTST204-FLUID CULTURE FOR ACID-FAST BAC: Negative-NO ACID-FAST BACILLI OBSERVED; OTHER PERICARDIAL FLUID NPTST205-FLUID FOR ANAEROBES: Negative-NO ANAEROBES ISOLATED; OTHER PERICARDIAL FLUID NPTST206-FLUID FOR CULTURE: Negative-NO ORGANISMS ISOLATED; [redacted]20[redacted] (RX DAY 661): OTHER MUCOSA NPTST238-HELICOBACTER PYLORI RAPID UREAS: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 653): CHEST X-RAY: NEW FINDING OF DIFFUSE CARDIAC ENLARGEMENT. THE POSSIBILITY OF A PERICARDIAL EFFUSION MAY BE CONSIDERED.; [redacted]20[redacted] (RX DAY 654): ECHOCARDIOGRAPHY: MODERATE-SIZED CIRCUMFERENTIAL PERICARDIAL EFFUSION WITH EARLY ECHOCARDIOGRAPHIC FEATURES OF TAMPONADE; [redacted]20[redacted] (RX DAY 655): CHEST X-RAY: NEW OPACITY IN THE LEFT LOWER LUNG ZONE ASSOCIATED WITH MILD PLEURAL EFFUSION. THE DIFFERENTIAL DIAGNOSIS INCLUDES ACTELECTASIS AND PNEUMONIA.; [redacted]20[redacted] (RX DAY 656): ABDOMINAL ULTRASOUND: CONGESTIVE HEPATOMEGALY IS SUSPECTED. NO EVIDENCE OF CHOLELITHIASIS/INTRAHEPATIC BILIARY DILATATION; [redacted]20[redacted] (RX DAY 657): ABDOMINAL X-RAY: FECAL RESIDUE AND GAS THROUGHOUT NONDISTENDED COLON. NO BOWEL OBSTRUCTION AND NO FREE AIR. NO ABNORMAL SOFT TISSUE MASSES OR CACLIFICATIONS; CHEST AP X-RAY: COMPARED TO PREVIOUS STUDY FROM THE SAME DAY. HEART REMAINS DIFFUSELY ENLARGED. SOME OF THE LINEAR ATELECTASIS IN THE LEFT MID TO LOWER LUNG HAS RESOLVED. A SMALLER PLEURAL EFFUSION IS SEEN ON THELEFT. NO NEW CONSOLIDATION OR ATELECTASIS. NO NEW ACUTE PROCESS OTHERWISE; CHEST X-RAY: PERSISTENT CARDIAC CONTOUR ENLARGEMENT IN THIS PATIENT WITH KNOWN PERICARDIAL EFFUSION, NOT SIGNIFICANTLY IMPROVED. A MODERATE LEFT-SIDED PLEURAL EFFUSION IS NOW PRESENT AND LINEAR DENSITIES IN THE MID TO LOWER LEFT LUNG MAY REPRESENT INCREASING ATELECTASIS IN ADDITION TO UNDERLYING SCARRING.; ECHOCARDIOGRAM-GUIDED PERICARDIOCENTESIS: PATIENT HAD CLINICAL SIGNS OF TAMPONADE. AFTER LOCALIZING THE SITE OF PUNCTURE ON THE LEFT PRECORDIUM. WE USED THE SELDINGER TECHNIQUE AND A PIGTAIL WAS INSERTED IN THE PERICARDIUM. WE MANAGED TO DRAIN 800 ML OF RED COLORED FLUID FROM THE PERICARDIUM. POST PERICARTIOCENTESIS, NO MORE PERICARDIAL EFFUSION WAS DOCUMENTED. NO COLLAPSE OF THE RIGHT VENTRICLE OR THE RIGHT ATRIUM WAS DOCUMENTED.THE LEFT VENTRICULAR EJECTION FRACTION WAS NORMAL. THERE ARE NO OBVIOUS VALVULAR ABNORMALITIES. SUCCESSFUL PERICARDIOCENTESIS UNDER ECHOCARDIOGRAPHY GUIDANCE. NO ORGANISMS FOUND IN FLUID; [redacted]20[redacted] (RX DAY 658): CHEST X-RAY: THE HEART REMAINS MINIMALLY DIFFUSELY ENLARGED. SINCE TH PREVIOUS EXAMINATION FROM THE PREVIOUS DAY, A SMALL LEFT PLEURAL EFFUSION STILL PERSISTS, MINIMALLY IMPROVED. THE ATELECTASIS IN THE LEFT LUNG BASE ALSO SHOWS SLIGHT IMPROVEMENT. THE LEFT LATERAL MIDLUNG ATELECTASIS PERSISTS. NO NEW AREAS OF CONSOLIDATION OR ATELECTASIS; [redacted]20[redacted] (RX DAY 661): CHEST/LIVER CT: MINIMAL PERICARDIAL EFFUSION ALONG THE RIGHT LOWER PERICARDIAL RECESS. MAXIMUM FLUID THICKNESS MEASURES APPROX 14 MM. MINIMAL LEFT-SIDED PLEURAL EFFUSION WITH LEFT BASAL SUBSEGMENTAL ATELECTASIS. INFERIOR, LINGULA SUBSEGMENTAL ATELECTASIS IS ALSO PRESENT. VISUALIZED UPPER LUNG FIELDS SHOW NO ABNORMAL OPACITY. MULTIPLE SMALL AXILLARY/MEDIASTINAL LYMPH NODES ARE NOTED WITH FATTY HILUM, THOUGHT TOBE REACTIVE. NO DESTRUCTIVE LESIONS ARE NOTED IN BONY THORACIC CAGE. FATTY LIVER IS NOTED. NO LESIONS NOTED IN THE SPLEEN, PANCREAS, ADRENAL GLANDS AND BOTH KIDNEYS; GASTROSCOPY: EROSIVE GASTRITIS DIAGNOSED; [redacted]20[redacted] (RX DAY 662):

ECHOCARDIOGRAPHY: FOLLOW-UP FOR PERICARDIAL EFFUSION. ACOUSTIC WINDOWS WERE SATISFACTORY. LEFT VENTRICULAR CAVITY NORMAL IN SIZE AND SYSTOLIC FUNCTION. NO REGIONAL WALL MOTION ABNORMALITIES, WALL THICKNESS NORMAL. DIASTOLIC FUNCTION INDETERMINATE. LEFT ATRIUM MILDLY DILATED. RIGHT CARDIAC CHAMBERS NORMAL IN SIZE WITH NORMAL RIGHT VENTRICULAR SYSTOLIC FUNCTION. ALL CARDIAC VALVES NORMAL IN MORPHOLOGY AND FUNCTION. TRIVIAL MITRAL REGURGITATION. NO TRICUSPID REGURGITATION. ASCENDING AORTA, AORTIC ROOT AND ARCH NORMAL IN SIZE. ABDOMINAL AORTA AND PULMONARY ARTERY NOT WELL VISUALIZED. IVC NORMAL IN SIZE.; ECHOCARDIOGRAPHY: (CONTINUED FROM PREVIOUS LINE): THERE IS A TRIVIAL PERICARDIAL EFFUSION WELL VISUALIZED ANTERIORLY. NO INTRACARDIAC MASS, THROMBUS OR SHUNT. IMPRESSION: 1. TRIVIAL PERICARDIAL EFFUSION WELL VISUALIZED ANTERIORLY 2.NO SIGNIFICANT VALVULAR ABNORMALITY 3. NORMAL LEFT AND RIGHT VE

