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
ABT-494 15 mg QD	7[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: POST MENOPAUSAL	19[redacted]
OTHER: LEFT KNEE TIBIAL PLATEAU FRACTURE	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA	20[redacted]
OTHER: TRIGGER FINGER RIGHT HAND	20[redacted]
DIABETES MELLITUS	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

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 393	224
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 394	[redacted]20[redacted] / 667	274

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SIMVASTATIN	20 mg	QD	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	6 mg/kg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	7 mg/kg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
METFORMIN	500 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
CERTOLIZUMAB PEGOL	200 mg	EVERY 2 WEEKS	Y-M: 20[redacted] / -358

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
SIMVASTATIN	20 mg	QD	Y-M: 20[redacted]	Not reported.
METFORMIN	500 mg	QD	Y-M: 20[redacted]	Not reported.
METOPROLOL	25 g	BID	Y-M: 20[redacted] / 632	ONGOING
ONDANSETRON	4 mg	OTHER: FOUR TIMES A DAY	Y-M: 20[redacted] / 632	ONGOING
TORASEMIDE	20 g	QD	Y-M: 20[redacted] / 632	ONGOING

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

Event Description	OVARIAN CANCER
Preferred term	卵巣癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 632
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	ONGOING

Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN ETIOLOGY
Discontinued Study Drug Due to the Event	YES
SAE Criteria	OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

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，卵巣癌の事象を発現した。

Event 1 の臨床経過：
関連する病歴は閉経後，局面型乾癬，乾癬性関節炎，糖尿病，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ウパダシチニブの盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は卵巣癌を発現した。

本報告時においてそれ以上の詳しい情報は得られていない。

The patient's past medications include:

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

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

REMICADE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], 12 [redacted] 20[redacted] - [redacted] 20[redacted])

FOLIC ACID for SUPPLEMENT ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

Causality for UPADACITINIB (Blinded)

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1) Ovarian cancer (10033128) (Ovarian cancer (10033128)) [v.23.0] [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: Unknown etiology.

- AbbVie: In the United States Ovarian canceris the second most common gynecologic malignancy with increasing age being a major risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CAT SCAN:** pending

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
狭心症	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	6[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
OTHER: BILATERAL SYNDACTLY OF 2ND/3RD TOES	19[redacted]
OTHER: CHICKEN POX	19
DRUG ALLERGIES/REACTIONS: ALLERGY TO LATEX	19
OTHER: UTERINE FIBROIDS	19
ASTHMA	20
EYE DISEASE/DISORDER: DRY EYES	20
EYE DISEASE/DISORDER: ENTROPIAN EYE LIDS	20
CHOLECYSTITIS	20
DRUG ALLERGIES/REACTIONS: ALLERGY TO MORPHINE	20
DRUG ALLERGIES/REACTIONS: ALLERGY TO ULTRAM	20
HYPERTENSION	20
OTHER: HASHIMOTO'S DISEASE	20
OTHER: LEFT SHOULDER PAIN	20
OTHER: PLAQUE PSORIASIS	20
OTHER: MASS ON OVARIES (BENIGN)	20
OTHER: SEASONAL ALLERGIES	20
OTHER: SINUS HEADACHES	20
DIABETES MELLITUS	20
DRUG ALLERGIES/REACTIONS: ALLERGY TO METOPROLOL	20
OTHER: LIPOMAS ON BILATERAL AXILLA, SUPRACLAVICULAR AREA	20
DEPRESSION: DEPRESSION	20
LIVER DISEASE (EXCLUDING HEPATITIS): FATTY LIVER	20
COGNITIVE OR PSYCHIATRIC DISORDER: ANXIETY	20
OTHER: TENSION HEADACHES	20
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COPD	20
OTHER: CHEST PALPITATIONS	20
OTHER: PULMONARY NODULES	20
PNEUMONIA	20
OTHER: ALOPECIA	20

Prior Procedures	Procedure Year
SURGERY: PARTIAL HYSTERECTOMY	19[redacted]
SURGERY: CHOLELYCYSECTOMY	20[redacted]
SURGERY: OVARIES EXTRACTED (SECONDARY TO BENIGN MASS)	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	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 384	215
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 385	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
GLIPIZIDE	10 mg	QD	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
USTEKINUMAB	90 mg	OTHER: EVERY 12 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
METHOTREXATE	0.6 mL	EVERY WEEK	Y-M: 20[redacted]-
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
APREMILAST	30 mg	BID	Y-M: 20[redacted]-
METHOTREXATE	2.5 mg	QD	Y-M: 20[redacted]-
MONTELUKAST	10 mg	QD	Y-M: 20[redacted]-[redacted] / -336
INSULIN ASPART	5 OTHER: UNITS	PRN	Y-M: 20[redacted]-[redacted] / -275
INSULIN DETEMIR	15 OTHER: UNITS	QD	Y-M: 20[redacted] / -275

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]	Not reported.
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / -336	Not reported.
GLIPIZIDE	5 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 510
LISINOPRIL	10 mg	QD	Y-M: 20[redacted] / 391	Y-M: 20[redacted] / 443
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted] / 396	Not reported.
AZITHROMYCIN	250 mg	QD	Y-M: 20[redacted] / 408	Y-M: 20[redacted] / 411
GLYCERYL TRINITRATE	.4 mg	PRN	Y-M: 20[redacted] / 441	Not reported.
METOPROLOL	25 mg	BID	Y-M: 20[redacted] / 443	Not reported.
ACICLOVIR	800 mg	QID	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 464
LISINOPRIL	20 mg	QD	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 500

Event #1: Serious Adverse Event

Event Description ANGINA

Preferred term 狭心症

AE Onset Date / Rx Day [redacted]20[redacted] / 441

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 441): NPTST034-BN PEPTIDE: 11.9 [0 - 100] pg/mL; NPTST209-TROPONIN-I: 0.03 [0 - 0.05] ng/mL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 441): CHEST X-RAY: NO ACUTE CARDIOPULMONARY ABNORMALITY; ECG: NORMAL SINUS RHYTHM. CANNOT RULE OUT ANTERIOR INFARCT, AGE UNDERTERMINED. ABNORMAL ECG; ECHOCARDIOGRAM: EF=55-60%. GRADE I DIASTOLIC DYSFUNCTION. MILD CONCENTRIC LEFT VENTRICULAR HYPERTROPHY. THE LEFT VENTRICLE IS NORMAL IN SIZE. THERE IS NO THROMBUS. LEFT VENTRICULAR SIZE AND FUNCTION APPEARS NORMAL.; [redacted]20[redacted] (RX DAY 445): NUCLEAR STRESS TEST: EVIDENCE OF SMALL SIZE OF MILD INTENSITY APICAL WALL INFARCT WITHOUT SIGNIFICANT ISCHEMIA.

AE Stopped Rx Day 442

Duration of AE 2 DAYS

Relation to Study Drug by Investigator NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	NEW DEVELOPMENT OF CORONARY ARTERY DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

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，アンギナの事象を発現した。

Event 1 の臨床経過：

関連する病歴は喘息，橋本病，高血圧，局面型乾癬，乾癬性関節炎，糖尿病，不安，胸部の動悸，非喫煙者，非飲酒者及び冠動脈疾患の家族歴であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

冠動脈疾患の家族歴もあった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はアンギナを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，アンギナは消失した。

[redacted] 月 [redacted] 日，被験者は，胸痛，左腕の痛み，嘔吐，発汗及び血圧上昇といった症状により，救急治療室を受診した。被験者は同日入院した。[redacted] 月 [redacted] 日，心電図検査，X 線検査及び心エコー検査が行われた。治療が行われ，アンギナは消失した。[redacted] 月 [redacted] 日，被験者は退院した。外来で核 GXT 検査を行ったところ，軽度の小さな心尖部壁梗塞の徴候が認められたが，著しい虚血は伴っていなかった（日付不明）。治験責任医師は，被験者には高血圧及び 2 型糖尿病の危険因子があると判断した。

投与された薬剤はニトログリセリンであった。

The patient's past medications include:

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

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

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

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

LEVEMIR for TYPE II DIABETES (20[redacted] - [redacted] 20[redacted])

ULTRAM for UNKNOWN INDICATION

MORPHINE for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Angina pectoris (10002383) (Angina pectoris (10002383)) [v.22.1] [10002383]

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 ANGINA

- Investigator: New development of coronary artery disease.

- AbbVie: Risk factors include pre-existing diabetes mellitus, hypertension, and obesity (BMI of 33 at screening).

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **BNP:** 11.9 PG/ML (normal 0.0 to 100.0)

[redacted] 20[redacted] **CHEST X-RAY:** No acute cardiopulmonary abnormality

[redacted] 20[redacted] **ECHOCARDIOGRAM:** EF=55-60%. Grade I diastolic dysfunction. Mild concentric left ventricular hypertrophy. The left ventricle is normal in size. There is no thrombus. Left ventricular size and

function appears normal.

[redacted] **20[redacted] ELECTROCARDIOGRAPHY:** Normal sinus rhythm. Cannot rule out anterior infarct, age undetermined. Abnormal ECG

[redacted] **20[redacted] NUCLEAR STRESS TEST:** Evidence of small size of mild intensity apical wall infarct without significant ischemia.

[redacted] **20[redacted] TROPONIN:** 0.028 NG/ML (normal 0.000 to 0.045)

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
徐脈	X			

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

Medical History	Onset Year
OTHER: CHILDHOOD RECURRING TONSILLITIS	19[redacted]
OTHER: OBESITY	19
OSTEOARTHRITIS	19
OTHER: PLAQUE PSORIASIS	19
HEARING DISORDER: SLIGHT HEARING LOSS	20
OTHER: SCROTAL MASS SEROMA	20
OTHER: RIGHT SHOULDER ROTATOR CUFF TEAR	20

Prior Procedures	Procedure Year
SURGERY: ADENOIDECTOMY	19[redacted]
SURGERY: TONSILLECTOMY	19
SURGERY: APPENDECTOMY	19
SURGERY: INGUINAL HERNIA REPAIR	20
SURGERY: SCROTAL MASS ASPIRATION	20
SURGERY: CORRECTIVE SURGERY SECONDARY TO HERNIA REPAIR	20
SURGERY: RIGHT TOTAL SHOULDER REPLACEMENT	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 166	166
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 167	[redacted]20[redacted] / 222	56

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]
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
ABATACEPT	50 mg	EVERY WEEK	Y-M: 20[redacted]
VICODIN	5/325 mg	BID	Y-M: 20[redacted]
POTASSIUM	4700 mg	QD	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted]	ONGOING
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	ONGOING
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
VICODIN	5/325 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 39
POTASSIUM	4700 mg	QD	Y-M: 20[redacted]	ONGOING
DEXTROMETHORPHAN HYDROBROMIDE W/DOX	2 OTHER: TABS	OTHER: Q4HRS	Y-M: 20[redacted] / 43	ONGOING

Event #1: Serious Adverse Event

Event Description	SYMPTOMATIC BRADYCARDIA
Preferred term	徐脈
AE Onset Date / Rx Day	[redacted]20[redacted] / 60
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 60): CHEST X-RAY: NORMAL; EKG: SINUS BRADYCARDIA W PREMATURE ATRIAL COMPLEX; [redacted]20[redacted] (RX DAY 61): BILATERAL CAROTID U/S: RIGHT CALCIFIED STENOSIS; CARDIAC STRESS TEST: ASYMPTOMATIC; ECHOCARDIOGRAM: MILD PULMONARY HYPERTENSION; EKG: SINUS BRADYCARDIA W PREMATURE VENTRICULAR COMPLEX

AE Stopped Rx Day	61
Duration of AE	2 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN ETIOLOGY
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: M15-554

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，症候性徐脈の事象を発現した。

Event 1 の臨床経過：

関連する病歴は肥満，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。

試験の盲検解除の情報を得た。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は症候性徐脈を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，症候性徐脈は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。診断検査が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

退院時サマリーより：被験者は浮動性めまいにより救急科を受診した。被験者の話では，これまでにこのようなことはなかった。しかし，この数日間は疲労感が増し，3 週間ほど前から胸の詰まりと咳嗽を自覚していた。最初に受診したウォークイン・クリニックでの心電図検査で徐脈性心房細動が認められ，詳細な検査のためそのまま救急科を受診することとなった。

救急科での検査で，頻回な PAC を伴う洞性徐脈が明らかとなった。臨床検査値に特に異常はなく，胸部 X 線検査でも重大な所見は見られなかった。救急科の医師は，被験者が組み入れられた本治験を行っていたリウマチ専門医に連絡した。リウマチ専門医は，徐脈は既知の副作用ではないとした。入院後，テレメトリー及びモニタリングが開始された。前回の心電図検査で徐脈性心房細動が疑われたとの報告があったため，心臓専門医の助言を受けた。入院翌日，心臓負荷検査及び心エコー検査が行われたが，いずれの検査でも重大な所見は認められなかった。被験者の状態は入院期間を通して変わらず，また [redacted] 月の心電図検査で頻回な PAC を伴う洞性徐脈が認められたとも報告された。現在の症状は，現在投与中の薬剤の治験とは無関連であると思われた。全体的に，入院中の経過は特に異常なく，悪化や臨床的代償不全も報告されなかった。被験者は医学的に安定していると思われ，退院して，今後はかかりつけ医による経過観察と，外来でのホルター心電図モニタリングのための心臓専門医による経過観察を行うのが妥当と判断された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

心臓専門医の診察結果より：被験者は症候性徐脈の状態で来院した。被験者は浮動性めまいを訴えたが，最近の疲労増加に伴う心拍数所見は見られなかった。被験者は AV ブロック治療薬を投与されていたわけではなかった。PCP から入手した過去（20[redacted] 年）のバイタルサイン測定結果を確認したところ，20[redacted] 年 [redacted] 月の 2 回の測定で心拍数が 51 及び 53 であり，徐脈が認められていた。これは，持病の乾癬性関節炎に対して，新たなリウマチ治療用治験薬の投与が開始される前であった。

被験者は病的肥満であり，早発性 CAD の家族歴を有していた。被験者には睡眠時無呼吸の一因が存在したと考えられた。実際，被験者は夜間にいびきをかいている。

Causality for UPADACITINIB (Blinded)

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1) Bradycardia (10006093) (Bradycardia (10006093)) [v.22.1] [10006093]

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 SYMPTOMATIC BRADYCARDIA

- Investigator: Unknown etiology.

- AbbVie: Event is more likely related to abnormal EKG at screening. Additionally bradycardia was noted on two occasions in [redacted] 20[redacted] and appears to be pre-existing.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BILATERAL CAROTID ULTRASOUNDS:** right calcified stenosis Interpretation Summary: The right common carotid artery shows no evidence of disease. The right external carotid artery shows evidence of <50% disease. The right bulb/internal carotid artery shows evidence of 20-39% calcified stenosis. Spectral Doppler flow evaluation of the innominate artery shows no evidence of a hemodynamically significant stenosis. Spectral Doppler flow evaluation of the right proximal subclavian artery shows no evidence of a hemodynamically significant stenosis. The right vertebral artery demonstrates antegrade flow. The left common carotid artery shows no evidence of disease. The left external carotid artery shows evidence of <50% disease. The left bulb/proximal internal carotid artery shows evidence of a 1-19%stenosis with homogeneous plaque. Spectral Doppler flow evaluation of the left proximal subclavian artery show no evidence of a hemodynamically significant stenosis. The left vertebral artery demonstrates antegrade flow.

[redacted] **20[redacted] BLOOD PRESSURE:** 157/88

Unknown date CALCIUM: 9.2 mg/dL

[redacted] **20[redacted] CARDIAC STRESS TEST:** asymptomatic In conclusion, low risk EKG portion of exercise nuclear stress test with the patient showing chronotropic competency.No evidence of ischemia Diaphragmatic attenuation. Normal left ventricular systolic function No evidence for transient ischemic dilatation.

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

[redacted] **20[redacted] CK MB FRACTION:** 3.10 NG/ML

[redacted] **20[redacted] ECHOCARDIOGRAM:** Interpretation Summary: The left ventricular ejection fraction is estimated at 60%. There is mild concentric left ventricular hypertrophy. The right ventricle demonstrates normal systolic function. The left atrium is normal in size. The estimated peak right ventricular systolic pressure

is 41 mmHg, consistent with mild pulmonary hypertension. There is no evidence of a pericardial effusion.