AE Stopped Rx Day	662
Duration of AE	10 DAYS
Severity	Severe
Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	LONG TERM SMOKER, PSORIATIC ARTHRITIS
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。本被験者はカナダの 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，心膜炎の事象を発現した。

Event 2 の臨床経過：

関連する病歴は，局面型乾癬，嚥下障害，胃内視鏡検査，乾癬性関節炎，閉経，紙巻タバコ喫煙者（1 日 0.5 箱を 30 年間），現飲酒者（1 日 2 杯未満），軽度の慢性閉塞性肺疾患，胃炎，脳卒中の家族歴及び離婚であった。

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

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。被験者は入院前日からの咽喉痛及び胸痛のため来院した。特に深呼吸時に激しい痛みがあった。医療記録によると，入院理由は，左胸水を伴う心膜炎（非重篤），うっ血性肝腫大及びうっ血性心不全の諸症状（非重篤）であった。入院中，基礎治療薬の投与は継続された。20[redacted] 年 [redacted] 月 [redacted] 日，心エコーガイド下で穿刺が行われ，800 mL の胸水が除去された。除去された胸水に病原菌は認められなかった。バイタルサインは入院期間を通して正常であった。心嚢水やタンポナーデは認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，胃内視鏡検査が行われ，びらん性胃炎（非重篤）と診断された。血液生化学検査及び血液学的検査の結果は正常であった。除去された心嚢液に病原菌は認められなかった。CT スキャン検査で，ごくわずかな左側胸水（非重篤），下縦舌筋，小腋窩リンパ節及び縦隔リンパ節の左亜区域性無気肺（非重篤）並びに脂肪肝（非重篤）が認められた。アルカリホスファターゼ，γGT 及び ALT がわずかに増加していたが，いずれも心不全によるうっ血に起因するものである可能性が最も高かった。C-反応性蛋白も高値であったが，これは当初から高値であった。ウイルス培養，抗酸性桿菌培養及び血液培養の結果はまだ出ていなかった。直近の心電図検査では，洞調律は正常であり，非特異的 T 波変化が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，心エコー再検査の結果は正常であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。担当医の判断では，心膜炎に続発した心嚢液貯留は乾癬性関節炎によるものである可能性が最も高かった。

投与された薬剤は，コルヒチン及び asa であった。

Causality for ABT-494 (Blinded)

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1) Pericarditis (10034484) (Pericarditis (10034484)) [v.22.0] [10034484]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of PERICARDITIS

- Investigator: Long term smoker, psoriatic arthritis

- AbbVie: Given diagnostic testing has not confirmed any identifiable cause of the pericarditis and frequently these cases are presumed to have a viral or autoimmune etiology, the event is more likely related to sore throat symptoms a day prior to admission with underlying autoimmune systemic inflammatory disease as an additional risk factor.

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		

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: 3.9 [1.8 - 7] 10^9/L; Monocytes: 0.44 [0.1 - 0.85] 10^9/L; NPTST053-APTT: 37.1 [22.6 - 28.6] SEC; NPTST396-PROTHROMBIN: 23.7 [11 - 13] SEC; NPTST470-TROPONIN: 0.01 [0 - 0.03] UG/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，アトルバスタチン及び asa 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.22.0] [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
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]20[redacted] / 1	[redacted]20[redacted] / 168	168
ADA	40MG	SC	EOW	[redacted]20[redacted] / 169	[redacted]20[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]20[redacted] / 32
Age at AE Onset	5[redacted]

Laboratory Testing
[redacted]20[redacted] (RX DAY 197): NPTST119-CEA: 6.9 [NOT REPORTED - 5] MG/ML

Microbiology
NOT REPORTED

SAE Supplemental Procedure
[redacted]20[redacted] (RX DAY 169): ENDOMETRIAL CYTOLOGY: UTERINE CANCER CLASS5; [redacted]20[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]20[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]20[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		

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

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 22 U/L (normal 0 to 32)

[redacted] **20[redacted] BLOOD PRESSURE:** During event: 132/78 mmHg

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

[redacted] **20[redacted] CREATININE:** 52 MCMOL/L (normal 44 to 80)

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

[redacted] **20[redacted] ECG:** NORMAL

[redacted] **20[redacted] HEMOGLOBIN:** 12.8 G/DL (normal 11.5 to 16)

[redacted] **20[redacted] PLATELET COUNT:** 331 X10**9/L (normal 150 to 400)

[redacted] **20[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	NOT REPORTED
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	NOT REPORTED
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 617	NOT REPORTED
TERRA-CORTRIL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 617	NOT REPORTED
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
PREGABALIN	25 mg	BID	Y-M: 20[redacted] / 619 Y-M: 20[redacted] / 623

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	50

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: 0.19 [0.96 - 4.75] 10^9/L; NPTST154-CRP: 1.66 [0 - 0.14] MG/DL; NPTST180-E-GFR: 85.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 3.3 [2.4 - 7.56] 10^9/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: 0.38 [0.96 - 4.75] 10^9/L; NPTST154-CRP: 7.81 [0 - 0.14] MG/DL; NPTST182-EGFR: 84.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 2.36 [2.4 - 7.56] 10^9/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: 0.76 [0.96 - 4.75] 10^9/L; NPTST154-CRP: 13.03 [0 - 0.14] MG/DL; NPTST182-EGFR: 85.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 3.14 [2.4 - 7.56] 10^9/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: 0.71 [0.96 - 4.75] 10^9/L; NPTST154-CRP: 1.11 [0 - 0.14] MG/DL; Neutrophils: 0.83 [2.4 - 7.56] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 541): SPUTUM NPTST450-STREPTOCOCCUS PNEUMONIAE: Positive-3+; [redacted]20[redacted] (RX DAY 543): URINE NPTST488-URINARY LEGIONELLA: Negative; URINE NPTST489-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): NPTST288-INFLUENZA TEST: NEGATIVE [NOT REPORTED - NOT REPORTED] ONCE

Microbiology

[redacted]20[redacted] (RX DAY 617): OTHER VESICULAR FLUID NPTST172-DERMAQUICK: Positive-SHINGLES

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
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] 20[redacted] **ALANINE AMINO TRANSFERASE:** 12 U/L (normal 10 to 12)

[redacted] 20[redacted] **ALANINE AMINO TRANSFERASE:** 11 U/L (normal 10 to 12)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 12 U/L (normal 10 to 42)

[redacted] 20[redacted] **ASPARATATE AMINO TRANSFERASE:** 25 U/L (normal 13 to 30)

[redacted] 20[redacted] **ASPARATATE AMINO TRANSFERASE:** 26 U/L (normal 13 to 30)

[redacted] 20[redacted] **ASPARATATE AMINO TRANSFERASE:** 16 U/L (normal 13 to 30)

[redacted] 20[redacted] **CHEST CT:** NO ABNORMAL FINDING. DIAGNOSED AS BRONCHITIS

[redacted] 20[redacted] **CHEST X-RAY:** SUSPECTED UPPER RESPIRATORY INFLAMMATION

[redacted] 20[redacted] **CHEST X-RAY:** SUSPECTED UPPER RESPIRATORY INFLAMMATION

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

[redacted] 20[redacted] **CHEST X-RAY (WEEK 56):** Normal

[redacted] 20[redacted] **CHEST XRAY:** no change

[redacted] 20[redacted] **CRP:** 1.66 mg/dL (normal 0 to 0.14)

[redacted] 20[redacted] **CRP:** 7.81 mg/dL (normal 0 to 0.14)

[redacted] 20[redacted] **CRP:** 13.03 mg/dL (normal 0 to 0.14)

[redacted] 20[redacted] **CRP:** 1.11 mg/dL (normal 0 to 0.14)

[redacted] 20[redacted] **E-GFR:** 85.2 no units

[redacted] 20[redacted] **E-GFR:** 85.2 no units

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 1.9 x10*2/uL

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 3.8 x10*2/uL

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 7.6 x10*2/uL

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 7.1 x10*2/uL

[redacted] 20[redacted] **NEUTROPHILS ABS:** 33.0 x10*2/uL

[redacted] 20[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，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。

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

The patient's past medications include:

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.22.1] [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

Event #1: Serious Adverse Event

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

Laboratory Testing

[redacted] (RX DAY 553): NPTST125-CK-MB: 14 [0 - 24] U/L; NPTST144-CPK: 140 [20 - 170] IU/L; [redacted] (RX DAY 554): NPTST125-CK-MB: 22 [0 - 24] U/L; NPTST144-CPK: 141 [20 - 170] IU/L; [redacted] (RX DAY 613): NPTST125-CK-MB: 13 [0 - 24] U/L; NPTST144-CPK: 178 [20 - 170] IU/L; NPTST478-TROPONIN-T: 5.4 [0 - 14] NG/L; [redacted] (RX DAY 614): NPTST125-CK-MB: 23 [0 - 24] U/L; NPTST144-CPK: 164 [20 - 170] IU/L; NPTST478-TROPONIN-T: 8.2 [0 - 14] NG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted] (RX DAY 554): TREADMILL EXERCISE TEST (TET): 6MIN32SEC, 85% (141/165), II, II, AVF, V4-6.; [redacted] (RX DAY 561): ECG REPORT: NORMAL SINUS RHYTHM NORMAL ECG; [redacted] (RX DAY 562): ULTRASOUND CARDIOGRAM(UCG): LVEF 65 % BY M-MODE, NO REGIONAL WALL MOTION ABNORMALITY.; [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] (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 [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，アスピリン，アトルバスタチン，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
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: [redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: [redacted]
CLOBETASOL	1 OTHER: TOPICAL	BID	Y-M: [redacted] / -245
CLOBETASOL	7.5 mL	PRN	Y-M: [redacted] / -245
BISOPROLOL	1.25 mg	QD	Y-M: [redacted] / -139
PIRACETAM	1200 mg	QD	Y-M: [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: [redacted]	NOT REPORTED
FOLIC ACID	5 mg	EVERY WEEK	Y-M: [redacted]	NOT REPORTED
PIRACETAM	1200 mg	QD	Y-M: [redacted] / -139	NOT REPORTED
BISOPROLOL	1.25 mg	QD	Y-M: [redacted] / -139	Y-M: [redacted] / 213
TEARS NATURALE	1 gtt	OTHER: ONCE	Y-M: [redacted] / 128	Y-M: [redacted] / 128
ATORVASTATIN	10 mg	OTHER: HS	Y-M: [redacted] / 129	Y-M: [redacted] / 156
NICAMETATE	50 mg	BID	Y-M: [redacted] / 162	NOT REPORTED
PARAFON	1 OTHER: TABLET	TID	Y-M: [redacted] / 162	NOT REPORTED
PARACETAMOL	500 mg	QID	Y-M: [redacted] / 162	Y-M: [redacted] / 197
ATORVASTATIN	20 mg	OTHER: HS	Y-M: [redacted] / 178	Y-M: [redacted] / 184
TEARS NATURALE	1 gtt	QID	Y-M: [redacted] / 213	ONGOING
CARTEOLOL	1 gtt	QD	Y-M: [redacted] / 213	Y-M: [redacted] / 244
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: [redacted] / 214	NOT REPORTED
ATORVASTATIN	20 mg	OTHER: HS	Y-M: [redacted] / 214	NOT REPORTED
NICORANDIL	5 mg	BID	Y-M: [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	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: 0 [0 - 0] G/L; LDL Cholesterol: 86 [NOT REPORTED - 130] mg/dL; Leukocytes: 10.8 [3.5 - 90.6] 10^9/L; NPTST182-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] %; NPTST267-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] %; NPTST012-ACTIVATED PARTIAL THROMBOPLASTI: 26.5 [NOT REPORTED - 33.8] sec; NPTST260-HIGH SENSITIVE CRP: 6.8 [0 - 3] MG/L; NPTST398-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; NPTST266-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，プラビックス及び bokey EM であった。

Causality for ABT-494 (Blinded)

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1) Coronary artery disease (10011078) (Coronary artery disease (10011078)) [v.21.1] [10011078]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (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] **20[redacted] ALANINE AMINO TRANSFERASE:** 25 U/L (normal 0 to 41)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 16.8 mg/dL (normal 7 to 25)

[redacted] **20[redacted] CHEST X-RAY:** NORMAL HEART SIZE. MILD AORTIC WALL CALCIFICATION. BILATERAL APICAL PLEURAL THICKENING. SHARP BILATERAL COSTOPHRENIC ANGLES.

[redacted] **20[redacted] CHOLESTEROL:** 147 mg/dL (normal >200)

[redacted] **20[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] **20[redacted] CREATININE:** 0.6 mg/dL (normal 0.6 to 1.3)

[redacted] **20[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] **20[redacted] ECG:** SINUS RHYTHM WITH PREMATURE VENTRICULAR COMPLEXES

[redacted] **20[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

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

[redacted] **20[redacted] HDL CHOLESTEROL:** 40 mg/dL

[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 >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] 201[redacted]

WEIMOK F.C. for PROPHYLAXIS PAINKILLER SIDE EFFECT ([redacted] 20[redacted] - [redacted] 201[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] **ACTIVATED PARTIAL THROMBOPLASTIN TIME:** 26.5 SEC (normal 24.6 to 33.8)

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

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

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

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

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

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

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

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

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

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

[redacted] **ERYTHROCYTE SEDIMENTATION RATE:** 12 mm/h (normal <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	
ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 392	168	

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
METHYLPREDNISOLONE	4 mg	OTHER: QDPRN	Y-M: 20[redacted] / 252	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
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
BUTENAFINE	1/10 %	QD	Y-M: 20[redacted] / 546	NOT REPORTED
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / 546	NOT REPORTED
METHYLPREDNISOLONE	4 mg	BID	Y-M: 20[redacted] / 546	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 20[redacted]

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，orotoretin，weil，アセトアミノフェン，テトラサイクリン，プレガバリン，塩化ナトリウム，アシクロビル及びバラシクロビルであった。

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] 201[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] **CXR:** NO INTERVAL CHANGE COMPARED TO CXR, PERFORMED ON 2019.07.03

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

[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
肺炎	X			X
出血性十二指腸潰瘍	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
LEFLUNOMIDE	10 mg	QD	Y-M: 20[redacted] / 113	NOT REPORTED
SALACTOL	167/167 OTHER: MG/G	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 141
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