[redacted] **20[redacted] EKG:** sinus bradycardia w premature atrial complex

[redacted] **20[redacted] EKG:** sinus bradycardia w premature ventricular complex

[redacted] **20[redacted] ELECTROCARDIOGRAM:** Screening ECG: atrial fibrillation;

[redacted] **20[redacted] GLUCOSE:** 84 mg/dL

[redacted] **20[redacted] HCT:** 42.7 %

[redacted] **20[redacted] HEART RATE:** 48 No units

[redacted] **20[redacted] HGB:** 14.4 G/DL

[redacted] **20[redacted] ISTAT TROPONIN:** 0.03 NG/ML

[redacted] **20[redacted] ISTAT TROPONIN:** 0.03 NG/ML

[redacted] **20[redacted] PLATELET COUNT:** 320 K/uL

[redacted] **20[redacted] POTASSIUM:** 4.6 MMOL/L

[redacted] **20[redacted] PULSE OXIMITER:** 95 No units

[redacted] **20[redacted] RESPIRATORY RATE:** 20 No units

[redacted] **20[redacted] TROPONIN:** 0.08 NG/ML

[redacted] **20[redacted] WBC:** 10.2 K/uL

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
子宮平滑筋腫	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 15 mg QD	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PREMENSTRUAL SYNDROME	20[redacted]
OTHER: UTERINE FIBROIDS	20
GASTROESOPHAGEAL REFLUX DISEASE	20
HYPERLIPIDEMIA	20
OTHER: ELEVATED C-REACTIVE PROTEIN BLOOD LEVEL	20
OTHER: PLAQUE PSORIASIS	20
DRUG ALLERGIES/REACTIONS: REMICADE - DRUG ALLERGY	20
DEPRESSION: MAJOR	20
OTHER: HAIR LOSS	20
OTHER: ABNORMAL LYMPHOCYTE RESULT	20
OTHER: ABNORMAL MONOCYTE RESULT	20
OTHER: ABNORMAL WHITE BLODD CELL COUNT	20

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	23	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 174	174
ABT-494	15MG	ORAL	QD	[redacted] / 175	[redacted] / 392	218
ABT-494	15MG	ORAL	QD	[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BIOTIN	1000 ug	QD	Y-M: [redacted]
CURCUMA LONGA	500 mg	QD	Y-M: [redacted]
DICLOFENAC	35 mg	QD	Y-M: [redacted]
ESOMEPRAZOLE	40 mg	QD	Y-M: [redacted]
PRAVASTATIN	20 mg	QD	Y-M: [redacted]
VICODIN	10 325 mg	PRN	Y-M: [redacted]
APREMILAST	30 mg	BID	Y-M: [redacted]
SECUKINUMAB	150 mg	OTHER: ONCE A MONTH	Y-M: [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
BIOTIN	1000 ug	QD	Y-M: [redacted]	ONGOING
CURCUMA LONGA	500 mg	QD	Y-M: [redacted]	ONGOING
DICLOFENAC	35 mg	QD	Y-M: [redacted]	ONGOING
ESOMEPRAZOLE	40 mg	QD	Y-M: [redacted]	ONGOING
PRAVASTATIN	20 mg	QD	Y-M: [redacted]	ONGOING
VICODIN	10 325 mg	PRN	Y-M: [redacted]	ONGOING
ESCITALOPRAM	20 mg	QD	Y-M: [redacted] / 84	ONGOING

Event #1: Serious Adverse Event

Event Description	UTERINE FIBROIDS
Preferred term	子宮平滑筋腫
AE Onset Date / Rx Day	[redacted]20[redacted] / 127
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 142): Hemoglobin: 134 [120 - 140] g/L; Leukocytes: 15 [4.8 - 10.8] 10^9/L; NPTST177-PT/INR: 0.9 [0.9 - 1.1] sec; Platelets: 561 [130 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 146): Hemoglobin: 125 [120 - 140] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 145): ROBOTIC LAPROSCOPIC HYSTERECTOMY WITH BILATERAL SALPINGECTOMY AND CYSTOSCOPY: SUCCESSFUL

AE Stopped Rx Day	145
Duration of AE	19 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HISTORY OF UTERINE FIBROIDS
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: M15-554

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，子宮類線維症の事象を発現した。

Event 1 の臨床経過：

関連する病歴は月経前症候群，子宮類線維症及び乾癬性関節炎であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は子宮類線維症を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，子宮類線維症は消失した。

被験者は，10 ヵ月に及ぶ不規則な月経周期，重度の大量凝血塊及び組織排出の訴えにより，産婦人科医を受診した。子宮摘出術が予定された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，ロボット支援腹腔鏡下子宮摘出術，両側卵管摘除術及び膀胱鏡検査が行われた。手術は成功し，合併症は見られなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

The patient's past medications include:

REMICADE for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

---

1) Uterine fibroids (10046784) (Uterine leiomyoma (10046798)) [v.22.1] [10046784]

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 UTERINE FIBROIDS

- Investigator: History of uterine fibroids.

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING HISTORY OF UTERINE FIBROIDS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] HEMOGLOBIN:** 13.4 G/DL (normal 12.0 to 14.0)

[redacted] **20[redacted] HEMOGLOBIN:** 12.5 G/DL (normal 12.0 to 14.0)

[redacted] **20[redacted] INR:** 0.9 SEC (normal 0.9 to 1.1)

[redacted] **20[redacted] PLATELET COUNT:** 561 X10**3/MCL (normal 130 to 400)

[redacted] **20[redacted] WBC:** 14.99 X10**3/MCL (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
失見当識	X			
浮動性めまい	X			
転倒	X			
会話障害	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	6[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: NEPHROLITHIASIS HISTORY	NOT REPORTED
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: DEEP VEIN THROMBOSIS	20[redacted]
DEPRESSION: NO SUICIDAL IDEATION NO EVENTS	20[redacted]
BENIGN PROSTATIC HYPERPLASIA	20[redacted]
HYPERTENSION	20[redacted]

Prior Procedures	Procedure Year
SURGERY: TRANSURETHRAL RESECTION OF THE PROSTATE	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	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 88	88

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CLOBETASOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
QUETIAPINE	200 mg	QD	Y-M: 20[redacted]
ETANERCEPT	UNK mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	UNK mg	EVERY WEEK	Y-M: 20[redacted]
IBUPROFEN	200 mg	OTHER: 3 TIME A WEEK	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
QUETIAPINE	200 mg	QD	Y-M: 20[redacted]	ONGOING
IBUPROFEN	200 mg	OTHER: 3 TIME A WEEK	Y-M: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL
Preferred term	失見当識
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
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
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DATA IS UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL
Preferred term	浮動性めまい
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
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
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DATA IS UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL
Preferred term	転倒
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
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
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DATA IS UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #4: Serious Adverse Event

Event Description	DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL
Preferred term	会話障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 88
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
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DATA IS UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者はプエルトリコの 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，浮動性めまい，発語困難，見当識障害及び転倒の事象を発現した。

Event 1～4 の臨床経過：

関連する病歴は深部静脈血栓症，うつ病，乾癬性関節炎，高血圧，非喫煙者及び非飲酒者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は浮動性めまい，発語困難，見当識障害及び転倒を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は転倒のため入院した。発語困難，失見当識及び浮動性めまいが認められた。被験者が追跡不能となったため，これ以上の情報の入手は不可能である。

Causality for UPADACITINIB (Blinded)

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1) Speech disorder (10041466) (Speech disorder (10041466)) [v.22.1] [10041466]

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

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

Dechallenge: No

2) Fall (10016173) (Fall (10016173)) [v.22.1] [10016173]

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

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

Dechallenge: No

3) Disorientated (10013394) (Disorientation (10013395)) [v.22.1] [10013394]

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

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

Dechallenge: No

4) Dizziness (10013573) (Dizziness (10013573)) [v.22.1] [10013573]

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 DIZZINESS, DIFFICULTY TO SPEAK, DISORIENTED, PATIENT FELL

- Investigator: Data is unknown

- **AbbVie:** Risk factors include age, hypertension, and history of deep vein thrombosis.

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
中咽頭扁平上皮癌	X	X		X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: DYSFUNCTIONAL UTERINE BLEEDING	20[redacted]
DRUG ALLERGIES/REACTIONS: NAPROSYN	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 166	166
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 167	[redacted]20[redacted] / 330	164

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETANERCEPT	UNK mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	UNK mg	EVERY WEEK	Y-M: 20[redacted]
OVIDON	0.3 mg	QD	Y-M: 20[redacted] / -291
FOLIC ACID	2 mg	QD	Y-M: 20[redacted] / -261
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted] / -261

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	2 mg	QD	Y-M: 20[redacted] / -261	ONGOING
FAMOTIDINE	UNKNOWN mg	OTHER: ONCE	Y-M: 20[redacted] / 56	ONGOING
CILEST	250 mg	QD	Y-M: 20[redacted] / 62	ONGOING
COLECALCIFEROL	20,000 IU	EVERY WEEK	Y-M: 20[redacted] / 167	ONGOING
THROAT PREPARATIONS	1 OTHER: SPRAY	BID	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 330
CEFALEXIN	500 mg	BID	Y-M: 20[redacted] / 330	ONGOING
PARACETAMOL	500 mg	BID	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 337
CEFAZOLIN	1 g	TID	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
KETOROLAC	15 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
KETOROLAC	30 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408
PARACETAMOL	325 mg	QID	Y-M: 20[redacted] / 381	Y-M: 20[redacted] / 408

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

Event Description RIGHT SIDE TONGUE SQUAMOUS CELL CARCINOMA, MODERATELY DIFFERENTIATED, INVASIVE IN SITU HYBRIDIZATION OF HPV IN PROGRESS.

Preferred term 中咽頭扁平上皮癌

AE Onset Date / Rx Day [redacted]20[redacted] / 323

Age at AE Onset 2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 330): BIOPSY TONGUE RIGHT LATERAL: SQUAMOUS CELL CARCINOMA,

MODERATELY DIFFERENTIATED, INVASIVE. IN SITU HYBRIDIZATION OF HPV IN PROGRESS, A REPORT WILL FOLLOW; [redacted]20[redacted] (RX DAY 346): PET/CT SCAN: 1. HYPERMATABOLIC DENSITY IN THE RIGHT SIDE OF THE TONGUE AS DESCRIBED ABOVE CONSISTENT WITH HEAD AND NECK CT SCAN WITH F-18 FDG AVID ACTIVE NEOPLSTIC PROCESS. CORRELATION WITH HEAD AND NECK CT SCAN W; [redacted]20[redacted] (RX DAY 365): CERVICAL/VAGINAL-THIN-PREP: NEGATIVE FOR INTRAEPITHELIAL; HPV GENOTYPE 18/45: NEGATIVE; HPV GENPTYPE 16: POSITIVE; HUMAN PAPILLOMA VIRUS- OTHER HIGH RISK TYPES: POSITIVE; [redacted]20[redacted] (RX DAY 385): EKG: T WAVE INVERSION NON SPECIFIC - NOT CLINICALLY SIGNIFICANT; [redacted]20[redacted] (RX DAY 392): TRACHEOSTOMY TUBE AND GASTRONOMY TUBE PLACEMENT: SUBJECT WAS DISCHARGED AFTER PROCEDURES

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INVASIVE IN SITU HYBRIDIZATION OF HPV IN PROGRESS.
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: M15-554

治験責任医師からの報告。本被験者はプエルトリコの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，右側舌扁平上皮癌（中分化型，浸潤性，HPV の in situ ハイブリダイゼーション実施中）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，非喫煙者及び少量の現飲酒者（1 日 2 杯未満）であった。

試験の盲検解除の情報を得た。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted]年[redacted]月[redacted]日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右側舌扁平上皮癌（中分化型，浸潤性，HPV の in situ ハイブリダイゼーション実施中）を発現した。

被験者は，右側舌の潰瘍のため，規定外来院した。被験者は，疼痛，腫脹及び痛みを伴う嚥下困難を発現した。治験責任医師は患部の生検を依頼した。20[redacted] 年 [redacted] 月 [redacted] 日，右側舌の生検が行われた。結果は，扁平上皮癌（中分化型，浸潤性）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は治療のため入院した。被験者は意識清明・見当識正常で協力的であった。被験者の予後は不良であった。同日，気管切開チューブ及び胃瘻造設術チューブの留置が行われた。放射線療法のための評価が進行中であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，sore throat spray，アセトアミノフェン及び cephalexin であった。

The patient's past medications include:

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

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

NAPROSYN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) HPV positive oropharyngeal squamous cell carcinoma (10081287) (Oropharyngeal squamous cell carcinoma (10031112)) [v.22.1] [10081287]

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 RIGHT SIDE TONGUE SQUAMOUS CELL CARCINOMA, MODERATELY DIFFERENTIATED, INVASIVE IN SITU HYBRIDIZATION OF HPV IN PROGRESS

- Investigator: Invasive in situ hybridization of HPV in progress.

- AbbVie: Risk factor includes HPV infection per PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BIOPSY TONGUE RIGHT LATERAL: Squamous cell carcinoma, moderately differentiated, invasive. In situ hybridization of HPV in progress, report will follow.

[redacted] 20[redacted] CERVICAL /VAGINAL THIN PREP: NEGATIVE FOR INTRAEPITHELIAL

[redacted] 20[redacted] EKG: T wave inversion non specific- not clinically significant

[redacted] 20[redacted] HPV GENOTYPE 16: positive

[redacted] 20[redacted] HPV GENOTYPE 18/45: negative

[redacted] 20[redacted] HUMAN PAPILLOMA: positive

[redacted] 20[redacted] PET/CT SCAN: HYPERMATABOLIC DENSITY IN THE RIGHT SIDE OF THE TONGUE AS DESCRIBED ABOVE CONSISTENT WITH HEAD AND NECK CT SCAN WITH F-18 FDG AVID ACTIVE NEOPLSTIC PROCESS. CORRELATION WITH HEAD AND NECK CT SCAN WITH IV CONTRAST IS RECOMENDED. 2. SYMMETRIC INTENSE F-18 FDG UPTAKE IN THE WALDEYERS RING IS NOTED. ALTHOUGHT IT COULD BE REACTIVE, PLEASE CORRELATE CLINICALLY TO EXCLUDE OTHER PATHOLOGY. 3. NO HYPERBOLIC FOCI TO SUGGEST F-18 FDG AVIS DISTANT METASTATIC DISEASE AT THE PRESENT TIME.

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
浮動性めまい	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 15 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: COMPRESSION FRACTURE T5	19[redacted]
OTHER: COMPRESSION FRACTURE L2	19
OTHER: PLAQUE PSORIASIS	19
DRUG ALLERGIES/REACTIONS: DARVON	20
OTHER: MYOFASCIAL PAIN SYNDROME	20
OTHER: POST MENOPAUSAL	20
PNEUMONIA	20
CORONARY ARTERY DISEASE: DILATED CARDIOMYOPATHY EJECTION FRACTION 45%	20
EYE DISEASE/DISORDER: IRITIS	20
MYOCARDIAL INFARCTION	20
OSTEOPOROSIS	20
OTHER: DYSLIPIDEMIA	20
OTHER: SCIATICA LEFT SIDE	20
GASTROESOPHAGEAL REFLUX DISEASE: DYSPEPSIA	20
OTHER: BURSITIS OF LEFT HIP	20
OTHER: BURSITIS OF RIGHT SHOULDER	20
OTHER: LESION SECONDARY TO PSORIASIS	20
HYPERTENSION	20
OTHER: FRACTURE LEFT WRIST	20
OTHER: HOARSENESS	20
DEGENERATIVE DISC DISEASE: L3-4, L4-5	20
OSTEOARTHRITIS: DEGENERATIVE CHANGES IN PROXIMAL INTERPHALANGES	20
OTHER: INSOMNIA	20
OTHER: VITAMIN D DEFICIENCY	20
OTHER: FRAGILITY FRACTURE LEFT 5TH FINGER	20
OTHER: HYPOKALEMIA	20
OTHER: LOW BACK PAIN	20
CONGESTIVE HEART FAILURE	20
OTHER: ANXIETY	20

OTHER: BIBASILAR STRANDS OF ATELECTASIS OR FIBROSIS	20
OTHER: BORDERLINE CARDIAC DECOMPENSATION	20
OTHER: MILD VASCULAR CONGESTION	20
OTHER: BORDERLINE CARDIOMEGALY	20

Prior Procedures	Procedure Year
SURGERY: LYMPH NODE DISSECTION	19

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	20 / 1	20 / 168	168
ABT-494	15MG	ORAL	QD	20 / 169	20 / 392	224
ABT-494	15MG	ORAL	QD	20 / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETANERCEPT	25 mg	OTHER: TWICE WEEKLY	Y-M: 20
FOLIC ACID	9 mg	EVERY WEEK	Y-M: 20
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20
CALCIUM	1 OTHER: TAB	QD	Y-M: 20 -
VERAPAMIL	240 mg	QD	Y-M: 20 -
ETANERCEPT	25 mg	EVERY WEEK	Y-M: 20 -
HYDROCHLOROTHIAZIDE W/LOSARTAN	12.5MG-50MG mg	QD	Y-M: 20 -
COLECALCIFEROL	50,000 IU	EVERY WEEK	Y-M: 20 -
INFLIXIMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20 -
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20 -
DENOSUMAB	60 mg	OTHER: EVERY 6	Y-M: 20 -

		MONTHS	
IBUPROFEN	800 mg	BID	Y-M: 20[redacted] / -351
AMITRIPTYLINE	100 mg	OTHER: HS	Y-M: 20[redacted] / -228
CYCLOBENZAPRINE	10 mg	QD	Y-M: 20[redacted] / -122

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	9 mg	EVERY WEEK	Y-M: 20[redacted]	Not reported.
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]	Not reported.
COLECALCIFEROL	50,000 IU	EVERY WEEK	Y-M: 20[redacted]	Not reported.
IBUPROFEN	800 mg	BID	Y-M: 20[redacted] / -351	Y-M: 20[redacted] / 168
AMITRIPTYLINE	100 mg	OTHER: HS	Y-M: 20[redacted] / -228	Not reported.
CYCLOBENZAPRINE	10 mg	QD	Y-M: 20[redacted] / -122	Not reported.
HYDROXYZINE	25 mg	TID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 126
ALPRAZOLAM	0.25 mg	BID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 154
CARVEDILOL	6.25 mg	BID	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 124
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 124
POTASSIUM	20 mEq	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 168
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 106	Not reported.
SACUBITRIL VALSARTAN SODIUM HYDRATE	1 OTHER: TAB	BID	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 278
FUROSEMIDE	40 mg	QD	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 153
CARVEDILOL	12.5 mg	QD	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 803
HYDROXYZINE	25 mg	PRN	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 154
FUROSEMIDE	20 mg	QD	Y-M: 20[redacted] / 154	Y-M: 20[redacted] / 171
POTASSIUM	20 mEq	BID	Y-M: 20[redacted]	Y-M: 20[redacted]

			[redacted] / 169	/ 171
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted]- [redacted] / 169	Y-M: 20[redacted]- [redacted] / 803
POTASSIUM	20 mEq	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]- [redacted] / 172	Y-M: 20[redacted]- [redacted] / 278
FUROSEMIDE	20 mg	OTHER: QOD	Y-M: 20[redacted]- [redacted] / 172	Y-M: 20[redacted]- [redacted] / 472
DENOSUMAB	60 mg	OTHER: Q 6 MONTHS	Y-M: 20[redacted]- [redacted] / 183	Not reported.
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted]- [redacted] / 228	Not reported.
SPIRONOLACTONE	25 mg	QD	Y-M: 20[redacted]- [redacted] / 473	Y-M: 20[redacted]- [redacted] / 803
LOSARTAN	100 mg	QD	Y-M: 20[redacted]- [redacted] / 487	Y-M: 20[redacted]- [redacted] / 803
CARVEDILOL	12.5 mg	BID	Y-M: 20[redacted]- [redacted] / 804	Not reported.
CYCLOBENZAPRINE	10 mg	QD	Y-M: 20[redacted]- [redacted] / 804	Not reported.
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted]- [redacted] / 804	Not reported.
FUROSEMIDE	20 mg	BID	Y-M: 20[redacted]- [redacted] / 804	Not reported.
SPIRONOLACTONE	12.5 mg	QD	Y-M: 20[redacted]- [redacted] / 805	Y-M: 20[redacted]- [redacted] / 873

Event #2: Serious Adverse Event

Event Description	ACUTE DIZZINESS
Preferred term	浮動性めまい
AE Onset Date / Rx Day	[redacted]20[redacted] / 803
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 803): NPTST035-BNP: 24 [0 - 0.1] ng/L; NPTST174-PROTIME: 8.9 [9 - 12] sec; NPTST207-TROPONIN I: 0.02 [0 - 0.05] ng/mL; [redacted]20[redacted] (RX DAY 804): NPTST076-D DIMER: 2.99 [0.19 - 0.5] mg/L; NPTST207-TROPONIN I: 0.02 [0 - 0.02] ng/mL; NPTST210-TSH: 2.8 [0.45 - 5.33] mIU/L; [redacted]20[redacted] (RX DAY 805): Alanine Aminotransferase: 16 [13 - 39] U/L; Alkaline Phosphatase: 78 [34 - 104] U/L; Bicarbonate: 24 [21 - 31] mmol/L; Creatinine: 106.08 [53.04 - 106.08] umol/L; Erythrocytes: 3.4 [4.3 - 5.1] 10^12/L; Hematocrit: 0.33 [0.35 - 0.45] fraction of 1; Hemoglobin: 112 [117 - 155] g/L; Leukocytes: 8.6 [4.5 - 11] 10^9/L; NPTST092-GFR: 48 [60 - 60] mL/min/1.73m2; NPTST136-MAGNESIUM: 2.5 [1.9 - 2.7] mg/dL; NPTST136-MAGNESIUM: 1.6 [1.9 - 2.7] mg/dL; Platelets: 421 [150 - 400] 10^9/L; Potassium: 3.6 [3.5 - 5.1] mmol/L; Sodium: 136 [136 - 145] mmol/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 803): CHEST X-RAY: NORMAL; CT ANGIOGRAPHY OF CHEST: NORMAL; ECG: LEFT AXIS DEVIATION, LOW QRS VOLTAGE IN PRECORDIAL LEADS, POSSIBLE ANTERIOR MYOCARDIAL INFARCTION, OF INDETERMINATE AG.BR/MODERATE T-WAVE ABNORMALITY,

CONSIDER LATERAL ISCHEMIA; [redacted]20[redacted] (RX DAY 804): CHEST X-RAY: NORMAL; [redacted]20[redacted] (RX DAY 805): BRCHOCARDIOGRAM SPECTRAL/COLOR FLOW COMP: NORMAL LEFT ATRIAL SIZE; NORMAL AORTIC VALUE STRUCTURE & FUNCTION, NO EVIDENCE OF PERICARDIAL EFFUSION

AE Stopped Rx Day	805
Duration of AE	3 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DEHYDRATION
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: M15-554

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，急性の浮動性めまいの事象を発現した。

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，心筋梗塞，高血圧，低カリウム血症，境界域心代償不全，うっ血性心不全，軽度血管うっ血，境界域心拡大，非喫煙者及び非飲酒者であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。高血圧の家族歴もあった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性の浮動性めまいを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性の浮動性めまいは消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は脱水によると思われる低血圧で入院した。被験者は急に浮動性めまいを発症した。臨床検査の結果は，マグネシウムと D ダイマーを除き正常であった。マグネシウムの補充が行われた。胸部 CT 血管造影で肺塞栓は否定された。うっ血性心不全の所見はなかった。心電図の変化はなかった。高血圧治療薬／利尿薬を調整し，被験者の症状は改善した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は良好な状態で退院した。

治験責任医師によれば，被験者の危険因子として，20[redacted] 年 [redacted] 月に生じた僧帽弁逆流症（非重篤）に加え，高血圧，うっ血性心不全のほか，心筋梗塞，腎前性高窒素血症，不眠症及び胃食道逆流の既往が挙げられる。

病院の記録によれば，被験者は急に浮動性めまいと嗜眠を発症して救急治療室を受診した。被験者には嗜眠及び疲労感があり，運動耐性の低下，全身脱力及び倦怠感を伴っていた。被験者は，入院前の 3～4 日間に食欲がひどく低下していて，極度の嗜眠と疲労感があったと述べた。

The patient's past medications include:

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

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

LOSARTAN-HYDROCHLOROTHIAZIDE for HYPERTENSION ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

INFLIXIMAB for PSORITAIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

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

HYDROXAZINE for PRURITUS SECONDARY TO PSORIASIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

ENTRESTO for MITRAL VALVE REGURGITATION ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

KCL for PROPHYLAXIS OF HYPOKALEMIA ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Dizziness (10013573) (Dizziness (10013573)) [v.22.1] [10013573]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE DIZZINESS

- Investigator: Dehydration

- AbbVie: Event is more likely related to decreased appetite for the past 3 to 4 days prior to admission with dehydration as noted in narrative. Additional risk factors include concomitant use of diuretic medication, antihypertensives and flexeril and pre-existing insomnia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 16 U/L (normal 13 to 39)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 78 U/L (normal 34 to 104)

[redacted] **20[redacted] BICARBONATE:** 24 MEQ/L (normal 21 to 31)

[redacted] **20[redacted] BLOOD PRESSURE:** 175/90 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 147/79 mmHg

[redacted] **20[redacted] BNP:** 24 PG/ML (normal 0 to 0.1)

[redacted] **20[redacted] BRONCHOCARDIOGRAM / SPECTRAL COLOR FLOW COMP:** Normal left atrial size; normal aortic value structure & function, no evidence of pericardial effusion

[redacted] **20[redacted] CHEST XRAY:** Normal

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

[redacted] **20[redacted] CT ANGIOGRAPHY OF CHEST:** Normal

[redacted] **20[redacted] D-DIMER:** 2.99 MG/L (normal 0.19 to 0.5)

[redacted] **20[redacted] ECG:** Left axis deviation, low QRS voltage in precordial leads, possible anterior myocardial infarction, of indeterminate AG.BR/Moderate T-Wave abnormality, consider Lateral ischemia

[redacted] **20[redacted] GFR:** 48 ml/min/1.72 (normal 60 to 60)

[redacted] **20[redacted] HEMATOCRIT:** 32.5 % (normal 35.0 to 45.0)

[redacted] **20[redacted] HEMOGLOBIN:** 11.2 G/DL (normal 11.7 to 15.5)

[redacted] **20[redacted] MAGNESIUM:** 1.6 mg/dL (normal 1.9 to 2.7)

[redacted] **20[redacted] MAGNESIUM:** 2.5 mg/dL (normal 1.9 to 2.7)

[redacted] **20[redacted] PLATELET COUNT:** 421 10^3/uL (normal 150 to 400)

[redacted] **20[redacted] POTASSIUM:** 3.6 MEQ/L (normal 3.5 to 5.1)

[redacted] **20[redacted] PRO TIME:** <8.9 SEC (normal 9.0 to 12.0)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.37 10^6/uL (normal 4.30 to 5.10)

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

[redacted] **20[redacted] TROPONIN I:** 0.022 NG/ML (normal 0 to 0.049)

[redacted] **20[redacted] TROPONIN I:** 0.02 NG/ML (normal 0 to 0.02)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.6 10^3/uL (normal 4.5 to 11.0)

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

Reason for Narrative

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

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

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: FIBROCYSTIC BREAST DISEASE	20[redacted]
DRUG ALLERGIES/REACTIONS: SULFA ALLERGY; HIVES WITH THROAT CLOSURE	20[redacted]
OTHER: DEVIATED SEPTUM	20[redacted]
OTHER: ANXIETY	20[redacted]
ANEMIA: DUE TO UTERINE FIBROIDS	20[redacted]
OTHER: LOW BACK PAIN (DEGENERATIVE DISC DISEASE LUMBAR SPINE)	20[redacted]
OTHER: UTERINE FIBROIDS	20[redacted]
OTHER: BENIGN CYST ON LIVER	20[redacted]
OTHER: OCCASIONAL ORAL ULCERS	20[redacted]
OTHER: ENVIRONMENTAL ALLERGIES	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: OCCASIONAL	20[redacted]
OTHER: CHRONIC GASTRITIS	20[redacted]
OTHER: DIVERTICULOSIS	20[redacted]
OTHER: EXTERNAL HEMORRHOIDS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: BENIGN BREAST CYST REMOVAL	20[redacted]
SURGERY: REPAIR DEVIATED SEPTUM	20[redacted]
SURGERY: HYSTERECTOMY (DUE TO FIBROIDS)	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	5	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 147	147

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VENLAFAXINE	37.5 mg	QD	Y-M: 20[redacted]
FAMOTIDINE	20 mg	PRN	Y-M: 20[redacted]
METHOTREXATE	17.5 mg	EVERY WEEK	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
ASCORBIC ACID	1000 mg	QD	Y-M: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted]
IBUPROFEN	600 mg	QD	Y-M: 20[redacted] / -308
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted] / -62

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
VENLAFAXINE	37.5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 330
FAMOTIDINE	20 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 167
ASCORBIC ACID	1000 mg	QD	Y-M: 20[redacted]	Not reported.
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	Not reported.
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted]	Not reported.
IBUPROFEN	600 mg	QD	Y-M: 20[redacted] / -308	Y-M: 20[redacted] / 163
HYDROXYCHLOROQUINE	200 mg	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 158
CIPROFLOXACIN	250 mg	BID	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 148
NITROFURANTOIN	100 mg	BID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 155
DIPHENHYDRAMINE	37.5 mg	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 187

PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 153	Y-M: 20[redacted] / 155
PHENAZOPYRIDINE	100 mg	TID	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 156
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 158	Y-M: 20[redacted] / 167
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 159	Y-M: 20[redacted] / 162
NYSTATIN	400,000 OTHER: UNIT	QID	Y-M: 20[redacted] / 160	Y-M: 20[redacted] / 169
DICYCLOVERINE	20 mg	QD	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 163
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 178
HYOSCYAMINE	0.125 mg	QID	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 184
MAALOX	1 OTHER: TABLESPOON	BID	Y-M: 20[redacted] / 168	Not reported.
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 168	Not reported.
BIFIDOBACTERIUM INFANTIS	4 mg	QD	Y-M: 20[redacted] / 176	Not reported.

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

Event Description	LEFT SIDE ABDOMINAL PAIN RADIATING TO LEFT FLANK UNKNOWN ETIOLOGY, DIARRHEA
Preferred term	腹痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 156 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 162): Glucose: 5.77 [3.89 - 5.5] mmol/L; Leukocytes: 8.1 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 9.6 [24 - 44] %; Neutrophils/Leukocytes: 81.3 [45 - 75] %; [redacted]20[redacted] (RX DAY 163): Calcium: 2.1 [2.12 - 2.52] mmol/L; Protein: 62 [64 - 82] g/L; [redacted]20[redacted] (RX DAY 164): Albumin: 33 [34 - 50] g/L; Calcium: 2.02 [2.12 - 2.52] mmol/L; Protein: 59 [64 - 82] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 157): CT SCAN OF ABDOMEN/PELVIS WITH CONTRAST: UNREMARKABLE; [redacted]20[redacted] (RX DAY 162): CHEST X-RAY: NORMAL; [redacted]20[redacted] (RX DAY 164): ENDOSCOPY: NORMAL EXCEPT FOR GASTRITIS AS IN MEDICAL HISTORY

AE Stopped Rx Day	184 (37 DAYS AFTER LAST TREATMENT)
Duration of AE	29 DAYS
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

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

Event Description	LEFT SIDE ABDOMINAL PAIN RADIATING TO LEFT FLANK UNKNOWN ETIOLOGY, DIARRHEA
Preferred term	下痢
AE Onset Date / Rx Day	[redacted]20[redacted] / 156 (9 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 162): Glucose: 5.77 [3.89 - 5.5] mmol/L; Leukocytes: 8.1 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 9.6 [24 - 44] %; Neutrophils/Leukocytes: 81.3 [45 - 75] %; [redacted]20[redacted] (RX DAY 163): Calcium: 2.1 [2.12 - 2.52] mmol/L; Protein: 62 [64 - 82] g/L; [redacted]20[redacted] (RX DAY 164): Albumin: 33 [34 - 50] g/L; Calcium: 2.02 [2.12 - 2.52] mmol/L; Protein: 59 [64 - 82] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 157): CT SCAN OF ABDOMEN/PELVIS WITH CONTRAST: UNREMARKABLE; [redacted]20[redacted] (RX DAY 162): CHEST X-RAY: NORMAL; [redacted]20[redacted] (RX DAY 164): ENDOSCOPY: NORMAL EXCEPT FOR GASTRITIS AS IN MEDICAL HISTORY

AE Stopped Rx Day	184 (37 DAYS AFTER LAST TREATMENT)
Duration of AE	29 DAYS
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: M15-554

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左側腹部に放散する原因不明の左腹部痛及び下痢の事象を発現した。

Event 2 及び 3 の臨床経過：

関連する病歴は局面型乾癬，良性肝嚢胞，乾癬性関節炎，慢性胃炎，胃食道逆流性疾患，元喫煙者（1 日 0.5 箱を 5 年間），憩室症及び元飲酒者（1 日 2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左側腹部に放散する原因不明の左腹部痛及び下痢を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左側腹部に放散する原因不明の左腹部痛及び下痢は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は尿路感染（非重篤）を発現した。UTI により治験薬の投与が中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はシプロフロキサシンに対するアレルギー反応（非重篤）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日にはピリジウム不耐性（非重篤）も認められた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は腹痛のため救急治療室（ER）を受診し，腹部／骨盤部の造影 CT スキャン検査及び臨床検査を受けた。検査結果はすべて異常なしであった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，痙攣性の鋭い痛みを伴って左側腹部に放散する間欠性で中等度の左腹部痛と，これに伴う下痢を訴えて，ER を受診した。被験者によると，発熱，悪寒，嘔吐，排尿困難，血便，食欲の変化及び体重減少はなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，清澄流動食が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，内視鏡検査が行われたが，結果は胃炎が認められた以外は異常なしであった。腹痛の原因は不明であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，マーロックス，pantoprazole，align probiotic，hyoscyamine，zofran 及び bentyl であった。

The patient's past medications include:

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

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

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

CIPROFLOXACIN for URINARY TRACT INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

MACROBID for URINARY TRACT INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ALLERGIC REACTION CIPROFLOXACIN ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Abdominal pain localized (10062367) (Abdominal pain (10000081)) [v.22.0] [10062367]

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

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

Dechallenge: Not Applicable

2) Diarrhea (10012727) (Diarrhoea (10012735)) [v.22.0] [10012727]

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 LEFT SIDE ABDOMINAL PAIN RADIATING TO LEFT FLANK UNKNOWN ETIOLOGY, DIARRHEA

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing chronic gastritis and diverticulosis, as well as recent urinary tract infection.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ALBUMIN:** 3.3 G/DL (normal 3.4 to 5.0)

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

[redacted] **CALCIUM:** 8.1 mg/dL (normal 8.5 to 10.1)

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

[redacted] **CT SCAN OF ABDOMEN AND PELVIS WITH CONTRAST:** Unremarkable

[redacted] **ENDOSCOPY:** Normal except for gastritis as in medical history

[redacted] **GLUCOSE:** 104 mg/dL (normal 70 to 99)

[redacted] **LYMPHOCYTES:** 9.6 % (normal 24 to 44)

[redacted] **NEUTROPHILS:** 81.3 % (normal 45 to 78)

[redacted] **TOTAL PROTEIN:** 6.2 G/DL (normal 6.4 to 8.2)

[redacted] **TOTAL PROTEIN:** 5.9 G/DL (normal 6.4 to 8.2)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.1 TH/UL (normal 4.5 to 11)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
上室性頻脈	X			