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+ [NOT REPORTED - NOT REPORTED] mg/dL; NPTST102-C-REACTIVE PROTEIN: 3.4 [0 - 1] MG/DL; NPTST134-COLD HEMAGGLUTININ: 128 X [NOT REPORTED - NOT REPORTED] NA; NPTST189-EPSTEIN-BARR VIRUS CAPSID ANTIG: + [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST381-PNEUMOCOCCUS RAPID SCREEN: - [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 53): NPTST337-MYCOPLASMA PNEUMONIA AB TEST: + [NOT REPORTED - NOT REPORTED] NA

Microbiology

[redacted]20[redacted] (RX DAY 52): BLOOD NPTST018-AEROBIC BLOOD CULTURE: Negative-NA; SPUTUM NPTST441-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] 20[redacted], [redacted] 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] %; NPTST376-PHOSPHORUS: 0.9 [0.97 - 1.62] MMOL/L; NPTST379-PLATELET DISTRIBUTION WIDTH: 9.1 [10 - 18.5] %; NPTST413-RBC VOLUME DISTRIBUTING WIDTH-S: 48.6 [39 - 46] FL; NPTST457-THE RATIO OF ASPARTATE AMINO TR: 1.7 [0.5 - 1.5] NA; NPTST462-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] %;

NPTST376-PHOSPHORUS: 0.9 [0.97 - 1.62] MMOL/L; NPTST379-PLATELET DISTRIBUTION WIDTH: 9.1 [10 - 18.5] %; NPTST413-RBC VOLUME DISTRIBUTING WIDTH-S: 48.6 [39 - 46] FL; NPTST457-THE RATIO OF ASPARTATE AMINO TR: 1.7 [0.5 - 1.5] NA; NPTST462-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; NPTST167-D-DIMER: 7.93 [0 - 0.5] UG/ML; NPTST198-FDP: 28 [0 - 5] UG/ML; NPTST296-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; NPTST014-ADENOSINE DEAMINASE: 54 [0 - 20] U/L; NPTST154-CRP: 149.4 [0 - 10] MG/L; NPTST224-GGT: 92 [0 - 50] IU/L; NPTST267-HSCRP: 42.98 [0 - 3] MG/L; NPTST430-SERUM FERRITIN: 1681.83 [21.8 - 274.66] NG/ML; Neutrophils: 1.74 [2 - 7] 10^9/L; [redacted]20[redacted] (RX DAY 291): NPTST073-BETA D GLUCAN: 16 [0 - 100] PG/ML; NPTST264-HIV: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; NPTST453-TB-AB-IGG: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; NPTST454-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; NPTST154-CRP: 97.5 [0 - 10] U/L; NPTST224-GGT: 110 [0 - 50] IU/L; NPTST386-PREALBUMIN: 94 [160 - 450] MG/L; NPTST485-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): NPTST485-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 NPTST068-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; BLOOD NPTST068-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; [redacted]20[redacted] (RX DAY 297): STOOL NPTST141-CONVENTIONAL STOOL OCCULT BLOOD: Negative; [redacted]20[redacted] (RX DAY 301): SPUTUM NPTST067-BACTERIAL CULTURE AND CHEMOSENS: Negative; [redacted]20[redacted] (RX DAY 305): CEREBROSPINAL FLUID

NPTST068-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; [redacted]20[redacted] (RX DAY 310): BLOOD NPTST068-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; [redacted]20[redacted] (RX DAY 311): SPUTUM NPTST068-BACTERIAL CULTURE+CHEMOSENSITIV: Positive-STOMATOCCUS++ STREPTOCOCCUS VIRIDANS++; [redacted]20[redacted] (RX DAY 313): CEREBROSPINAL FLUID NPTST033-ANAEROBIC CULTURE: Negative; CEREBROSPINAL FLUID NPTST068-BACTERIAL CULTURE+CHEMOSENSITIV: Negative; [redacted]20[redacted] (RX DAY 317): BLOOD NPTST068-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，炭酸カルシウム D3 粒子製剤，ブプレノルフィン経皮吸収型製剤及び henggu gushangyu heji（タイツリオウギ，ニンジン，コウカ）であった。

Causality for ABT-494 (inded)

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1) Comminuted fracture (10052614) (Comminuted fracture (10052614)) [v.22.0] [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.22.0] [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 ABT-494 (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] **AO 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] **20[redacted] ABDOMEN CT:** 1. CONSIDER MULTIPLE INTRAPERITONEAL INFARCTS; 2. PROSTATE CALCIFICATION; 3. PARTIAL THORACIC VERTEBRA AND RIGHT RIB BONE DESTRUCTION.

[redacted] **20[redacted] B ULTRASOUND OF PROSTATE:** PROSTATE ENLARGEMENT AND CALCIFICATION OF THE FORMATION OF LESIONS, PROSTATE CYSTS

[redacted] **20[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] **20[redacted] B-MODE ULTRASOUND:** GALLBLADDER STONE, CHOLECYSTITIS CAN, ACCESSORY SPLEEN

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

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

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

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

[redacted] **20[redacted] BONE DNA BIOPSY:** TB TEST NEGATIVE

[redacted] **20[redacted] BONE MINERAL DENSITY:** Osteoporosis

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

[redacted] **20[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		

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	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -86	NOT REPORTED
ISONIAZID	0.3 g	QD	Y-M: 20[redacted] / -19	NOT REPORTED
AMBROXOL	30 mg	QD	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 312
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 315
AMBROXOL	30 mg	BID	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

Event #1: Serious Adverse Event

Event Description LEFT SPONTANEOUS PNEUMOTHORAX

Preferred term 自然気胸

AE Onset Date / Rx Day [redacted]20[redacted] / 309

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; NPTST174-DETERMINATION OF SERUM HYDROXYB: 0.72 [0.02 - 0.27] MMOL/L; NPTST286-INFLUENZA A ANTIGEN TESTING: NEGATIVE [NOT REPORTED - NOT REPORTED] NEGATIVE; NPTST287-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] %; NPTST061-B B E ANTIBODY SEMI - QUANTITAT: 1.640 [NOT REPORTED - NOT REPORTED] COI; NPTST137-COMBINED DETECTION OF HIV ANTIG: 0.19 [0 - 0.9] COI; NPTST165-D - DIMER: 0.63 [NOT REPORTED - NOT REPORTED] mg/L; NPTST236-HCV: 0.04 [0 - 0.9] COI; NPTST245-HEPATITIS B CORE ANTIBODY SEMI: 2.280 [NOT REPORTED - NOT REPORTED] COI; NPTST247-HEPATITIS B E ANTIGEN SEMI - QU: 0.11 [0 - 1] COI; NPTST251-HEPATITIS B SURFACE ANTIBODY SE: ?2.000 [0 - 10] IU/L; NPTST252-HEPATITIS B SURFACE ANTIGEN SEM: 0.46 [0 - 0.9] COI; NPTST468-TREPONEMA PALLIDUM ANTIBODY: 0.1 [0 - 1] S/CO; Neutrophils/Leukocytes: 77.4 [40 - 75] %; [redacted]20[redacted] (RX DAY 315): NPTST162-CYTOMEGALOVIRUS ANTIBODY IGG: 125 [NOT REPORTED - NOT REPORTED] 099,U/ML; NPTST163-CYTOMEGALOVIRUS ANTIBODY IGM: 5.10 [NOT REPORTED - NOT REPORTED] 099,AU/ML