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

Medical History	Onset Year
OTHER: INTERMITTENT HEADACHES	19[redacted]
OTHER: PLAQUE PSORIASIS	19
OTHER: INDIGESTION	20
HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA; NO MEDS; DIET CONTROLLED	20
OTHER: HERPES ZOSTER	20
DEGENERATIVE DISC DISEASE: LUMBAR	20
OTHER: LOW BACK PAIN	20
OTHER: DYSPAREUNIA	20
CARDIAC ARRHYTHMIA: PALPITATIONS	20
OSTEOARTHRITIS: BILATERAL OSTEOARTHRITIS OF HANDS	20
OTHER: POSTMENOPAUSAL	20
OTHER: LUMBAR SPONDYLOLITHESIS	20
OTHER: SACROILIITIS	20
OTHER: INSOMNIA	20
OTHER: OCCASIONAL BLURRY VISION	20
OTHER: ANKYLOSED TOE LEFT 3RD	20
OTHER: THORACIC SPONDYLOSIS	20
OTHER: PSORIATIC NAIL DYSTROPHY	20

Prior Procedures	Procedure Year
SURGERY: LASIK BOTH EYES	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	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 393	225
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 394	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CORTISONE	1 OTHER: APPLICATION	QID	Y-M: 20[redacted]
ALKA SELTZER	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]
CALCIUM CARBONATE	2 OTHER: TABS	PRN	Y-M: 20[redacted]
IBUPROFEN	200 mg	QID	Y-M: 20[redacted]
CALCIUM WITH VITAMIN D	1 OTHER: TABLET	QD	Y-M: 20[redacted]
FISH OIL	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
OSPEMIFENE	60 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]-[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]
PROBIOTICS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]-[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]
METHYLPREDNISOLONE	80 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted]-[redacted]
CERTOLIZUMAB PEGOL	400 mg	OTHER: Q 4 WEEKS	Y-M: 20[redacted]-[redacted] / -236
CURCUMA LONGA	2 OTHER: TABLETS	QD	Y-M: 20[redacted]-[redacted] / -145
DOXYLAMINE	12.5 mg	PRN	Y-M: 20[redacted]-[redacted] / -114
MELATONIN	3 mg	PRN	Y-M: 20[redacted]-[redacted] / -114

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
ALKA SELTZER	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]	Not reported.
CALCIUM CARBONATE	2 OTHER: TABS	PRN	Y-M: 20[redacted]	Not reported.
IBUPROFEN	200 mg	QID	Y-M: 20[redacted]	Not reported.
CALCIUM WITH VITAMIN D	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Not reported.
FISH OIL	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]	Not reported.
OSPEMIFENE	60 mg	QD	Y-M: 20[redacted]	Not reported.
PROBIOTICS	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Not reported.
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 561
CURCUMA LONGA	2 OTHER: TABLETS	QD	Y-M: 20[redacted] / -145	Not reported.
DOXYLAMINE	12.5 mg	PRN	Y-M: 20[redacted] / -114	Not reported.
MELATONIN	3 mg	PRN	Y-M: 20[redacted] / -114	Not reported.
ESTROGENS CONJUGATED	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 2	Not reported.
MAGNESIUM	400 mg	QD	Y-M: 20[redacted] / 43	Not reported.
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 114	Not reported.
BIOTIN	10,000 ug	QD	Y-M: 20[redacted] / 118	Not reported.
FOLIC ACID	4 mg	QD	Y-M: 20[redacted] / 169	Y-M: 20[redacted] / 756
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 372	Not reported.
COLECALCIFEROL	4000 IU	QD	Y-M: 20[redacted] / 373	Not reported.
FOLINIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted] / 394	Y-M: 20[redacted] / 756
MACROGOL 3350	17 g	PRN	Y-M: 20[redacted] / 460	Not reported.
DILTIAZEM	30 mg	TID	Y-M: 20[redacted] / 493	Not reported.
ACETYLSALICYLIC ACID	324 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 493	Y-M: 20[redacted] / 493
ADENOSINE	12 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 493	Y-M: 20[redacted] / 493
ADENOSINE	6 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 493	Y-M: 20[redacted] / 493
CEPACOL ANESTHETIC	1 OTHER: LOZENGE	OTHER: SINGLE	Y-M: 20[redacted] /	Y-M: 20[redacted] /

		DOSE	493	493
MYLANTA	30 mL	OTHER: SINGLE	Y-M: 20[redacted] /	Y-M: 20[redacted] /
		DOSE	493	493

Event #1: Serious Adverse Event

Event Description	PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA
Preferred term	上室性頻脈
AE Onset Date / Rx Day	[redacted]20[redacted] / 493
Age at AE Onset	5[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 493): NPTST160-PC BN PEPTIDE: LESS THAN 20.0 [0 - 100] pg/mL; NPTST161-PC TROPONIN 1: 0.01 [0 - 0.06] ng/mL; NPTST208-TROPONIN-1: 0.02 [0 - 0.05] ng/mL; NPTST210-TSH: 2.54 [0.36 - 3.74] ng/mL; [redacted]20[redacted] (RX DAY 494): NPTST034-BN PEPTIDE: 52.2 [0 - 100] pg/mL
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 493): CHEST X-RAY 1 VIEW: NORMAL; ECHOCARDIOGRAM: WITHIN NORMAL LIMITS; EKG: SINUS TACHYCARDIA WITH SHORT PR OTHERWISE NORMAL; [redacted]20[redacted] (RX DAY 494): EKG: NORMAL SINUS RHYTHM NONSPECIFIC T WAVE ABNORMALITY
AE Stopped Rx Day	493
Duration of AE	1 DAY
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HISTORY OF PALPITATIONS; PREEXISTING CONDUCTION ISSUE
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: M15-554

治験責任医師からの報告。本被験者は米国の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，発作性上室性頻脈（悪化）の事象を発現した。

Event 1 の臨床経過：

関連する病歴は局面型乾癬，高脂血症，発作性上室性頻脈，閉経後，乾癬性関節炎，不眠症，胸部脊椎症，非喫煙者及び非飲酒者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は発作性上室性頻脈（悪化）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，発作性上室性頻脈（悪化）は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は運転中に動悸を自覚し，脱力感及び頭のふらつきが出現し，気分が悪くなり，発汗も来した。友人によると，被験者の血圧は 200/110 mmHg で，心拍数は速すぎて数えられなかった。救急隊員が要請された。到着時，被験者は PSVT の状態にあり，アスピリン及びアデノシンが投与された。2 回目のアデノシン投与で PSVT が消失し，心電図検査により NSR が確認された。同日，被験者は入院した。被験者によると，過去数年間に同様の事象が起こっていたが，それらは不安によるものと思われ，気分が落ち着くと治まった。Cardizem の投与が開始された。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，アデノシン，cardizem 及びプラバスタチンであった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Paroxysmal supraventricular tachycardia (10034044) (Supraventricular tachycardia (10042604)) [v.22.1] [10034044]

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 PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA (WORSENING)

- Investigator: History of palpitations, preexisting conduction issue.

- AbbVie: Risk factor includes pre-existing palpitations since 20[redacted].

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** 200/110 mmHg

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

[redacted] **20[redacted] ECHOCARDIOGRAM:** WITHIN NORMAL LIMITS

[redacted] **20[redacted] EKG:** SINUS TACHYCARDIA WITH SHORT PR OTHERWISE NORMAL; VENTRICULAR RATE: 105 bpm

[redacted] **20[redacted] EKG:** NORMAL SINUS RHYTHM NONSPECIFIC T WAVE ABNORMALITY

[redacted] **20[redacted] PC BN PEPTIDE:** <20.0 pg/mL

[redacted] **20[redacted] PC BN PEPTIDE:** 52.2 PG/ML (normal 0.00 to 100.0)

[redacted] **20[redacted] POTASSIUM:** 4.4 no unit

[redacted] **20[redacted] RBC:** 3.72 no unit

[redacted] **20[redacted] TOTAL CHOLESTEROL:** 210 no unit

[redacted] **20[redacted] TROPONIN 1:** 0.01 NG/ML (normal 0.00 to 0.06)

[redacted] **20[redacted] TROPONIN 1:** 0.016 NG/ML (normal 0.00 to 0.06)

[redacted] **20[redacted] TSH:** 2.540 NG/ML (normal 0.358 to 3.740)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
急性腎障害	X			X
蜂巣炎	X			X

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

Medical History	Onset Year
OTHER: INGUINAL HERNIA	NOT REPORTED
OTHER: ROTATOR CUFF TEAR	NOT REPORTED
OTHER: SEASONAL ALLERGIES	NOT REPORTED
OTHER: JOINT PAIN	19[redacted]
HYPOTHYROIDISM	20[redacted]
OSTEOARTHRITIS: KNEE	20[redacted]
KIDNEY DISORDER: ABNORMAL KIDNEY FUNCTION	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: LEFT KNEE REPLACEMENT	20[redacted]
SURGERY: RIGHT HIP REPLACEMENT	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	4.5	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 170	[redacted]20[redacted] / 392	223
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LEVOTHYROXINE	200 OTHER: MCG	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	UNK mg	OTHER: UNKNOWN	Y-M: 20[redacted]-[redacted]
ETANERCEPT	UNK mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	UNK mg	EVERY 2 WEEKS	Y-M: 20[redacted]-[redacted]
DICLOFENAC	1 OTHER: APPLICATION	QID	Y-M: 20[redacted]-[redacted]
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]-[redacted]
TRIAMCINOLONE	80 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / -57

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	200 OTHER: MCG	QD	Y-M: 20[redacted]-[redacted]	Not reported.
DICLOFENAC	1 OTHER: APPLICATION	QID	Y-M: 20[redacted]-[redacted]	Not reported.
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]-[redacted]	Not reported.
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]-[redacted]	Not reported.
NYSTATIN	2 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted] / 113	Not reported.
CLINDAMYCIN	300 mg	TID	Y-M: 20[redacted]-[redacted] / 499	Not reported.
ERGOCALCIFEROL	1.25 mg	QD	Y-M: 20[redacted]-[redacted] / 510	Not reported.
MUPIROCIN	1 OTHER: APP	TID	Y-M: 20[redacted]-[redacted] / 510	Not reported.
PARACETAMOL	650 mg	OTHER: Q6HR PRN	Y-M: 20[redacted]-[redacted] / 510	Not reported.
CEFEPIME	50 mL	OTHER: Q8HR	Y-M: 20[redacted]-[redacted] / 510	Y-M: 20[redacted]-[redacted] / 518
ERGOCALCIFEROL	50000 OTHER:	EVERY WEEK	Y-M: 20[redacted]-[redacted] /	Y-M: 20[redacted]-[redacted] /

	INTL_UNITS CAP		510 518
MORPHINE	2 mg	OTHER: Q4HR PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 510 518
ONDANSETRON	4 mg	OTHER: Q4HR PRN	Y-M: 20[redacted] / Y-M: 20[redacted] / 510 518
PIP/TAZO	15 mL	OTHER: Q6HR	Y-M: 20[redacted] / Y-M: 20[redacted] / 510 518
AMLODIPINE	5 mg	BID	Y-M: 20[redacted] / Not reported. 516
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 518 528
TRAMADOL	50 mg	BID	Y-M: 20[redacted] / Not reported. 648

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	CELLULITIS LEFT LEG, ACUTE RENAL FAILURE
Preferred term	急性腎障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 510
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 510): Creatinine: 160.01 [56.58 - 112.27] umol/L; Glucose: 9.55 [3.89 - 5.5] mmol/L; Hematocrit: 0.39 [0.4 - 0.5] fraction of 1; Hemoglobin: 134 [137 - 170] g/L; Leukocytes: 24.7 [4 - 11] 10^9/L; Lymphocytes: 0.25 [0.5 - 4.8] 10^9/L; NPTST027-BAND MAN: 8 [0 - 5] %; NPTST079-EGFR AA: 48 [30 - 59] mL/min/1.73m2; NPTST134-LYMPH MAN: 1 [19 - 48] %; NPTST189-SED RATE: 84 [0 - 10] mm/h; NPTST190-SEGS MAN: 91 [40 - 74] %; Neutrophils: 24.5 [1.6 - 8.5] 10^9/L; [redacted]20[redacted] (RX DAY 518): Creatinine: 162.66 [56.58 - 112.27] umol/L; Erythrocytes: 3.35 [4.2 - 5.6] mU/L; Glucose: 5.77 [3.89 - 5.5] mmol/L; Hematocrit: 0.32 [0.4 - 0.5] fraction of 1; Hemoglobin: 111 [137 - 170] g/L; NPTST135-LYMPHOCYTES: 10.4 [19 - 48] %; NPTST152-NEUTRO ABSOLUTE: 8.8 [1.6 - 8.5] 10^3/uL; NPTST153-NEUTROPHILS: 84.5 [40 - 74] %; Platelets: 563 [150 - 400] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 510): WOUND NPTST154-NON-CULTURE MICROBIOLOGY: NEGATIVE-MRSA NAAT - NEGATIVE 2+ STREPTOCOCCUS PYOGENES (GROUP A)

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 510): MAGNETIC RESONANCE IMAGING: BONE MARROW THERE IS A PARTIALLY INCLUDED KNEE PROSTHESIS. NORMAL SIGNAL, WITHOUT EVIDENCE FOR EDEMA OR FRACTURE. MUSCULOTENDIOUS STRUCTURES. NORMAL APPEARANCE. SUBCUTANEOUS SOFT TISSUES NO EVID

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	TRAUMA TO THE LEG
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	CELLULITIS LEFT LEG, ACUTE RENAL FAILURE
Preferred term	蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 510
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 510): Creatinine: 160.01 [56.58 - 112.27] umol/L; Glucose: 9.55 [3.89 - 5.5] mmol/L; Hematocrit: 0.39 [0.4 - 0.5] fraction of 1; Hemoglobin: 134 [137 - 170] g/L; Leukocytes: 24.7 [4 - 11] 10^9/L; Lymphocytes: 0.25 [0.5 - 4.8] 10^9/L; NPTST027-BAND MAN: 8 [0 - 5] %; NPTST079-EGFR AA: 48 [30 - 59] mL/min/1.73m2; NPTST134-LYMPH MAN: 1 [19 - 48] %; NPTST189-SED RATE: 84 [0 - 10] mm/h; NPTST190-SEGS MAN: 91 [40 - 74] %; Neutrophils: 24.5 [1.6 - 8.5] 10^9/L; [redacted]20[redacted] (RX DAY 518): Creatinine: 162.66 [56.58 - 112.27] umol/L; Erythrocytes: 3.35 [4.2 - 5.6] mU/L; Glucose: 5.77 [3.89 - 5.5] mmol/L; Hematocrit: 0.32 [0.4 - 0.5] fraction of 1; Hemoglobin: 111 [137 - 170] g/L; NPTST135-LYMPHOCYTES: 10.4 [19 - 48] %; NPTST152-NEUTRO ABSOLUTE: 8.8 [1.6 - 8.5] 10^3/uL; NPTST153-NEUTROPHILS: 84.5 [40 - 74] %; Platelets: 563 [150 - 400] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 510): WOUND NPTST154-NON-CULTURE MICROBIOLOGY: NEGATIVE-MRSA NAAT - NEGATIVE 2+ STREPTOCOCCUS PYOGENES (GROUP A)

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 510): MAGNETIC RESONANCE IMAGING: BONE MARROW THERE IS A PARTIALLY INCLUDED KNEE PROSTHESIS. NORMAL SIGNAL, WITHOUT EVIDENCE FOR EDEMA OR FRACTURE. MUSCULOTENDIOUS STRUCTURES. NORMAL APPEARANCE. SUBCUTANEOUS SOFT TISSUES NO EVID

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	TRAUMA TO THE 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: M15-554

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左脚の蜂巣炎及び急性腎不全の事象を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は元紙巻タバコ喫煙者（1 日 1 箱を 4.5 年間），甲状腺機能低下症，血清反応陽性関節リウマチ，腎機能異常，局面型乾癬及び元飲酒者（1 日 2 杯未満）であった。

試験の盲検を解除。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左脚の蜂巣炎及び急性腎不全を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は金づちで負傷した左下肢の蜂巣炎のため入院した。膝下に紅斑が見られ，右下肢と比べると中等度の浮腫が認められた。創傷はすねの中央の高さにあり，淡黄色の排出液を伴っており，触ると温感があった。被験者は白血球増加症，杆状核球増加症及び急性腎障害を発現した。被験者は感染症のため診察を受け，創傷培養で連鎖球菌が検出された。バンコマイシンの静脈内投与が 3 日間行われた後，セフェピム投与下で退院となった。被験者の状態ははるかに良くなり，発熱，悪寒及び寝汗は認められなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，クリンダマイシン，タイレノール，セフェピム，モルヒネ，ムピロシン，セフトリアキソン及びゾシンであった。

The patient's past medications include:

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

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

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

TRIAMCINOLONE ACETONIDE for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute renal failure (10001041) (Acute kidney injury (10069339)) [v.22.1] [10001041]

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

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

Dechallenge: Not Applicable

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

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 CELLULITIS LEFT LEG, ACUTE RENAL FAILURE

- Investigator: Trauma to the leg

- AbbVie: Event is more likely related to accidental trauma sustained to the left lower extremity and pre-existing abnormal kidney function.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABSOLUTE LYMPHOCYTES:** 0.25 K/UL (normal 0.5 to 4.8)

[redacted] **20[redacted] ABSOLUTE NEUTROPHIL:** 24.5 K/UL (normal 1.60 to 8.50)

[redacted] **20[redacted] ABSOLUTE NEUTROPHIL:** 8.80 K/UL (normal 1.60 to 8.50)

[redacted] **20[redacted] BAND MAN:** 8 % (normal 0 to 5)

[redacted] **20[redacted] CREATININE:** 1.81 mg/dL (normal 0.64 to 1.27)

[redacted] **20[redacted] CREATININE:** 1.84 mg/dL (normal 0.64 to 1.27)

[redacted] **20[redacted] CULTURE:** WOUND CULTURE: MRSA NAAT - NEGATIVE 2+ STREPTOCOCCUS PYOGENES (GROUP A)

[redacted] **20[redacted] ERYTHROCYTE SEDIMENTATION RATE:** 84 MM/HR (normal 0 to 10)

[redacted] **20[redacted] GFR:** 48 ML/Min (normal 30 to 59)

[redacted] **20[redacted] GLUCOSE:** 172 mg/dL (normal 70 to 99)

[redacted] **20[redacted] GLUCOSE:** 104 mg/dL (normal 70 to 99)

[redacted] **20[redacted] HCT:** 39.3 % (normal 40 to 50)

[redacted] **20[redacted] HCT:** 31.6 % (normal 40 to 50)

[redacted] **20[redacted] HGB:** 13.4 G/DL (normal 13.7 to 17)

[redacted] **20[redacted] HGB:** 11.1 G/DL (normal 13.7 to 17)

[redacted] **20[redacted] LYMPH MAN:** 1 % (normal 19 to 48)

[redacted] **20[redacted] LYMPHOCYTES:** 10.4 % (normal 19 to 48)

[redacted] **20[redacted] MAGNETIC RESONANCE IMAGING:** Bone marrow there is a partially included knee prosthesis. Normal signal, without evidence for edema or fracture. Musculotendious structures. Normal appearance. Subcutaneous soft Tissues no evidence of a mass or fluid collection is seen by the noncontrast technique. There is extensive subcutaneous soft tissue edema seen circumferentially about the leg.

[redacted] **20[redacted] NEUTROPHILS:** 84.5 % (normal 40 to 74)

[redacted] **20[redacted] PLATELET COUNT:** 563 X10**9/L (normal 150 to 450)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.35 X10**6/MCL (normal 4.20 to 5.60)

[redacted] **20[redacted] SEGS MAN:** 91 % (normal 40 to 74)

[redacted] **20[redacted] WBC:** 24.7 K/uL (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
全身性炎症反応症候群	X			

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

Medical History	Onset Year
OTHER: PHOTOSENSITIVITY	19[redacted]
OTHER: SEASONAL ALLERGIES	19
OTHER: CERVICAL DYSPLASIA LEADING TO HYSTERECTOMY	19
GASTROESOPHAGEAL REFLUX DISEASE	19
OTHER: INTERMITTENT CONSTIPATION	19
OTHER: INTERMITTENT DIARRHEA	19
OTHER: GELLING PHENOMENON	19
OTHER: JOINT SWELLING	19
OTHER: PLAQUE PSORIASIS	19
OTHER: MORNING STIFFNESS	19
OTHER: DRY EYES/MOUTH	20
OTHER: ELEVATED LIVER TRANSAMINASIS	20
CHOLECYSTITIS	20
DIABETES MELLITUS	20
LIVER DISEASE (EXCLUDING HEPATITIS): METHOTREXATE INDUCED LIVER CHANGES	20
HYPERLIPIDEMIA: HIGH CHOLESTEROL	20
HYPERTENSION	20
OTHER: LEFT LATERAL EPICONDYLITITS	20
DEGENERATIVE DISC DISEASE: LUMBER SPINE L3-L5	20
OTHER: ROTOSCOLIOSIS LUMBER SPINE	20
MIGRAINE HEADACHE: MIGRAINE WITH TIA SYMPTOMS	20
OTHER: RIGHT SACROILIITIS	20
OTHER: SCLEROSIS LEFT SACROILIAC JOINT	20
OTHER: TRANSIENT APHASIA	20
PERIPHERAL NERVE DISORDER: RIGHT LEG NUMBNESS	20
OTHER: FRACTURE L SECOND METATARSAL	20
OTHER: ALOPECIA	20
HYPOTHYROIDISM	20

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	19[redacted]
SURGERY: NOSE RECONSTRUCTION DUE TO TRAUMA	19[redacted]
SURGERY: CHOLESCYSTECTOMY	20[redacted]
SURGERY: LUMBER RADICULOPATHY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 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	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 177	177
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 178	[redacted]20[redacted] / 402	225
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 403	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETANERCEPT	25.0 mg	OTHER: TWICE/WK	Y-M: 20[redacted]
FOLIC ACID	1.0 mg	QD	Y-M: 20[redacted]
LEFLUNOMIDE	20.0 mg	QD	Y-M: 20[redacted]
INSULIN ASPART	100.0 OTHER: UNITS	QD	Y-M: 20[redacted]
ADALIMUMAB	40.0 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
SULINDAC	200.0 mg	BID	Y-M: 20[redacted]
OMEPRAZOLE	20.00 mg	QD	Y-M: 20[redacted]
GOLIMUMAB	50.0 mg	OTHER: QMONTH	Y-M: 20[redacted]
LOSARTAN	25.0 mg	QD	Y-M: 20[redacted]
PRAVASTATIN	10.0 mg	QD	Y-M: 20[redacted]
FLUTICASONE	50.0 ug	QD	Y-M: 20[redacted]
SECUKINUMAB	300.0 mg	OTHER: Q MONTH	Y-M: 20[redacted]
INSULIN DEGLUDEC	65.0 OTHER: UNITS	QD	Y-M: 20[redacted]
LEVOTHYROXINE	25.0 ug	QD	Y-M: 20[redacted] / -337

METHOTREXATE	25.0 mg	EVERY WEEK	Y-M: 20[redacted]- / - 156

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	1.0 mg	QD	Y-M: 20[redacted]-	Not reported.
INSULIN ASPART	100.0 OTHER: UNITS	QD	Y-M: 20[redacted]	Y-M: 20[redacted]- / 377
SULINDAC	200.0 mg	BID	Y-M: 20[redacted]-	Not reported.
OMEPRAZOLE	20.00 mg	QD	Y-M: 20[redacted]-	Not reported.
LOSARTAN	25.0 mg	QD	Y-M: 20[redacted]-	Not reported.
PRAVASTATIN	10.0 mg	QD	Y-M: 20[redacted]-	Not reported.
FLUTICASONE	50.0 ug	QD	Y-M: 20[redacted]-	Y-M: 20[redacted]- / 194
INSULIN DEGLUDEC	65.0 OTHER: UNITS	QD	Y-M: 20[redacted]-	Y-M: 20[redacted]- / 377
LEVOTHYROXINE	25.0 ug	QD	Y-M: 20[redacted]- / -337	Not reported.
GLUCOSE	4.0 g	PRN	Y-M: 20[redacted]- / 61	Not reported.
PILOCARPINE	.005 ug	QD	Y-M: 20[redacted]- / 73	Not reported.
CEFDINIR	300 mg	BID	Y-M: 20[redacted]- / 76	Y-M: 20[redacted]- / 86
METHOTREXATE	25.00 mg	EVERY WEEK	Y-M: 20[redacted]- / 83	Y-M: 20[redacted]- / 262
IOPAMIDOL	70.0 mg	OTHER: ONCE	Y-M: 20[redacted]- / 115	Y-M: 20[redacted]- / 115
IOPAMIDOL	70.00 mL	OTHER: ONCE	Y-M: 20[redacted]- / 115	Y-M: 20[redacted]- / 115
VANCOMYCIN	125.00 mg	TID	Y-M: 20[redacted]- / 115	Y-M: 20[redacted]- / 116
ONDANSETRON	4.0 mg	BID	Y-M: 20[redacted]- / 115	Y-M: 20[redacted]- / 120
SODIUM CHLORIDE	2000.00 mL	OTHER: CONTINUOUS DRIP	Y-M: 20[redacted]- / 115	Y-M: 20[redacted]- / 121
LACTOBACILLUS ACIDOPHILUS	1.0 OTHER: CAPSULE	QD	Y-M: 20[redacted]- / 116	Not reported.
PIP/TAZO	3.3 g	TID	Y-M: 20[redacted]- / 116	Y-M: 20[redacted]- / 117

VANCOMYCIN	10 mg/kg	TID	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 118
ENOXAPARIN	40.0 mg	QD	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 119
FLEBOBAG RING LACT	2000.00 mL	OTHER: CONTINUOUS	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 120
LATANOPROST	1.0 gtt	BID	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 120
LIDOCAINE	2.0 %	PRN	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 120
MAGNESIUM SULFATE	2.0 g	QD	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 120
MEROPENEM	500.00 mg	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 120
VALSARTAN	80.0 mg	QD	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 120
AUGMENTIN	125.0 mg	BID	Y-M: 20[redacted]- [redacted] / 116	Y-M: 20[redacted]- [redacted] / 125
NEUTRA-PHOS	10.0 mEq	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 117	Y-M: 20[redacted]- [redacted] / 117
POTASSIUM	20.0 mEq	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 117	Y-M: 20[redacted]- [redacted] / 117
VANCOMYCIN	125.00 mg	OTHER: 6 TIMES/DAY	Y-M: 20[redacted]- [redacted] / 117	Y-M: 20[redacted]- [redacted] / 121
DICYCLOVERINE	10.0 mg	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 118	Y-M: 20[redacted]- [redacted] / 118
PARACETAMOL	650.0 mg	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 118	Y-M: 20[redacted]- [redacted] / 118
LACTOBACILLUS ACIDOPHILUS	1.0 OTHER: CAPSULE	QD	Y-M: 20[redacted]- [redacted] / 118	Y-M: 20[redacted]- [redacted] / 120
PANTOPRAZOLE	40.0 mg	QD	Y-M: 20[redacted]- [redacted] / 118	Y-M: 20[redacted]- [redacted] / 120
KETOTIFEN	1.00 gtt	BID	Y-M: 20[redacted]- [redacted] / 119	Not reported.
EMOLLIENTS AND PROTECTIVES	1 OTHER: APPL	BID	Y-M: 20[redacted]- [redacted] / 119	Y-M: 20[redacted]- [redacted] / 119
FLUCONAZOLE	150.0 mg	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 119	Y-M: 20[redacted]- [redacted] / 119
MAALOX	30.0 mL	QD	Y-M: 20[redacted]- [redacted] / 119	Y-M: 20[redacted]- [redacted] / 120
ALUMINIUM W/MAGNESIUM HYDROXIDE/SIMETICONE	30.00 mL	TID	Y-M: 20[redacted]- [redacted] / 120	Y-M: 20[redacted]- [redacted] / 120
LOPERAMIDE	4.0 mg	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 120	Y-M: 20[redacted]- [redacted] / 120
PROMETHAZINE	12.5 mg	OTHER: ONCE	Y-M: 20[redacted]- [redacted] / 120	Y-M: 20[redacted]- [redacted] / 120
COLESEVELAM	1250.0 mg	BID	Y-M: 20[redacted]- [redacted] / 120	Y-M: 20[redacted]- [redacted] / 125

Event #1: Serious Adverse Event

Event Description	SYSTEMIC INFLAMMATORY RESPONSE SYNDROME
Preferred term	全身性炎症反応症候群
AE Onset Date / Rx Day	[redacted]20[redacted] / 115
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 115): Albumin: 41 [34 - 48] g/L; Alkaline Phosphatase: 88 [25 - 150] U/L; Aspartate Aminotransferase: 44 [5 - 34] U/L; Basophils: 0 [0 - 0.2] 10^9/L; Bilirubin: 22.24 [0 - 20.52] umol/L; Calcium: 2.3 [2.17 - 2.57] mmol/L; Calcium: 2.27 [2.1 - 2.64] mmol/L; Chloride: 100 [98 - 109] mmol/L; Creatinine: 96.36 [50.39 - 88.4] umol/L; Eosinophils: 0 [0 - 0.5] 10^9/L; Erythrocytes: 4.6 [3.8 - 5.3] 10^12/L; Glucose: 11.27 [3.61 - 5.5] mmol/L; Hemoglobin: 144 [111 - 159] g/L; Leukocytes: 13.5 [3.4 - 10.8] 10^9/L; Lymphocytes: 0.7 [0.7 - 3.1] 10^9/L; Monocytes: 0.5 [0.1 - 0.9] 10^9/L; NPTST033-BLOOD UREA NITROGEN: 30 [8 - 25] mg/dL; Neutrophils: 12.3 [1.4 - 7] 10^9/L; Platelets: 300 [150 - 379] 10^9/L; Potassium: 4.5 [3.5 - 5.3] mmol/L; Protein: 79 [60 - 85] g/L; Sodium: 133 [134 - 144] mmol/L; [redacted]20[redacted] (RX DAY 480): Hematocrit: 0.43 [0.34 - 0.47] fraction of 1; NPTST127-LACTIC ACID: 1.9 [0.5 - 2.2] mmol/L; NPTST205-TROPONIN: 0.02 [0 - 0.78] ng/mL

Microbiology

[redacted]20[redacted] (RX DAY 115): BLOOD NPTST063-CULTURE: NOT APPLICABLE-NEGATIVE CULTURE;
[redacted]20[redacted] (RX DAY 482): STOOL NPTST203-TOXIGENIC CLOSTRIDIUM DIFFICILE: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 115): CHEST RADIOGRAPHS: NO ACUTE FINDINGS; CT ABD AND PELVIS WITH CONTRAST: NO ACUTE FINDING; EKG: SINUS RHYTHM WITH 1ST DEGREE A=V BLOCK; [redacted]20[redacted] (RX DAY 116): CT NECK WITH CONTRAST: MILD ASYMMETRIC THICKENING OF LEFT PALATINE TONSIL WITH NO EVIDENCE OF ABCESS; [redacted]20[redacted] (RX DAY 117): NASAL ENDOSCOPY: ENLARGED TONSILLS; [redacted]20[redacted] (RX DAY 480): VITAL SIGNS: BP=145/70 HR=108 TEMP=101.2 O2 SAT=94%

AE Stopped Rx Day	121
Duration of AE	7 DAYS
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: M15-554

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，全身性炎症反応症候群の事象を発現した。

Event 1 の臨床経過：

関連する病歴は元喫煙者（1 日 0.5 箱を 10 年間），乾癬性関節炎，糖尿病，高血圧，甲状腺機能低下症及び非飲酒者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は全身性炎症反応症候群を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，全身性炎症反応症候群は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は扁桃炎（非重篤な事象）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，CK 値増加（非重篤な事象）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，発熱を伴う急性の激しい嘔吐及び突発性の下痢のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，本事象は消失し，被験者は退院した。本事象に関連する家族歴はなかった。

医療記録によると，被験者は当初，原因不明の SIRS／敗血症の症状のために入院した。被験者は最近（数週間前），クリンダマイシンを投与されており，入院時には経験的にバンコマイシンの投与が開始された。症状は改善し，経口抗生物質に切り替えられた。被験者はその後，安定状態で退院し，経口抗生物質を継続することとなった。被験者には，ここ最近において，旅行歴，病人との接触，キャンプ歴はなかった。

投与された薬剤は，ロペラミド，バンコマイシン，ゾシン，アシドフィルス菌，メロペネム，生理食塩液，水酸化アルミニウム・水酸化マグネシウム・シメチコン合剤，enoxa，硫酸マグネシウム，乳酸リンゲル液，塩化カリウム，neutraphos，タイレノール，bentyl，lactocap，protonix，マーロックス，ジフルカン及びオーグメンチンであった。

The patient's past medications include:

ENBREL for PSA THERAPY ([redacted] 20[redacted] - [redacted] 20[redacted])

ARAVA for PSA ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for PSA ([redacted] 20[redacted] - [redacted] 20[redacted])

SIMPONI for PSA ([redacted] 20[redacted] - [redacted] 20[redacted])

COSENTYX for PSA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Systemic inflammatory response syndrome (10051379) (Systemic inflammatory response syndrome (10051379)) [v.22.0] [10051379]

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 SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

- Investigator: Not applicable.