Microbiology

[redacted]20[redacted] (RX DAY 312): OTHER NA NPTST426-RHINOVIRUS: Positive-TEST POSITIVE; SPUTUM NPTST436-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 NPTST436-SMEAR FOR BACTERIA + SMEAR FOR: Positive-SMEAR GRAM STAINING: NO FUNGUS DETECTED LESS G-BACILLI (++) OLIGG + COCCI (+) OLIGG + STREPTOCOCCUS (+); SPUTUM NPTST438-SMEAR FOR MYCOBACTERIA: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE DETECTED; SPUTUM NPTST442-SPUTUM. CULTURE OF PHARYNGEAL B: Negative-NORMAL MIXED FLORA, NO HAEMOPHILUS ISOLATED; [redacted]20[redacted] (RX DAY 315): BLOOD NPTST451-TB ANTIBODY TEST: Negative; [redacted]20[redacted] (RX DAY 316): SPUTUM NPTST159-CULTURE OF SPUTUM FUNGI: Negative-NONFUNGAL GROWTH; SPUTUM NPTST436-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 NPTST439-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	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，乾癬性関節炎，活動性局面型乾癬，貧血，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，被験者は左胸痛を伴って悪化した咳嗽を発現した。また，胸部絞扼感を伴う持続的な鈍痛も発現した。鈍痛は午前中によりひどく，午後や夕方には消失し，運動後にわ

ずかに「空気が薄く感じられ」，少量の白色泡沫様喀痰，しつこい風邪及び発熱を伴う咳嗽の症状が見られた。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。

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

The patient's past medications include:

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

SULFASALAZINE for PSORIATITHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

The patient took TOTAL GLUCOSIDES OF PAEONY CAPSULES, 600 mg BID orally from [redacted] 20[redacted] to [redacted] 20[redacted] for Psoriatic arthritis.

Causality for UPADACITINIB (Blinded)

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1) Pneumothorax spontaneous (10035763) (Pneumothorax spontaneous (10035763)) [v.22.1] [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 also is 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:** Blood: 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 (+).

[redacted] **20[redacted] SPUTUM TEST:** Positive: (Smear for bacteria + fungi): Smear gram staining: no fungus detected Less g-bacilli (++) Oligg + cocci (+) Oligg + streptococcus (+)

[redacted] **20[redacted] SPUTUM TEST:** Positive: smear for bacteria and fungi: 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:** Negative (Smear mycobacterium): Smear acid-fast staining: No acid-fast bacilli were detected.

[redacted] **20[redacted] SPUTUM TEST:** Negative (Culture of sputum fungi): 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	NOT REPORTED
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -119	NOT REPORTED
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / 113	NOT REPORTED
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1.4 g	TID	Y-M: 20[redacted] / 197	ONGOING
CEFTIZOXIME	2 g	BID	Y-M: 20[redacted] / 208	ONGOING
LEVOFLOXACIN;SODIUM CHLORIDE	0.3 g	BID	Y-M: 20[redacted] / 208	ONGOING
PYRIDOXINE	0.1 g	QD	Y-M: 20[redacted] / 208	NOT REPORTED

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; NPTST008-ABNORMAL LYMPHOCYTE RATIO: 2.4 [0 - 2] %; NPTST028-ALT: 125 [5 - 40] U/L; NPTST058-AST: 75 [8 - 45] U/L; NPTST176-DIRECT BILIRUBIN: 12.55 [0 - 6.8] UMOL/L; NPTST270-HYPERSENSITIVE C-REACTIVE PROTE: 1.1 [1 - 1] MG/L; NPTST285-INDIRECT BILIRUBIN: 23.17 [4 - 18] UMOL/L; NPTST322-MEAN ERYTHROCYTE HEMOGLOBIN CON: 314 [320 - 360] G/L; NPTST447-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

Microbiology

[redacted]20[redacted] (RX DAY 206): BLOOD NPTST467-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	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，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，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。

投与された薬剤は，cefuroxime sodium，レボフロキサシン塩酸塩，塩化ナトリウム注射剤及び jie shi tong pian であった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Urinary tract infection (10046571) (Urinary tract infection (10046571)) [v.22.1] [10046571]

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

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

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

[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)

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] / 64	64

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	BID	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 67
ASCORBIC ACID	2 g	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 70
CEFMETAZOLE	2 g	OTHER: EVERY 12H	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 70
DIGNOWELL	1 g	OTHER: (APPLY THE AFFECTED AREA IF NECESSARY)	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67

GLYCYRRHIZA GLABRA	50 mg	QD	Y-M: 20[redacted]- [redacted] / 67	Y-M: 20[redacted]- / 67
HALOMETASONE	0.5 g	OTHER: APPLY THE AFFECTED AREA IF NECESSARY	Y-M: 20[redacted]- [redacted] / 67	Y-M: 20[redacted]- / 67
ACETYLSALICYLIC ACID	1.8 g	QD	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- / 68
CAFFEIC ACID	0.3 g	QD	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- / 68
HYDROCORTISONE	0.1 g	QD	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- / 68
LEUCOGEN	20 mg	QD	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- / 68
VERAMID	2 mL	QD	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- / 68
CALCIUM GLUCONATE	1 g	QD	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- / 70
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- / 70
POTASSIUM	10 mL	QD	Y-M: 20[redacted]- [redacted] / 68	Y-M: 20[redacted]- / 70
NAPROXEN	100 mg	QD	Y-M: 20[redacted]- [redacted] / 71	Y-M: 20[redacted]- / 71
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 mL	QD	Y-M: 20[redacted]- [redacted] / 71	Y-M: 20[redacted]- / 72
VERAMID	2 mL	QD	Y-M: 20[redacted]- [redacted] / 71	Y-M: 20[redacted]- / 72
MEROPENEM	500 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted]- [redacted] / 72	Y-M: 20[redacted]- / 73
GANCICLOVIR	250 mg	OTHER: EVERY 12 HOURS	Y-M: 20[redacted]- [redacted] / 72	Y-M: 20[redacted]- / 86
VORICONAZOLE	400 mg	OTHER: EVERY 12 HOURS	Y-M: 20[redacted]- [redacted] / 73	Y-M: 20[redacted]- / 74
MANNITOL	125 mL	OTHER: EVERY 12 HOURS	Y-M: 20[redacted]- [redacted] / 73	Y-M: 20[redacted]- / 82
MEROPENEM	1000 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted]- [redacted] / 73	Y-M: 20[redacted]- / 82
SULFAMETHOXAZOLE	0.8 g	BID	Y-M: 20[redacted]- [redacted] / 74	Y-M: 20[redacted]- / 75
ASCORBIC ACID	3 g	QD	Y-M: 20[redacted]- [redacted] / 74	Y-M: 20[redacted]- / 82
GLUCOSE	500 mL	QD	Y-M: 20[redacted]- [redacted] / 74	Y-M: 20[redacted]- / 82
SULFAMETHOXAZOLE	0.8 g	TID	Y-M: 20[redacted]- [redacted] / 75	Y-M: 20[redacted]- / 80
PHOSPHATIDYL CHOLINE	15 mL	QD	Y-M: 20[redacted]- [redacted] / 76	Y-M: 20[redacted]- / 87
IMMUNOGLOBULIN HUMAN NORMAL	10 g	QD	Y-M: 20[redacted]- [redacted] / 77	Y-M: 20[redacted]- / 85
SULPERAZON	3 g	OTHER: EVERY 12 HOURS	Y-M: 20[redacted]- [redacted] / 82	Y-M: 20[redacted]- / 87

Event #2: 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] / 60
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] %; NPTST020-AFP? ALPHA FETOPROTEIN?: ?0.24 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST053-APTT: 33.8 [20 - 40] SEC; NPTST055-ASO?ANTI-STREPTOLYSIN "O ?: 142 [0 - 200] IU/ML; NPTST064-BACT?BACTERIA?: 1 [0 - 7] 099,/UL; NPTST091-BNP: 40 [NOT REPORTED - NOT REPORTED] 099,PG/ML; NPTST099-BYST: 0 [0 - 1] 099,/UL; NPTST106-CA-125: 12.96 [NOT REPORTED - NOT REPORTED] 099,U/ML; NPTST107-CA-153: 5.69 [NOT REPORTED - NOT REPORTED] 099,U/ML; NPTST108-CA-199: 8.25 [NOT REPORTED - NOT REPORTED] 099,U/ML; NPTST109-CA-242: 3.08 [NOT REPORTED - NOT REPORTED] 099,U/ML; NPTST120-CEA?CARCINOEMBRYONIC ANTIGEN?: 0.98 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST125-CK-MB: 23 [NOT REPORTED - NOT REPORTED] U/L; NPTST131-CO2: 25.1 [22 - 29] MMOL/L; NPTST136-COLOR, CHARACTER, LARVAE EGGS,: NOT DETECTED [NOT REPORTED - NOT REPORTED] NA; NPTST154-CRP: 100.9 [0 - 10] MG/L; NPTST169-DBIL: 3.8 [0 - 8] UMOL/L; NPTST170-DD? D-DIMER?: 1.1 [0 - 1.5] 099,UG/ML; NPTST196-FBG?FIBRINOGEN?: 3.62 [2 - 4] G/L; NPTST197-FBIL: 15.4 [1.7 - 17] UMOL/L; NPTST199-FDP?FIBRINOGEN DEGRADATION PROD: 3.8 [0 - 5] UG/ML; NPTST207-FPSA?FREE PROSTATE SPECIFIC ANT: 0.07 [0 - 1.04] NG/ML; NPTST224-GGT: 107 [5 - 54] U/L; NPTST225-GLOBULIN: 28.1 [20 - 35] G/L; NPTST234-HBDH?A-HYDROXYBUTYRATE DEHYDROG: 177 [90 - 180] U/L; NPTST259-HGH?HUMAN GROWTH HORMONE?: ?0.01 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST268-HYAL?HYALINE CAST?: 0 [0 - 1] 099,/HPF; NPTST300-LDH: 323 [109 - 250] U/L; NPTST313-MALB(MICROALBUMIN): NEGATIVE [NOT REPORTED - NOT REPORTED] 099,NEGATIVE; NPTST316-MCH: 31 [27 - 34] PG; NPTST320-MEAN CORPUSCULAR HEMOGLOBIN CON: 337 [316 - 354] G/L; NPTST321-MEAN CORPUSCULAR VOLUME: 92 [82 - 100] FL; NPTST325-MG?MAGNESIUM?: 0.78 [0.65 - 1.1] MMOL/L; NPTST336-MUCS?VISCOSE RAYON?: 14 [0 - 28] 099,/UL; NPTST348-NSE?NEURONE SPECIFIC ENOLASE?: 2.91 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST349-NSE?NON-SQUAMOUS EPITHELIAL CEL: 0 [0 - 6] 099,/UL; NPTST357-OSM: 275.34 [275 - 295] 099,MOSM/KG; NPTST387-PROCALCITONIN: 0.63 [0 - 0.5] NG/ML; NPTST401-PSA: 0.13 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST402-PT: 13.2 [9 - 14] SEC; NPTST419-RED BLOOD CELL DISTRIBUTION WID: 50.8 [35 - 56] FL; NPTST425-RF?RHEUMATOID FACTOR?: 9.9 [0 - 20] IU/ML; NPTST431-SF?FERRITIN?: ?600.00 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST443-SQEP?SQUAMOUS EPITHELIAL CELL?: 1 [0 - 28] 099,/UL; NPTST481-TT?THROMBIN TIME?: 16.7 [14 - 21] SEC; NPTST483-UNCX?UNCLASSIFIED CRYSTALLIZATI: 0 [0 - 28] 099,/UL; NPTST485-UREA: 4 [2.1 - 7.2] MMOL/L; NPTST496-VARIATION COEFFICIENT OF ERYTHR: 15.7 [11.5 - 14.5] %; NPTST497-VC: ?=5.7 [NOT REPORTED - NOT REPORTED] 099,NA; NPTST503-WHITE BLOOD CELL GROUP: 0 [0 - 2] 099,/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: 38 [40 - 55] G/L; Albumin: 50 [56 - 66] 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; NPTST024-ALPHA 1: 7.1 [2.9 - 4.9] %; NPTST056-ASPERGILLUS GALACTOMANNAN: 0.04 [NOT REPORTED - NOT REPORTED] 099,GMI; NPTST061-B B E