- AbbVie: Risk factors include age, diabetes mellitus and obesity.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ASPARTATE AMINOTRANSFERASE:** 44 U/L (normal 5 to 34)

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

[redacted] **20[redacted] BNP:** 10 PG/ML (normal <100)

[redacted] **20[redacted] BUN:** 30 mg/dL (normal 8 to 25)

[redacted] **20[redacted] CBC WITH DIFFERENTIAL:** WBC =13.5 (REF 3.4-10.8)

[redacted] **20[redacted] CHEST RADIOGRAPHS:** No acute findings

[redacted] **20[redacted] CMP:** CO2 = 16 (20-32)/NA 133(134-144)

[redacted] **20[redacted] CREATININE:** 1.09 mg/dL (normal 0.57 to 1.00)

[redacted] **20[redacted] CT ABDOMEN AND PELVIS WITH CONTRAST:** No acute finding

[redacted] **20[redacted] CT NECK WITH CONTRAST:** Mild asymmetric thickening of left palatine tonsil with no evidence of abscess

[redacted] **20[redacted] EKG:** Sinus rhythm with 1st degree AV block

[redacted] **20[redacted] GLUCOSE:**203 mg/dL (normal 65 to 99)

[redacted] **20[redacted] NASAL ENDOSCOPY:** Enlarged tonsils

[redacted] **20[redacted] NEUTROPHILS:** 12.3 X10**3/MM**3 (normal 1.4 to 7.0)

[redacted] **20[redacted] SEPSIS LACTIC ACID:** 1.9 MMOL/L (normal 0.5 to 5.2)

[redacted] **20[redacted] STOOL FOR C. DIFF:** negative

[redacted] **20[redacted] TROPONIN:** 0.02 NG/ML (normal 0.00 to 0.78)

[redacted] **20[redacted] URINALYSIS:** Within normal limits

[redacted] **20[redacted] WHITE BLOOD CELLS:** 13.5 X10**3/MM**3 (normal 3.4 to 10.8)

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

Reason for Narrative

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

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

Medical History	Onset Year
OTHER: SEASONAL ALLERGIES	19[redacted]
OTHER: VITILIGO	19
OTHER: PLAQUE PSORIASIS	19
OTHER: PSORIASIS	19
HYPERTENSION	19
OTHER: ABNORMAL LIVER FUNCTION TEST	19
OTHER: NERVE PAIN	20
OTHER: MENOPAUSE	20
LIVER DISEASE (EXCLUDING HEPATITIS): FATTY LIVER	20
SLEEP APNEA	20
OTHER: LEFT ANKLE FRACTURE	20
OTHER: LOW VITAMIN D	20

Prior Procedures	Procedure Year
SURGERY: MYOMECTOMY	20[redacted]
SURGERY: UMBILICAL HERNIA REPAIR	20

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	36	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 160	160

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DIPHENHYDRAMINE	25 mg	QD	Y-M: 19[redacted]
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 19[redacted]
LISINOPRIL	40 mg	QD	Y-M: 19[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 19[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted]
AMLODIPINE	5 mg	QD	Y-M: 20[redacted]
GABAPENTIN	1200 mg	TID	Y-M: 20[redacted]
METOPROLOL	25 mg	QD	Y-M: 20[redacted]
USTEKINUMAB	90 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
METHOTREXATE	20 mg	EVERY WEEK	Y-M: 20[redacted]
HEPATITIS B IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
SECUKINUMAB	300 mg	OTHER: UNKNOWN	Y-M: 20[redacted]
IXEKIZUMAB	160 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
GUSELKUMAB	100 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
ERGOCALCIFEROL	50000 IU	OTHER: EVERY MONTH	Y-M: 20[redacted]-[redacted] / -97

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
DIPHENHYDRAMINE	25 mg	QD	Y-M: 19[redacted]	ONGOING
LISINOPRIL	40 mg	QD	Y-M: 19[redacted]	ONGOING
AMLODIPINE	5 mg	QD	Y-M: 20[redacted]	ONGOING
GABAPENTIN	1200 mg	TID	Y-M: 20[redacted]	ONGOING
METOPROLOL	25 mg	QD	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	50000 IU	OTHER: EVERY MONTH	Y-M: 20[redacted] / -97	ONGOING
CEFUROXIME	500 mg	QD	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 67
LEVOFLOXACIN	750 mg	OTHER: ONCE	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
LEVOFLOXACIN	750 mg	QD	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 72
SALBUTAMOL	1 OTHER: PUFF	TID	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 74

Event #1: Serious Adverse Event

Event Description	ACUTE HYPOXEMIC RESPIRATORY FAILURE
Preferred term	急性呼吸不全
AE Onset Date / Rx Day	[redacted]20[redacted] / 67
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 67): CHEST COMPUTED TOMOGRAPHY ANGIOGRAPHY: NEGATIVE FOR PULMONARY EMBOLISM; CHEST X-RAY: NEGATIVE FOR INFILTRATE; OXYGEN THERAPY: TOLERATED; TEMPERATURE ONSET: 101.6 F

AE Stopped Rx Day	68
Duration of AE	2 DAYS
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: M15-554

治験責任医師からの報告。本被験者は米国の 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，急性低酸素血症性呼吸不全の事象を発現した。

Event 1 の臨床経過：

関連する病歴は季節性アレルギー，乾癬，現紙巻タバコ喫煙者（1 日 1 箱を 36 年間），現飲酒者（2 杯未満）であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は急性低酸素血症性呼吸不全を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，急性低酸素血症性呼吸不全は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日以前から 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は咽喉痛（非重篤）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで，被験者は連鎖球菌性咽頭炎（非重篤）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，咳嗽，息切れ及び発熱のため，救急治療室を受診した。同日，被験者は，酸素投与，抗生物質の静脈内投与及びネブライザーによる治療のため，一晩入院した。診断検査が行われた。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，levoquin 及び albuterol であった。

The patient's past medications include:

CIPROFLOXACIN for STREP THROAT ([redacted] 20[redacted] - [redacted] 20[redacted])

AUGMENTIN for STREP THROAT ([redacted] 20[redacted] - [redacted] 20[redacted])

CEFUROXIME for STREP THROAT ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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

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 ACUTE HYPOXEMIC RESPIRATORY FAILURE

- Investigator: NOT APPLICABLE

- AbbVie: ETIOLOGY OF THE EVENT IS UNLIKELY RELATED TO STUDY DRUG'S MECHANISM OF ACTION. ADDITIONAL RISK FACTORS INCLUDE CURRENT SMOKING STATUS AND PRECEDING STREP THROAT.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **CHEST COMPUTED TOMOGRAPHY ANGIOGRAPHY:** Negative for pulmonary embolism.

[redacted] **CHEST X-RAY:** Negative for infiltrate.

[redacted] **TEMPERATURE ONSET:** 101.6 F

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
ブドウ球菌感染性滑液包炎	X			X

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
OTHER: BILATERAL WRIST PAIN	19[redacted]
OTHER: INSOMNIA	19
OTHER: POST MENOPAUSAL	20
DEPRESSION: MILD DEPRESSION	20
HYPERTENSION	20
OTHER: BILATERAL CARPAL TUNNEL	20
OTHER: LOWER BACK PAIN	20
OTHER: NECK PAIN	20
OTHER: PLAQUE PSORIASIS	20
GASTROESOPHAGEAL REFLUX DISEASE	20
INFLAMMATORY BOWEL DISEASE: NOT SYMPTOMATIC AT THIS TIME	20
OTHER: BENIGN HEPATIC LESION	20
OTHER: DIVERTICULOSIS	20
OTHER: LACTOSE INTOLERANT	20
OTHER: RIGHT ADRENAL ADENOMA	20
OTHER: HISTORY MICROSCOPIC C0LITIS	20

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	37	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 80	80

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]
FLUOXETINE	20 mg	QD	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]
INFLIXIMAB	300 mg	OTHER: Q4W	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: MONTHLY	Y-M: 20[redacted]
COLON HEALTH	1 OTHER: TAB	QD	Y-M: 20[redacted]
NAPROXEN	220 mg	PRN	Y-M: 20[redacted] / -53

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
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]	ONGOING
FLUOXETINE	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 83
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 83
VITAMINS NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]	ONGOING
COLON HEALTH	1 OTHER: TAB	QD	Y-M: 20[redacted]	ONGOING
NAPROXEN	220 mg	PRN	Y-M: 20[redacted] / -53	Y-M: 20[redacted] / 83
PARACETAMOL	1000 mg	OTHER: Q6H	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 54
DOCUSATE	100 mg	BID	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 79
ACETYLSALICYLIC ACID	162 mg	BID	Y-M: 20[redacted] / 49	Y-M: 20[redacted] / 79
ERGOCALCIFEROL	1000 IU	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 60
PARACETAMOL	1000 mg	BID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 79
ERGOCALCIFEROL	2000 IU	QD	Y-M: 20[redacted] / 61	ONGOING
CEFALEXIN	500 mg	QID	Y-M: 20[redacted] / 79	Y-M: 20[redacted] / 80
OXYCOCET	5/325 mg	PRN	Y-M: 20[redacted] /	Y-M: 20[redacted] / 84

DOCUSATE	100 mg	BID	Y-M: 20[redacted]-[redacted] / 79	ONGOING
OMEPRAZOLE	40 mg	BID	Y-M: 20[redacted]-[redacted] / 80	ONGOING
CEPHALOSPORIN C	1 g	OTHER: Q8H	Y-M: 20[redacted]-[redacted] / 80	Y-M: 20[redacted]-[redacted] / 84
ONDANSETRON	4 mg	OTHER: Q8H	Y-M: 20[redacted]-[redacted] / 80	Y-M: 20[redacted]-[redacted] / 84
PARACETAMOL	650 mg	OTHER: Q6H	Y-M: 20[redacted]-[redacted] / 80	Y-M: 20[redacted]-[redacted] / 84
PNEUMOCOCCAL VACCINE	0.5 mL	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 82	Y-M: 20[redacted]-[redacted] / 82
FLUOXETINE	40 mg	QD	Y-M: 20[redacted]-[redacted] / 84	ONGOING
IBUPROFEN	600 mg	PRN	Y-M: 20[redacted]-[redacted] / 84	ONGOING
OXYCODONE	5 mg	OTHER: PRN	Y-M: 20[redacted]-[redacted] / 84	Y-M: 20[redacted]-[redacted] / 84
CEFALEXIN	500 mg	OTHER: Q6H	Y-M: 20[redacted]-[redacted] / 85	Y-M: 20[redacted]-[redacted] / 98

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description ACUTE SEPTIC PREPATELLAR BURSITIS OF THE LEFT KNEE (MSSA)

Preferred term ブドウ球菌感染性滑液包炎

AE Onset Date / Rx Day [redacted]20[redacted] / 79

Age at AE Onset 6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 49): Erythrocytes: 3.7 [4 - 5.1] 10^12/L; Platelets: 291 [130 - 350] 10^9/L; [redacted]20[redacted] (RX DAY 80): Hematocrit: 0.35 [0.33 - 0.44] fraction of 1; Hemoglobin: 113 [110 - 147] g/L; Leukocytes: 18.5 [4.1 - 9.3] 10^9/L; Lymphocytes/Leukocytes: 13 [28 - 42] %; Monocytes/Leukocytes: 10 [4 - 8.5] %; NPTST056-CRP: 253 [0 - 8] mg/L; NPTST176-PT: 11 [9.8 - 11.8] sec; Neutrophils/Leukocytes: 77 [41 - 67] %; [redacted]20[redacted] (RX DAY 82): Erythrocytes: 3 [4.5 - 5.1] 10^12/L; Hematocrit: 0.28 [0.33 - 0.44] fraction of 1; Hemoglobin: 92 [110 - 147] g/L; Leukocytes: 11.8 [4.1 - 9.3] 10^9/L; Lymphocytes/Leukocytes: 25 [28 - 42] %; Monocytes/Leukocytes: 8 [4 - 8.5] %; NPTST017-APTT: 25 [24 - 32] sec; NPTST176-PT: 10.1 [9.8 - 11.8] sec; Neutrophils/Leukocytes: 65 [41 - 67] %; Platelets: 276 [130 - 350] 10^9/L; [redacted]20[redacted] (RX DAY 84): Erythrocytes: 3.4 [4 - 5.1] 10^12/L; Hematocrit: 0.31 [0.33 - 0.44] fraction of 1; Hemoglobin: 101 [110 - 147] g/L; Leukocytes: 7.3 [4.1 - 9.3] 10^9/L; Lymphocytes/Leukocytes: 25 [28 - 42] %; Monocytes/Leukocytes: 12 [4 - 8.5] %; Neutrophils/Leukocytes: 61 [41 - 67] %; Platelets: 368 [130 - 350] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 80): OTHER LEFT KNEE BURSA FLUID NPTST014-ANAEROBIC CULTURE ONLY: NEGATIVE-NO ANAEROBIC GROWTH AFTER 5 DAYS; OTHER LEFT KNEE BURSA FLUID NPTST063-CULTURE: NEGATIVE-NO GROWTH IN 5 DAYS; OTHER LEFT KNEE BURSA FLUID NPTST088-FLUID CULTURE AND SMEAR: POSITIVE-POLYMORPHONUCLEAR CELLS, NO ORGANISM SEEN; [redacted]20[redacted] (RX DAY 81): OTHER LEFT KNEE BURSA FLUID NPTST088-FLUID CULTURE AND SMEAR: POSITIVE-2+,POLYMORPHONUCLEAR CELLS; OTHER LEFT KNEE BURSA FLUID NPTST088-FLUID CULTURE AND SMEAR: POSITIVE-1+,STAPHYLOCOCCUS AUREUS, METHICILLIN SUSCEPTIBLE; OTHER LEFT KNEE BURSA FLUID NPTST088-FLUID

CULTURE AND SMEAR: NEGATIVE-RARE GRAM POSITIVE COCCI; OTHER LEFT KNEE BURSA FLUID NPTST202-TISSUE CULTURE AND STAIN: POSITIVE-4+ POLYMORPHONUCLEAR CELLS, NO ORGANISM SEEN

SAE Supplemental Procedure

[redacted] 20[redacted] (RX DAY 80): X-RAY LEFT KNEE: PREPATELLAR EDEMA, SMALL EFFUSION; 20[redacted] (RX DAY 81): ECG: NORMAL; IRRIGATION, DEBRIDEMENT AND EXCISION OF LEFT PREPATELLAR BURSA: SUBJECT IMPROVED

AE Stopped Rx Day	121 (41 DAYS AFTER LAST TREATMENT)
Duration of AE	43 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECT RECENTLY HAD LEFT ANKLE REPAIR SURGERY. THIS AE MAY BE RELATED BUT LEFT ANKLE SURGERY SITE DID NOT SHOW SIGNS OF INFECTION.
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: M15-554

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，左膝関節の急性化膿性膝蓋前滑液包炎（MSSA）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，両手根管，高血圧，乾癬性関節炎，炎症性腸疾患及び禁酒であった。

20[redacted] 年 [redacted] 月 [redacted] 日，左膝関節の急性化膿性膝蓋前滑液包炎（MSSA）を発現した。
20[redacted] 年 [redacted] 月 [redacted] 日以前に，被験者は左足関節三果骨折（非重篤）を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日以降，左足関節三果骨折修復が軽快していた。20[redacted] 年 [redacted] 月 [redacted] 日，耐え難い左膝痛，紅斑，温感，腫脹及び発熱が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，症状が悪化し，整形外科医は被験者に救急治療室の受診を勧めた。X 線検査により著しい膝蓋骨内滲出液が認められ，左膝関節のデブリードマンが行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。再度，左膝関節の洗浄とデブリードマンが行われた。滑液包切除術も行われた。培養を行ったところ，メチシリ

ン感受性黄色ブドウ球菌（MSSA）が検出された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

この被験者の治験参加は完全に中止された。20[redacted] 年 [redacted] 月 [redacted] 日，左膝関節の急性化膿性膝蓋前滑液包炎（MSSA）は消失した。

投与された薬剤は，ケフレックス，percocet，ゾシン，タイレノール，イブプロフェン，オキシコドン，セファロスポリン及びセファゾリン IV であった。

Causality for ABT-494 (Blinded)

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1) Bursitis infectivetaphylococcal (10048894) (Bursitis infective staphylococcal (10048894)) [v.21.0] [10048894]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of ACUTE SEPTIC PREPATELLAR BURSITIS OF THE LEFT KNEE (MSSA)

- Investigator: The patient recently had left ankle repair surgery. This AE may be related but left ankle surgery site did not show signs of infection.

- AbbVie: The most common mechanisms involved in septic superficial bursitis consist of direct inoculation due to puncture of the overlying skin or contiguous spread from cellulitis. Additional risk factor includes recent ankle surgery.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANAEROBIC CULTURE ONLY:** Negative: No anaerobic growth after 5 days

[redacted] **20[redacted] APTT:** 25 SEC (normal 9.8 to 32)

[redacted] **20**[redacted] **CRP:** 253 MG/L (normal 0 to 8)

[redacted] **20**[redacted] **CULTURE:** Negative: No growth in 5 days

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

[redacted] **20**[redacted] **FLUID CULTURE AND SMEAR:** Positive: Polymorphonuclear cells, no organism seen

[redacted] **20**[redacted] **FLUID CULTURE AND SMEAR:** Positive: 2+, polymorphonuclear cells

[redacted] **20**[redacted] **FLUID CULTURE AND SMEAR:** Negative: Rare gram positive cocci

[redacted] **20**[redacted] **FLUID CULTURE AND SMEAR:** Positive: 1+, staphylococcus aureus, methicillin susceptible

[redacted] **20**[redacted] **HEMATOCRIT:** 34.7 % (normal 33.0 to 44.0)

[redacted] **20**[redacted] **HEMATOCRIT:** 28.2 % (normal 33.0 to 44.0)

[redacted] **20**[redacted] **HEMATOCRIT:** 31 % (normal 33.0 to 44.0)

[redacted] **20**[redacted] **HEMOGLOBIN:** 11.3 G/DL (normal 11.0 to 14.7)

[redacted] **20**[redacted] **HEMOGLOBIN:** 9.2 G/DL (normal 11.0 to 14.7)

[redacted] **20**[redacted] **HEMOGLOBIN:** 10.1 G/DL (normal 11.0 to 14.7)

[redacted] **20**[redacted] **LYMPHOCYTES %:** 13 % (normal 28 to 42)

[redacted] **20**[redacted] **LYMPHOCYTES %:** 25 % (normal 28 to 42)

[redacted] **20**[redacted] **LYMPHOCYTES %:** 25 % (normal 28 to 42)

[redacted] **20**[redacted] **MONOCYTES %:** 10 % (normal 4 to 8.5)

[redacted] **20**[redacted] **MONOCYTES %:** 8 % (normal 4 to 8.5)

[redacted] **20**[redacted] **MONOCYTES %:** 12 % (normal 4 to 8.5)

[redacted] **20**[redacted] **NEUTROPHILS %:** 77 % (normal 41 to 67)

[redacted] **20**[redacted] **NEUTROPHILS %:** 65 % (normal 41 to 67)

[redacted] **20**[redacted] **NEUTROPHILS %:** 61 % (normal 41 to 67)

[redacted] **20**[redacted] **PLATELET COUNT:** 291 10^3/uL (normal 130 to 350)

[redacted] **20**[redacted] **PLATELET COUNT:** 276 10^3/uL (normal 130 to 350)

[redacted] **20**[redacted] **PLATELET COUNT:** 368 10^3/uL (normal 130 to 350)

[redacted] **20**[redacted] **PT:** 11.0 SEC (normal 9.8 to 11.8)