ANTIBODY SEMI - QUANTITAT: 0.820 [NOT REPORTED - NOT REPORTED] 099,POSITIVE; NPTST102-C-REACTIVE PROTEIN: 157 [NOT REPORTED - NOT REPORTED] mg/L; NPTST116-CD3 COUNT: 3333 [941 - 2226] 099,CELL/UL; NPTST117-CD4 COUNT: 1375 [471 - 1220] 099,CELL/UL; NPTST118-CD8 COUNT: 1905 [303 - 1003] 099,CELL/UL; NPTST124-CHLORINE: 122.5 [120 - 130] MMOL/L; NPTST137-COMBINED DETECTION OF HIV ANTIG: 0.19 [0 - 0.9] 099,COI; NPTST210-FUNGI 1, 3-B-D GLUCAN: 40.66 [NOT REPORTED - NOT REPORTED] 099,PG/ML; NPTST214-GAMMA: 22.5 [11.1 - 18.8] %; NPTST227-GLUTAMYL TRANSPEPTIDASE: 80 [NOT REPORTED - NOT REPORTED] IU/L; NPTST237-HCV-AB: 0.04 [0 - 0.9] 099,COI? NEGATIVE; NPTST245-HEPATITIS B CORE ANTIBODY SEMI: 0.008 [NOT REPORTED - NOT REPORTED] 099,POSITIVE; NPTST246-HEPATITIS B E ANTIBODY: POSITIVE [NOT REPORTED - NOT REPORTED] 099,COI; NPTST250-HEPATITIS B SURFACE ANTIBODY QU: ?2.000 [0 - 10] 099,NEGATIVE; NPTST252-HEPATITIS B SURFACE ANTIGEN SEM: 0.46 [0 - 0.9] 099,COI ?NEGATIVE; NPTST269-HYDROXYBUTYRATE DEHYDROGENASE: 248 [72 - 182] IU/L; NPTST280-IMMUNOGLOBULIN G: 16 [8 - 15.5] G/L; NPTST281-IMMUNOGLOBULIN M: 3170 [700 - 2200] MG/L; NPTST291-INTERLEUKIN 6: 148.2 [0 - 7] 099,PG/ML; NPTST294-KARYOCYTE: 0 [0 - 16] 099,10^6/L; NPTST298-LACTIC DEHYDROGENASE: 331 [110 - 220] IU/L; NPTST328-MICROPROTEIN: 0.5 [0.15 - 0.45] G/L; NPTST332-MONOVESICULAR VIRUS ANTIBODY I/: 2.65 [NOT REPORTED - NOT REPORTED] 099,INDEX; NPTST343-NON-WRINKLED ERYTHROCYTES: 100 [NOT REPORTED - NOT REPORTED] %; NPTST387-PROCALCITONIN: 0.19 [NOT REPORTED - NOT REPORTED] ng/mL; NPTST418-REAL-TIME FLUORESCENCE DETECTIO: 1.43*10^4 [NOT REPORTED - NOT REPORTED] 099,COPIES/ML/; NPTST460-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): NPTST154-CRP: 329 [NOT REPORTED - NOT REPORTED] mg/L; [redacted]20[redacted] (RX DAY 79): NPTST130-CMV-DNA: 2.28?10? [NOT REPORTED - NOT REPORTED] 099,COPIES/ML; [redacted]20[redacted] (RX DAY 85): NPTST154-CRP: 13.90 [NOT REPORTED - NOT REPORTED] mg/L; NPTST387-PROCALCITONIN: 0.19 [NOT REPORTED - NOT REPORTED] ng/mL; [redacted]20[redacted] (RX DAY 103): NPTST247-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 ACID-RESISTANT BACTERIA, NO FUNGUS, A SMALL AMOUNT OF G+ COCCI, WHITE BLOOD CELLS > 25/LP, EPITHELIAL CELLS > 10/LP WERE DETECTED; SPUTUM NPTST441-SPUTUM CULTURE: Negative-NORMAL MIXED FLORA; [redacted]20[redacted] (RX DAY 72): BLOOD NPTST032-ANAEROBIC BLOOD CULTURE: Negative-NO ANAEROBIC GROWTH; BLOOD NPTST080-BLOOD AND BONE MARROW CULTURE: Negative-NO BACTERIA AND FUNGUS GROWTH AFTER 5 DAYS CULTURE; CEREBROSPINAL FLUID NPTST209-FUNGAL CULTURE: Negative-NO FUNGUS GROWTH AT 2 WEEKS?CULTURE WAS EXTENDED TO 21 DAYS; CEREBROSPINAL FLUID NPTST284-INDIA INK STAIN: Negative-SMEAR INK STAINING: NO CRYPTOCOCCUS WAS FOUND; CEREBROSPINAL FLUID NPTST435-SMEAR FOR BACTERIA + FUNGUS: Negative-SMEAR GRAM STAINING: NO FUNGUS AND BACTERIA WERE DETECTED; CEREBROSPINAL FLUID NPTST437-SMEAR FOR DISMITOBACTERIUM: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE FOUND; CEREBROSPINAL FLUID NPTST439-SMEAR MYCOBACTERIUM: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE DETECTED; [redacted]20[redacted] (RX DAY 73): SPUTUM NPTST158-CULTURE OF SPUTUM AND PHARYNGEA: Negative-NORMAL MIXED BACTERIUM IS OVERGROWN LONG, DID NOT ISOLATE HAEMOPHILUS BACTERIUM; CEREBROSPINAL FLUID NPTST173-DETECTION OF CRYPTOCOCCAL ANTIG: Negative; SPUTUM NPTST434-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 NPTST439-SMEAR MYCOBACTERIUM: Negative-SMEAR ACID-FAST STAINING: NO ACID-FAST BACILLI WERE DETECTED; [redacted]20[redacted] (RX DAY 78): OTHER ALVEOLAR LAVAGE NPTST382-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

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 2 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，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，スルファメトキサゾール，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，柴胡注射剤，ナプロキセン，メロペネム，ボリコナゾール，スルペラゾン，セフメタゾール，lysine acetylsalicylate 及び aminophenazone／barbital であった。

The patient's past medications include:

XUESHANJINLUOHAN ZHITONGTUMOJI for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 201[redacted]

Causality for UPADACITINIB (Blinded)

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1) Lung infection (10061229) (Lung infection (10061229)) [v.22.0] [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 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 CHT:** 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] 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
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] / 426
DRACAENA COCHINCHINENSIS	1 OTHER: PILL	QD	Y-M: 20[redacted] / 422	Y-M: 20[redacted] / 425
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / 427	NOT REPORTED
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / 435	Y-M: 20[redacted] / 437
BENZYLPENICILLIN	1.6 MILLION OTHER: U	OTHER: ONCE	Y-M: 20[redacted] / 437	Y-M: 20[redacted] / 437
BENZYLPENICILLIN	16000 OTHER: U	TID	Y-M: 20[redacted] / 437	Y-M: 20[redacted] / 437
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

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] / 422 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 437): Hemoglobin: 126 [130 - 175] G/L; NPTST261-HIGH-SENSITIVITY 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; NPTST202-FIBRINOGEN: 5.7 [2 - 4] G/L; NPTST354-OCCULT BLOOD IN STOOL: ++ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 60 [65 - 85] G/L; [redacted]20[redacted] (RX DAY 439): NPTST354-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; NPTST270-HYPERSENSITIVE C-REACTIVE PROTE: 9.25 [0 - 5] MG/L; NPTST354-OCCULT BLOOD IN STOOL: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 38 [40 - 55] G/L; [redacted]20[redacted] (RX DAY 445): NPTST354-OCCULT BLOOD IN STOOL: +++ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE

Microbiology

[redacted]20[redacted] (RX DAY 437): BLOOD NPTST082-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	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 11 月 12 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。

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）を発現したが，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。治験責任医師によると，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。

投与された薬剤は，セフトリアキソン，エリスロマイシン，モキシフロキサシン及びペニシリンであった。

The patient's past medications include:

TRIPTERYGIUM GLYCOSIDES 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], [redacted] 20[redacted] - [redacted] 20[redacted])

LEFLUNOMIDE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[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.22.1] [10007882]

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 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] **ALBUMIN:** 35.9 G/L (normal 40 to 55)

[redacted] **BLOOD CULTURE:** No bacterial growth observed after 120 hours of culture.

[redacted] **FIBRINOGEN:** 5.7 G/L (normal 2 to 4)

[redacted] **HEMATOCRIT:** 38.6 % (normal 40 to 50)

[redacted] **HEMOGLOBIN:** 126 G/L (normal 130 to 175)

[redacted] **HS-CRP:** 38.55 MG/L (normal 0 to 5)

[redacted] **HS-CRP:** 9.25 MG/L (normal 0 to 5)

[redacted] **TOTAL PROTEIN:** 60.1 G/L (normal 65 to 85)

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	19[redacted]

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		

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，ヘパリン，イグザレルト及びクレキサンであった。

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) 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[redacted]
PSORIATIC ARTHRITIS	19[redacted]
HYPERTENSION	19[redacted]
OTHER: HEPATITIS C	19[redacted]
OTHER: CATARACTS ON BOTH EYES	20[redacted]
OSTEOPOROSIS	20[redacted]
CHOLELITHIASIS	20[redacted]
OTHER: ATHEROSCLEROSIS	20[redacted]
OTHER: LEFT VENTRICULAR HYPERTROPHY	20[redacted]
OTHER: ABDOMINAL EXPLORATION DUE TO CAR ACCIDENT	20[redacted]
OTHER: PAROXYSMAL ATRIAL FLUTTER	20[redacted]
OTHER: ABDOMINAL HERNIA	20[redacted]
OTHER: ANGINA PECTORIS	20[redacted]
OTHER: HYPERCHOLESTERINAEMIA	20[redacted]
DIABETES MELLITUS	20[redacted]
OTHER: LATENS TB	20[redacted]
OTHER: ABDOMINAL HERNIA SURGERY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: SURGERY DUE TO LEFT FEMUR FRACTURE	19[redacted]
SURGERY: SURGERY DUE TO CATARACTS ON BOTH EYES	20[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]

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	NOT REPORTED
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 NPTST326-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] [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
OTHER: NODULAR GOITER	20
GASTROESOPHAGEAL REFLUX DISEASE	20
OTHER: MENOPAUSE	20
PSORIATIC ARTHRITIS	20
PERIPHERAL VASCULAR DISEASE-VENOUS: VARICOSE VEINS	20

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	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: 2016

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] **20[redacted] BLOOD PRESSURE:** 130/70 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 134/90 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 116/74 mmHg

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

[redacted] **20[redacted] ECG:** Changes in the anterior lower wall of the left ventricle (NCS).