[redacted] **20[redacted] PT:** 10.1 SEC (normal 9.8 to 11.8)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.65 10^6/uL (normal 4.00 to 5.1)

[redacted] **20[redacted] RED BLOOD CELLS:** 2.99 10^6/uL (normal 4.00 to 5.1)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.35 10^6/uL (normal 4.00 to 5.1)

[redacted] **20[redacted] TISSUE CULTURE AND STAIN:** Positive: 4+ polymorphonuclear cells, no organism seen

[redacted] **20[redacted] WHITE BLOOD CELLS:** 18.5 10^3/uL (normal 4.1 to 9.3)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.8 10^3/uL (normal 4.1 to 9.3)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.3 10^3/uL (normal 4.1 to 9.3)

[redacted] **20[redacted] X-RAY LEFT KNEE:** Prepatellar edema, small effusion

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
胃炎	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 15 mg QD	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
ASTHMA	19[redacted]
OTHER: BILATERAL HIP PAIN	19
OTHER: PSORIATIC PLAQUES	20
OTHER: FATIGUE	20
DEPRESSION: MILD DEPRESSION	20
OTHER: ANXIETY	20
OTHER: BILATERAL-HEEL PAIN	20
OTHER: HISTORY LYME DISEASE	20
OTHER: NIGHT SWEATS	20
OTHER: NAUSEA	20
OTHER: HISTORY PICC LINE PORT	20
OTHER: RESTLESS LEG SYNDROME	20
OTHER: CERVICALGIA	20
OTHER: VITAMIN D DEFICIENCY	20
OTHER: ELEVATED TRANSAMINASES	20
OTHER: TRAMADOL HYDROCHLORIDE/ ULTRAM ALLERGY	20
LIVER DISEASE (EXCLUDING HEPATITIS): FATTY LIVER	20
OTHER: HISTORY EPSTEIN BARR VIRUS	20
OTHER: MOTOR VEHICLE ACCIDENT	20
OTHER: SORE MUSCLES- RELATED TO MVA	20

Prior Procedures	Procedure Year
SURGERY: TONSILLECTOMY/ ADENOIDECTOMY	19[redacted]
SURGERY: CHOLECYSTECTOMY	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

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] / 170	170
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 171	[redacted]20[redacted] / 392	222
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted]
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
CLONAZEPAM	0.5 mg	PRN	Y-M: 20[redacted]
PAROXETINE	20 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	50000 IU	EVERY WEEK	Y-M: 20[redacted] / -273
TACROLIMUS	2 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -218
HYDROXYZINE	25 mg	PRN	Y-M: 20[redacted] / -180
ETANERCEPT	50 mg	EVERY WEEK	Y-M: 20[redacted] / -133
METHOCARBAMOL	750 mg	PRN	Y-M: 20[redacted] / -91
ANOVLAR	1.5 mg	QD	Y-M: 20[redacted] / -31
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -22
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -15
CYCLOBENZAPRINE	5 mg	QD	Y-M: 20[redacted] / -8
ONDANSETRON	4 mg	QD	Y-M: 20[redacted] / -8

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	800 mg	PRN	Y-M: 20[redacted]	Not reported.
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]	Not reported.
ERGOCALCIFEROL	50000 IU	EVERY WEEK	Y-M: 20[redacted] / -273	Not reported.
TACROLIMUS	2 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -218	Not reported.
HYDROXYZINE	25 mg	PRN	Y-M: 20[redacted] / -180	Not reported.
METHOCARBAMOL	750 mg	PRN	Y-M: 20[redacted] / -91	Not reported.
PAROXETINE	40 mg	QD	Y-M: 20[redacted] / 1	Not reported.
CYCLOBENZAPRINE	5 mg	PRN	Y-M: 20[redacted] / 196	Not reported.
CILEST	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 224	Not reported.
MAGIC MOUTHWASH	1 TO 2 OTHER: TSP	EVERY 2 WEEKS	Y-M: 20[redacted] / 280	Not reported.
SALBUTAMOL	90 OTHER: MCG	OTHER: QD PRN	Y-M: 20[redacted] / 280	Not reported.
DIAZEPAM	5 mg	OTHER: QD PRN	Y-M: 20[redacted] / 298	Y-M: 20[redacted] / 634
MELOXICAM	15 mg	QD	Y-M: 20[redacted] / 315	Y-M: 20[redacted] / 477
NYSTATIN	100,000/ 5 mL	QID	Y-M: 20[redacted] / 477	Y-M: 20[redacted] / 484
NAPROXEN	500 mg	BID	Y-M: 20[redacted] / 477	Y-M: 20[redacted] / 541
HYDROMORPHONE	1.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 542	Y-M: 20[redacted] / 542
MORPHINE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 542	Y-M: 20[redacted] / 542
DICYCLOVERINE	10 mg	TID	Y-M: 20[redacted] / 543	Not reported.
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 543	Not reported.
ONDANSETRON	4 mg	QID	Y-M: 20[redacted] / 543	Not reported.
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 543	Not reported.
SUCRALFATE	10 mL	QID	Y-M: 20[redacted] / 543	Not reported.

METOCLOPRAMIDE	5 mg	TID	Y-M: 20[redacted]- [redacted] / 547	Y-M: 20[redacted]- [redacted] / 548
TRAMADOL	50 mg	TID	Y-M: 20[redacted]- [redacted] / 547	Y-M: 20[redacted]- [redacted] / 548
GLYCOPYRRONIUM	1 mg	TID	Y-M: 20[redacted]- [redacted] / 634	Not reported.
DIAZEPAM	60 mg	PRN	Y-M: 20[redacted]- [redacted] / 635	Not reported.

Event #2: Serious Adverse Event

Event Description	GASTRITIS
Preferred term	胃炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 513
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 542): Albumin: 49 [35 - 52] g/L; Alkaline Phosphatase: 56 [30 - 115] U/L; Basophils: 0 [0 - 1] UNIT NOT REPORTED; Bilirubin: 8.55 [1.71 - 20.52] umol/L; Calcium: 2.32 [2.15 - 2.57] mmol/L; Chloride: 102 [99 - 102] mmol/L; Creatinine: 69.84 [53.04 - 106.08] umol/L; Eosinophils: 1 [0 - 5] UNIT NOT REPORTED; Erythrocytes: 4.6 [4 - 5.1] 10^12/L; Glucose: 4.72 [3.61 - 5.5] mmol/L; Hematocrit: 0.44 [0.33 - 0.44] fraction of 1; Hemoglobin: 140 [110 - 147] g/L; Leukocytes: 10 [4.1 - 10.3] 10^9/L; Lymphocytes: 2.7 [1.1 - 3.9] UNIT NOT REPORTED; Lymphocytes: 27 [28 - 42] UNIT NOT REPORTED; Monocytes/Leukocytes: 8 [4 - 8.5] %; NPTST051-CO2: 27 [21 - 30] mmol/L; NPTST129-LACTIC ACID LEVEL: 0.75 [0.4 - 2] mmol/L; NPTST136-MAGNESIUM: 2 [1.5 - 2.6] mg/dL; NPTST138-MCHC: 31.5 [32.5 - 35.1] g/L; NPTST139-MCV: 97.4 [82.3 - 93.2] fL; NPTST146-MPV: 10.9 [7.5 - 10.7] fL; NPTST165-PIMG: 0 [0 - 1] UNIT NOT REPORTED; NPTST170-PREGNANCY (SERUM): NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST181-RDW: 12.2 [12 - 15] %; NPTST215-UREA NITROGEN: 15 [7 - 22] mg/dL; Neutrophils: 6.4 [1.6 - 6.2] UNIT NOT REPORTED; Neutrophils/Leukocytes: 64 [41 - 67] %; Platelets: 359 [130 - 350] 10^9/L; Potassium: 4.3 [3.4 - 4.8] mmol/L; Protein: 80 [60 - 80] g/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 542): CT OF THE ABDOMEN: CT OF THE ABDOMEN & PELVIS WITH CONTRAST: LUNGS: NORMAL LIVER: NORMAL, NO MASSES GALLBLADDER: S/P CHOLECYSTECTOMY SPLEEN: UNREMARKABLE PANCREAS: UNREMARKABLE ADRENAL GLANDS: UNREMARKABLE AO; [redacted]20[redacted] (RX DAY 548): EGD: MILD ERYTHEMA FOUND IN THE GASTRIC ANTRUM. NEG FOR CELIAC DISEASE. NORMAL STOMACH. NORMAL ESOPHAGUS.

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NO REASONABLE POSSIBILITY, DUE TO NSAID USE
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: M15-554

治験責任医師からの報告。本被験者は米国の 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，グレード 1 の胃炎の事象を発現した。

Event 2 の臨床経過：
関連する病歴は扁桃摘出及びアデノイド切除，乾癬プラーク，両側の踵部痛，胆嚢切除，乾癬性関節炎，自動車事故，MVA による筋肉痛，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ウパダシチニブの盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胃炎を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は突然左腹部痛が出現したため入院した。疼痛で目が覚め，食事と労作で疼痛が悪化し，鎮痛剤を使用しないと改善しなかった。被験者は疼痛による悪心を発現し，2 日前から下痢があったが，発熱はなくメレナもなかった。関節痛をコントロールするため，被験者のナプロキセンの用量が 2 週間前に 2 倍になった。診察時に被験者の左肺基部に粗い断続性ラ音が聞かれ，腹部の触診で左上腹部に圧痛が認められた。腹部 CT 検査で所見は認められなかった。被験者は輸液の静脈内投与による治療を受け，パントプラゾールが BID に増量された。被験者のナプロキセンは保留とされた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，carafate，dicyclomine，ファモチジン，メトクロプラミド，モルヒネ，zofran 及びパントプラゾールであった。

The patient's past medications include:

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

PREDNISONE 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])

ULTRAM for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Gastritis (10017853) (Gastritis (10017853)) [v.22.1] [10017853]

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 GASTRITIS

- Investigator: No reasonable possibility; due to NSAID use.

- AbbVie: Event with multiple underlying etiologies. Additional risk factor includes NSAID use as reported by primary investigator.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] CT ABDOMEN: Negative

[redacted] **20[redacted] EGD:** Mild erythema found in the gastric antrum, negative for celiac disease. Normal stomach. Normal esophagus.

[redacted] **20[redacted] LACTIC ACID:** 0.75 MMOL/L (normal 0.40 to 2.00)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 27 % (normal 28 to 42)

[redacted] **20[redacted] NEUTROPHILS %:** 64 % (normal 41 to 67)

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

[redacted] **20[redacted] WBC:** 10.0 U/L (normal 4.1 to 10.3)

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
腎結石症	X			
側腹部痛	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	4[redacted]	MALE	WHITE

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	19[redacted]
OTHER: DIARRHEA OCCASIONAL	19
GASTROESOPHAGEAL REFLUX DISEASE	20
OTHER: TOE FUNGUS	20
OTHER: TRANSAMINITIS	20
OTHER: ANXIETY INTERMITTENT	20
OTHER: SICCA SYNDROME OCCASIONAL	20
OTHER: HEADACHES INTERMITTENT	20
OTHER: SEBACEOUS CYST IN LEFT ARMPIT	20

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.75 PACK	13	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted] / 1	[redacted] / 167	167
ABT-494	15MG	ORAL	QD	[redacted] / 168	[redacted] / 385	218
ABT-494	15MG	ORAL	QD	[redacted] / 386	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CELECOXIB	100 mg	BID	Y-M: 19[redacted]
ROFECOXIB	50 mg	QD	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: APP	QD	Y-M: 20[redacted]
DICLOFENAC	100 ng	QD	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: Q6WK	Y-M: 20[redacted]
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]
ESCITALOPRAM	10 mg	QD	Y-M: 20[redacted]
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	25 ug	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
SULFASALAZINE	3000 mg	QD	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]
METHOTREXATE	7.5 mg	EVERY WEEK	Y-M: 20[redacted]
EFINACONAZOLE	1 OTHER: APP	QD	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: MONTHLY	Y-M: 20[redacted]
IBUPROFEN	400 mg	PRN	Y-M: 20[redacted]
METHOTREXATE	12.5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -255
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -183
MOMETASONE	1 OTHER: APP	QD	Y-M: 20[redacted] / -139
LORAZEPAM	1 mg	PRN	Y-M: 20[redacted] / -50
CEFALEXIN	500 mg	OTHER: 4 TIMES/DAY	Y-M: 20[redacted] / -35
CELECOXIB	200 mg	BID	Y-M: 20[redacted] / -29
DESONIDE	1 OTHER: APP	OTHER: BID PRN	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted]	Not reported.
ERGOCALCIFEROL	25 ug	QD	Y-M: 20[redacted]	Not reported.
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	Not reported.
EFINACONAZOLE	1 OTHER: APP	QD	Y-M: 20[redacted]	Not reported.
METHOTREXATE	15 mg	EVERY WEEK	Y-M: 20[redacted] / -255	Y-M: 20[redacted] / 313
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -183	Not reported.
LORAZEPAM	1 mg	PRN	Y-M: 20[redacted] / -50	Y-M: 20[redacted] / -1
CELECOXIB	200 mg	BID	Y-M: 20[redacted] / -29	Y-M: 20[redacted] / 455
DESONIDE	1 OTHER: APP	OTHER: BID PRN	Y-M: 20[redacted] / -8	Not reported.
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 19
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 28
ULTRACET	2 OTHER: TABLET	PRN	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 28
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 62

Event #1: Serious Adverse Event

Event Description	STONE IN RIGHT KIDNEY
Preferred term	腎結石症
AE Onset Date / Rx Day	[redacted]20[redacted] / 12
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 14): INSERTION OF RENAL STENT: SUCCESSFUL INSERTION.; LAPAROSCOPIC SURGICAL REMOVAL OF RENAL CALCULI: SUCCESSFUL REMOVAL OF RENAL CALCULI

AE Stopped Rx Day	16
Duration of AE	5 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN AT THIS TIME
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	RIGHT SIDE FLANK PAIN
Preferred term	側腹部痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 47
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 56): SURGICAL REMOVAL OF RENAL STENT.: SUCCESSFUL REMOVAL OF RENAL STENT.	
AE Stopped Rx Day	56
Duration of AE	10 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PATIENT HAS TEMPORARY STENT IN RIGHT KIDNEY
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: M15-554

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，右腎結石及び右側腹部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，間欠熱，現紙巻タバコ喫煙者（1 日 0.75 箱を 13 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，被験者は右腎結石を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右腎結石は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右側腹部痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右側腹部痛は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，極度の腰痛及び排尿困難により，救急治療室を受診した。被験者は腎結石と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，腹腔鏡下腎結石摘出術及び腎ステント挿入が行われた。手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右側腹部痛のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，腎ステントが無事抜去された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。被験者には腎結石の既往歴があったことが治験責任医師から報告された。

投与された薬剤は，タムスロシン，シプロフロキサシン及び tramacet であった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Kidney stone (10023436) (Nephrolithiasis (10029148)) [v.22.1] [10023436]

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

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

Dechallenge: Not Applicable

2) Flank pain (10016750) (Flank pain (10016750)) [v.22.1] [10016750]

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 STONE IN RIGHT KIDNEY

- Investigator: Unknown at this time.

- AbbVie: Weak temporal association with only 2 week exposure to study drug. Calculi were likely pre-existing. Obesity is an additional risk factor.