[redacted] **20[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] **20[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
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; NPTST089-BLOOD GROUP: A(II) RH(+) [NOT REPORTED - NOT REPORTED] NA; NPTST427-RW (WASSERMANN REACTION): NEGATIVE [NOT REPORTED - NOT REPORTED] NA; NPTST445-SQUAMOUS EPITHELIUM: 1-2 [NOT REPORTED - NOT REPORTED] HPF; NPTST485-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): NPTST007-ABHCV: NEGATIVE [NOT REPORTED - NOT REPORTED] NA; NPTST235-HBSAG: NEGATIVE [NOT REPORTED - NOT REPORTED] NA

Microbiology

(RX DAY): OTHER:

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

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 1 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

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		

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: 67600 [53 - 97] UMOL/L; 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] %; NPTST031-AMYLASE: 74.1 [NOT REPORTED - NOT REPORTED] U/L; NPTST389-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，paracetamol 500 mg を服用したと報告された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，左臀部の開放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，invanz，セフトリアキソン及びデキサメタゾンであった。

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: No rechallenge was done, recurrence is not applicable

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
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		

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	ONGOING
Duration of AE	ONGOING
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，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.22.0] [10043827]

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 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]-[redacted]

ISOSORBIDE MONONITRATE	20 mg	BID	Y-M: 20
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20
NEBIVOLOL	5 mg	QD	Y-M: 20
VITAMINS, OTHER COMBINATIONS	2 OTHER: TABLETS	QD	Y-M: 20 -
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20 -
ALFACALCIDOL	0.25 OTHER: MCG	BID	Y-M: 20 - / -32
IBANDRONIC ACID	150 mg	OTHER: MONTHLY	Y-M: 20 - / -32
ISONIAZID	300 mg	QD	Y-M: 20 - / -19
PYRIDOXINE	25 mg	QD	Y-M: 20 - / -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	ONGOING
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20	ONGOING
NEBIVOLOL	5 mg	QD	Y-M: 20	ONGOING
VITAMINS, OTHER COMBINATIONS	2 OTHER: TABLETS	QD	Y-M: 20 -	ONGOING
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20 -	ONGOING
ALFACALCIDOL	0.25 OTHER: MCG	BID	Y-M: 20 - / -32	ONGOING
IBANDRONIC ACID	150 mg	OTHER: MONTHLY	Y-M: 20 - / -32	ONGOING
ISONIAZID	300 mg	QD	Y-M: 20 - / -19	ONGOING
PYRIDOXINE	25 mg	QD	Y-M: 20 - / -19	ONGOING
MOXIFLOXACIN	400 mg	QD	Y-M: 20 - / 140	Y-M: 20 - / 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 20 / 145 (18 DAYS AFTER LAST TREATMENT)

Age at AE Onset 6

Laboratory Testing

20 (RX DAY 148): NPTST106-CA-125: 239.8 [0 - 35] U/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

20 (RX DAY 145): CT IMAGING OF ABDOMEN: MESENTERIAL CARCINOMATOSIS WITH LYMPHADENOPATHY AND PERITONEAL FREE-LIQUID-SUSPECTED NEOPLASTIC OVARIAN PROCESS;DILATED LEFT OVARIAN VEIN; 20 (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 THERE ARE NO MEDICAL CONDITION IN MEDICAL HISTORY THAT ARE IN

Alternative Etiology 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）。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		

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
ISONIAZID	100 mg	BID	Y-M: 20[redacted] / - 115	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: 0.787 [0 - 2.5] 10^3/uL; 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: 5819.88 [0 - 8699.83] U/L; Creatinine: 52 [45 - 84] UMOL/L; Eosinophils: 0.181 [0 - 0.7] 10^9/L; Eosinophils/Leukocytes: 1.34 [0 - 7] 10^9/L; Erythrocytes: 4.82 [4.04 - 6.13] 099,M/UL; Hematocrit: 0.43 [0.38 - 0.54] FRACTION OF 1; Hemoglobin: 148 [122 - 181] G/L; Leukocytes: 13.5 [4.6 - 10.2] 099,K/UL; Lymphocytes: 1.8 [0.6 - 3.4] 10^9/L; Lymphocytes/Leukocytes: 13.4 [10 - 50] 10^9/L; Monocytes: 0.755 [0 - 0.99] 10^9/L; Monocytes/Leukocytes: 5.6 [0 - 12] K/UL; NPTST428-SEDIMENTATION: 6 [NOT REPORTED - NOT REPORTED] HOURS; NPTST501-VITAMIN B12: 279 [187 - 883] G/DL; Neutrophils: 10.6 [2 - 6.9] 10^9/L; Neutrophils/Leukocytes: 78.9 [37 - 80] K/UL; Platelets: 236 [142 - 424] 099,K/UL; 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，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，aprol，diklojik 及び dikloron 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] **20[redacted] RBC:** 4.82 M/uL (normal 4.04 to 6.13)

[redacted] **20[redacted] SED RATE:** 6 /hr

[redacted] **20[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		

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] / -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]-[redacted] / -96	NOT REPORTED
IMIQUIMOD	1 OTHER: CENTIMETER	PRN	Y-M: 20[redacted]-[redacted] / 99	Y-M: 20[redacted]-[redacted] / 143
DEXPANTHENOL	1 OTHER: CENTIMETER	PRN	Y-M: 20[redacted]-[redacted] / 128	NOT REPORTED
VERRUMAL	1 APPLICATION OTHER: APPLICATION	TID	Y-M: 20[redacted]-[redacted] / 197	NOT REPORTED

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 NPTST263-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
NOT REPORTED

AE Stopped Rx Day	309 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	55 DAYS
Severity	Severe

Relation to Study Drug by Investigator	No Reasonable Possibility
Investigator Alternative Etiology	ANAL FISTULA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]
Program Source Code: [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，bepanthen クリーム，novalgin，ボルタレン及び dafalgan であった。

Causality for ABT-494 (Blinded)

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1) Perianal abscess (10034447) (Anal abscess (10048946)) [v.22.0] [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 ABT-494 (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] **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。

被験者は痔瘻に対する瘻孔切開の待期的手術のため入院した。

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.22.1] [10002156]

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 ANAL FISTULA

- Investigator: Anal Fistula

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

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	NOT REPORTED
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; NPTST054-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	HYPERTROPHY 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，アセトアミノフェン，amotaks，アトロピン，klacid，midanium，モルヒネ及び nimesil であった。

Causality for UPADACITINIB (Blinded)

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1) Tonsillar hypertrophy (10044003) (Tonsillar hypertrophy (10044003)) [v.22.1] [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: Hypertrophy 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)