Event of RIGHT SIDE FLANK PAIN

- Investigator: Patient has temporary stent in right kidney

- AbbVie: Event more likely a complication of recent renal calculi and recent 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
肛門性器疣贅	X			X
肺炎	X			X

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

Medical History	Onset Year
OTHER: POLLINOSIS	NOT REPORTED
OTHER: CHICKENPOX	19[redacted]
HYPERTENSION	20[redacted]
OTHER: PLAQUE PSORIASIS	20[redacted]
OTHER: INTERSTITIAL PNEUMONIA	20[redacted]
OTHER: GINGIVITIS	20[redacted]
OTHER: LATENT TUBERCULOSIS	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	10	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 167	167
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 168	[redacted]20[redacted] / 391	224
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 392	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
CANDESAR A	1 OTHER: TABLET	QD	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
DIFLUPREDNATE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
INDOMETACIN	25 mg	BID	Y-M: 20[redacted]
MAXACALCITOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
ADALIMUMAB	80 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
FAMOTIDINE	150 mg	BID	Y-M: 20[redacted] / -296
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / -296
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -282
DAIVOBET	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -282
MELOXICAM	10 mg	QD	Y-M: 20[redacted] / -282
SECUKINUMAB	300 mg	EVERY WEEK	Y-M: 20[redacted] / -258
APREMILAST	30 mg	BID	Y-M: 20[redacted] / -174
ISONIAZID	150 mg	BID	Y-M: 20[redacted] / -21
PYRIDOXINE	0.25 g	BID	Y-M: 20[redacted] / -21
CEFDINIR	100 mg	BID	Y-M: 20[redacted] / -15

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
CANDESAR A	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Not reported.
CARBAZOCHROME	30 mg	QD	Y-M: 20[redacted] / 384	Y-M: 20[redacted] / 386
HEMONASE	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 384	Y-M: 20[redacted] / 390
FEXOFENADINE	60 mg	PRN	Y-M: 20[redacted] / 392	Not reported.
AMENAMEVIR	200 mg	QD	Y-M: 20[redacted] / 589	Y-M: 20[redacted] / 595
VIDARABINE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 589	Y-M: 20[redacted] / 595
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 589	Y-M: 20[redacted] / 601
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / 589	Y-M: 20[redacted] / 601
VONOPRAZAN	10 mg	QD	Y-M: 20[redacted] / 594	Y-M: 20[redacted] / 596
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 601	Y-M: 20[redacted] / 643
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / 601	Y-M: 20[redacted] / 643
MECOBALAMIN	500 ug	TID	Y-M: 20[redacted] / 601	Y-M: 20[redacted] / 672
BETAMETHASONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 609	Y-M: 20[redacted] / 644
PREDNISOLONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 611	Y-M: 20[redacted] / 644
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 622	Y-M: 20[redacted] / 643
OTHER ANTIEPILEPTICS	5 mg	BID	Y-M: 20[redacted] / 623	Y-M: 20[redacted] / 636
OTHER ANTIEPILEPTICS	10 mg	BID	Y-M: 20[redacted] / 637	Y-M: 20[redacted] / 657
OTHER ANTIEPILEPTICS	5 mg	QD	Y-M: 20[redacted] / 667	Y-M: 20[redacted] / 672
ADENOSINE		TID	Y-M: 20[redacted] / 777	Y-M: 20[redacted] / 781
ISOSORBIDE		TID	Y-M: 20[redacted] / 777	Y-M: 20[redacted] / 781
MECOBALAMIN	500 mg	TID	Y-M: 20[redacted] / 777	Y-M: 20[redacted] / 781
CEFCAPENE	100 mg	TID	Y-M: 20[redacted] / 801	Y-M: 20[redacted] / 802

PARACETAMOL	600 mg	PRN	Y-M: 20[redacted] / 801	Y-M: 20[redacted] / 803
METOCLOPRAMIDE	5 mg	PRN	Y-M: 20[redacted] / 803	Y-M: 20[redacted] / 803
AZITHROMYCIN	500 mg	BID	Y-M: 20[redacted] / 803	Y-M: 20[redacted] / 804
OSMOSAL	500 mL	PRN	Y-M: 20[redacted] / 803	Y-M: 20[redacted] / 805
PIP/TAZO	4.5 g	PRN	Y-M: 20[redacted] / 803	Y-M: 20[redacted] / 813
PARACETAMOL	500 mL	QD	Y-M: 20[redacted] / 804	Y-M: 20[redacted] / 805
DEXAMETHASONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 809	ONGOING
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 809	ONGOING
HYDROCORTISONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 809	ONGOING
DIFLUPREDNATE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 811	ONGOING
BEPOTASTINE	10 mg	PRN	Y-M: 20[redacted] / 814	Y-M: 20[redacted] / 818

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	CONDYLOMA
Preferred term	肛門性器疣贅
AE Onset Date / Rx Day	[redacted]20[redacted] / 365
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 384): DUE TO THE CONDILOMA, HE WAS ADDMITED TO THE OTHER HOSIPITAL.THE CONDYLOMA WAS RESECTED.: THE LESION DISAPPERAED AFTER THE RESECTION.	
AE Stopped Rx Day	392
Duration of AE	28 DAYS
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 #5: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted] / 802
Age at AE Onset	[redacted]

Laboratory Testing

[redacted] (RX DAY 804): NPTST107-HBS ANTIGEN: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted] (RX DAY 807): NPTST074-CYTOMEGALOVIRUS IGG: 24.8 [2 - NOT REPORTED] UNIT NOT REPORTED; NPTST075-CYTOMEGALOVIRUS IGM: 0.14 [0.8 - NOT REPORTED] UNIT NOT REPORTED

Microbiology

[redacted] (RX DAY 801): OTHER NASAL CAVITY NPTST118-INFLUENZA VIRAL: NEGATIVE; [redacted] (RX DAY 802): SPUTUM NPTST099-GRAM-NEGATIVE BACILLARY: POSITIVE-2+; URINE NPTST099-GRAM-NEGATIVE BACILLARY: NEGATIVE; SPUTUM NPTST100-GRAM-NEGATIVE COCCAL: NEGATIVE; URINE NPTST100-GRAM-NEGATIVE COCCAL: NEGATIVE; SPUTUM NPTST101-GRAM-POSITIVE BACILLARY: POSITIVE-4+; URINE NPTST101-GRAM-POSITIVE BACILLARY: NEGATIVE; SPUTUM NPTST102-GRAM-POSITIVE COCCAL: POSITIVE-4+; URINE NPTST102-GRAM-POSITIVE COCCAL: NEGATIVE; [redacted] (RX DAY 803): SPUTUM NPTST054-COVID-19 PCR: NEGATIVE; OTHER NASAL CAVITY NPTST054-COVID-19 PCR: NEGATIVE; SPUTUM NPTST211-TUBERCLE BACILLUS: NEGATIVE; [redacted] (RX DAY 807): SPUTUM NPTST054-COVID-19 PCR: NEGATIVE; SPUTUM NPTST099-GRAM-NEGATIVE BACILLARY: POSITIVE-4+; SPUTUM NPTST100-GRAM-NEGATIVE COCCAL: NEGATIVE; SPUTUM NPTST101-GRAM-POSITIVE BACILLARY: NEGATIVE; SPUTUM NPTST102-GRAM-POSITIVE COCCAL: POSITIVE-3+

SAE Supplemental Procedure

[redacted] (RX DAY 801): CHEST X RAY: NORMAL; TEMPERATURE: 39.0C; [redacted] (RX DAY 802): CT: CT FINDINGS SHOW A CONSOLIDATION AT RIGHT INFERIOR LOBE.; [redacted] (RX DAY 803): TEMPERATURE: 39.4C; [redacted] (RX DAY 804): TEMPERATURE: 38.2; [redacted] (RX DAY 805): TEMPERATURE: 38.7C; [redacted] (RX DAY 806): TEMPERATURE: 36.5C; [redacted] (RX DAY 807): TEMPERATURE: 36.2C; [redacted] (RX DAY 808): TEMPERATURE: 36.2C; [redacted] (RX DAY 815): TEMPERATURE: 36.6C

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
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: M15-554

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，コンジローマの事象を発現した。

Event 1 の臨床経過：

関連する病歴は元喫煙者（1 日 1 箱を 10 年間），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。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はコンジローマを発現した。20[redacted] 年 [redacted] 月 [redacted] 日，コンジローマは消失した。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肛門周囲の疼痛及び腫脹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院し，コンジローマ切除術を受けた。手術は成功した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

投与された薬剤は，アドナ及びヘモナーゼであった。

The patient's past medications include:

ANTEBATE for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

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

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

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Condyloma (10053433) (Anogenital warts (10059313)) [v.22.0] [10053433]

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 CONDYLOMA

- Investigator: NOT APPLICABLE

- AbbVie: EVENT'S ETIOLOGY MORE LIKELY RELATED TO HPV INFECTION WHICH IS COMMON IN THE GENERAL POPULATION.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

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，肺炎の事象を発現した。

Event 5 の臨床経過：
関連する病歴は元喫煙者（1 日 1 箱を 10 年間），高血圧，局面型乾癬，乾癬性関節炎，間質性肺炎，潜伏結核，花粉症及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ウパダシチニブの盲検投与が開始された。

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

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は発熱と頭痛の症状で近医を受診した。胸部 X 線検査は正常で，インフルエンザの検査は陰性であった。被験者はカロナールとフロモックスを処方された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は肺炎のため入院した。CT 検査で右下葉に浸潤影が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，抗生物質が開始された。COVID-19 の検査は陰性であった。20[redacted] 年 [redacted] 月 [redacted] 日，抗生物質により炎症は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

肝損傷の事象のグレードは重篤から非重篤に下げられた。

投与された薬剤は，フロモックス，カロナール，アセリオ静注液バッグ，ゾシン，アセリオ，メサデルム，ロコイド，メトクロプラミド，ジフルプレドナート，ソルデム 3AG 輸液及びジスロマックであった。

The patient's past medications include:

ANTEBATE for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

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

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

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

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

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

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

Causality for UPADACITINIB (Blinded)

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

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMONIA

- **Investigator:** Not applicable.

- **AbbVie:** Risk factor includes prior history of interstitial pneumonia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **BODY TEMPERATURE:** 39.0 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 39.4 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 38.2 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 38.7 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 36.5 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 36.2 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 36.2 Degrees C

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

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

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

[redacted] 20[redacted] **CT CHEST:** Consolidation at right inferior lobe

[redacted] 20[redacted] **CYTOMEGALOVIRUS IGG:** 24.8 No units (normal >2.0)

[redacted] 20[redacted] **CYTOMEGALOVIRUS IGM:** 0.14 No units (normal >0.80)

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

[redacted] 20[redacted] **NASAL CULTURE:** Negative for COVID-19 PCR

[redacted] 20[redacted] **SPUTUM CULTURE:** Positive for Gram-Positive coccal (4+) and Gram Positive bacillary (4+) [redacted] 20[redacted] SPUTUM CULTURE: Negative for Gram-Negative coccal and Positive for Gram-Negative bacillary (2+)

[redacted] 20[redacted] **SPUTUM CULTURE:** Negative for COVID-19 PCR

[redacted] 20[redacted] **SPUTUM CULTURE:** Negative for Tubercle Bacillus

[redacted] 20[redacted] **SPUTUM CULTURE:** Positive for Gram-Positive coccal (3+), Negative for Gram-Positive bacillary

[redacted] **20**[redacted] **SPUTUM CULTURE:** Negative for Gram-Negative coccal, Positive for Gram-Negative bacillary (4+)

[redacted] **20**[redacted] **SPUTUM CULTURE:** Negative for COVID-19 PCR

[redacted] **20**[redacted] **URINE CULTURE:** Negative for Gram Positive coccal and Gram positive bacillary

[redacted] **20**[redacted] **URINE CULTURE:** Negative for Gram-Negative coccal and Gram- Negative bacillary

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		X
卵巣癌	X			X

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	5[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: DYSMENORRHOEA	NOT REPORTED
OTHER: POLLINOSIS	19[redacted]
OTHER: VARICELLA	19[redacted]
OTHER: PSORIASIS VULGARIS	19[redacted]
OTHER: SINUSITIS	20[redacted]
OTHER: JOINT FLUID DRAINAGE	20[redacted]
ANEMIA: IRON DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: ADENOTONSILLECTOMY	19[redacted]
SURGERY: SYNOVECTOMY	19[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 99	99

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]
CICLOSPORIN	50 mg	BID	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
INFLIXIMAB	350 mg	OTHER: ONCE DOSE	Y-M: 20[redacted]
INFLIXIMAB	480 mg	OTHER: EVERY 2 MONTHS	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	OTHER: ONCE DOSE	Y-M: 20[redacted]
LIDOCAINE	1 OTHER: APPLICATION	OTHER: ONCE DOSE	Y-M: 20[redacted]
PREDNISOLONE	5 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
MAXACALCITOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
METHOTREXATE	4 mg	EVERY WEEK	Y-M: 20[redacted]
FLURBIPROFEN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
LOXOPROFEN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
BETAMETHASONE BUTYRATE PROPIONATE W/MAXACALCI	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
MAXACALCITOL	1 OTHER: 1	OTHER: APPLICATION	Y-M: 20[redacted]
TACALCITOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted]
IXEKIZUMAB	160 mg	OTHER: ONCE DOSE	Y-M: 20[redacted] / -202
IXEKIZUMAB	80 mg	EVERY 2 WEEKS	Y-M: 20[redacted] / -166
TEPRENONE	100 mg	BID	Y-M: 20[redacted] / -166
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / -152
IXEKIZUMAB	80 mg	OTHER: ONCE DOSE	Y-M: 20[redacted] / -68

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	PRN	Y-M: 20[redacted] / -152	Y-M: 20[redacted] / 73
IRON	100 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 29
PENCICLOVIR	500 mg	TID	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 51
PREGABALIN	25 mg	QD	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 51
NADIFLOXACIN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 66
MECOBALAMIN	500 ug	TID	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 87
NEUROTONIC	2 OTHER: TABLET	PRN	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 87
PREGABALIN	50 mg	QD	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 57
ACICLOVIR	1 OTHER: APPLICATION	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 66
BETAMETHASONE	1 OTHER: APPLICATION	QID	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 66
CLINDAMYCIN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 52	Y-M: 20[redacted] / 66
TEPRENONE	50 mg	PRN	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 100
LIDOCAINE	1 mL	EVERY WEEK	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 100
LIDOCAINE	7 mL	EVERY WEEK	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 100
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 74	Y-M: 20[redacted] / 112
REBAMIPIDE	100 mg	PRN	Y-M: 20[redacted] / 101	ONGOING
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 101
RINGER-LACTATE	500 mL	QD	Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 101
PHYSIO 140	500 mL	TID	Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 102
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	QD	Y-M: 20[redacted] / 102	Y-M: 20[redacted] / 102
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 102	Y-M: 20[redacted] / 104
TRIFLUID	500 mL	QD	Y-M: 20[redacted]	Y-M: 20[redacted]

			[redacted] / 102 / 105
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted] / 102 - Y-M: 20[redacted] / 118
VITAMEDIN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 102 - Y-M: 20[redacted] / 118
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	1000 mL	QD	Y-M: 20[redacted] / 102 - Y-M: 20[redacted] / 122
SENNOSIDE A+B	24 mg	PRN	Y-M: 20[redacted] / 104 - ONGOING
PIP/TAZO	4.5 g	TID	Y-M: 20[redacted] / 104 - Y-M: 20[redacted] / 108
GLYCEROL	30 g	PRN	Y-M: 20[redacted] / 108 - Y-M: 20[redacted] / 108
MEROPENEM	0.5 g	BID	Y-M: 20[redacted] / 108 - Y-M: 20[redacted] / 108
MEROPENEM	0.5 g	TID	Y-M: 20[redacted] / 109 - Y-M: 20[redacted] / 112
DIMETICONE	5 mL	OTHER: ONCE DOSE	Y-M: 20[redacted] / 112 - Y-M: 20[redacted] / 112
LIDOCAINE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 112 - Y-M: 20[redacted] / 112
LIDOCAINE	5 mL	OTHER: ONCE DOSE	Y-M: 20[redacted] / 112 - Y-M: 20[redacted] / 112
PRONASE	20000 OTHER: UNIT/KG	OTHER: ONCE DOSE	Y-M: 20[redacted] / 112 - Y-M: 20[redacted] / 112
SODIUM BICARBONATE	1 g	OTHER: ONCE DOSE	Y-M: 20[redacted] / 112 - Y-M: 20[redacted] / 112
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 113 - ONGOING
PARACETAMOL	1000 mg	OTHER: ONCE DOSE	Y-M: 20[redacted] / 113 - Y-M: 20[redacted] / 113
IOPAMIDOL	100 mL	OTHER: ONCE DOSE	Y-M: 20[redacted] / 114 - Y-M: 20[redacted] / 114
MICAFUNGIN	150 mg	QD	Y-M: 20[redacted] / 114 - Y-M: 20[redacted] / 120
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 115 - Y-M: 20[redacted] / 121
TRIFLUID	1000 mL	QD	Y-M: 20[redacted] / 116 - Y-M: 20[redacted] / 122
BENZETHONIUM	10 mL	OTHER: ONCE DOSE	Y-M: 20[redacted] / 121 - Y-M: 20[redacted] / 121
ALBUMIN HUMAN	12.5 g	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
ANTITHROMBIN III	1500 IU	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
ATROPINE	0.5 mg	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122

CALCIUM GLUCONATE	10 mL	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
DEXAMETHASONE	6.6 mg	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
DICLOFENAC	25 mg	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
EPHEDRINE	4 mg	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
GLUCOSE INJECTION	10 mL	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
GLYCEROL	60 mL	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
HETASTARCH	500 mL	QD	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
INSULIN HUMAN	1 IU	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
LEVOBUPIVACAINE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
LIDOCAINE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
PHENYLEPHRINE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
PHYSIO 140	1000 mL	QD	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
PROPOFOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
RED BLOOD CELLS	400 mL	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
REMIFENTANIL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
ROCURONIUM	60 mg	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
SEVOFLURANE	3 %	OTHER: CONTINUOUS	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
SUGAMMADEX	200 mg	OTHER: ONCE DOSE	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 122
FENTANYL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 123
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	QID	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 124
CEFAZOLIN	1 g	BID	Y-M: 20[redacted] / 122 - Y-M: 20[redacted] / 124
ENOXAPARIN	2000 IU	BID	Y-M: 20[redacted] / 124 - Y-M: 20[redacted] / 124
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 124 - Y-M: 20[redacted] / 127

MAGNESIUM OXIDE	330 mg	TID	Y-M: 20[redacted]- [redacted] / 126	ONGOING
BENZETHONIUM	10 mL	OTHER: ONCE DOSE	Y-M: 20[redacted]- [redacted] / 128	Y-M: 20[redacted]- / 128
BENZETHONIUM	10 mL	OTHER: ONCE DOSE	Y-M: 20[redacted]- [redacted] / 129	Y-M: 20[redacted]- / 129
CEFACLOR	250 mg	TID	Y-M: 20[redacted]- [redacted] / 129	Y-M: 20[redacted]- / 132

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

Event Description	URINARY TRACT INFECTION
Preferred term	尿路感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 83
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 101): Blood: 2+ [-1 - 0] UNIT NOT REPORTED; Creatinine: 43.32 [35.36 - 70.72] umol/L; Erythrocytes: 25 [0 - 4] /HPF; Leukocytes: 55 [0 - 5] /HPF; Leukocytes: 9.8 [3.5 - 8.5] 10^9/L; NPTST001- BACTERIUM: 1+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST056-CRP: 26.34 [0 - 0.3] mg/dL; Protein: 2+ [-1 - 0] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 104): Creatinine: 38.01 [35.36 - 70.72] umol/L; Erythrocytes: 22 [0 - 4] /HPF; Leukocytes: 11 [0 - 5] /HPF; Leukocytes: 8.5 [3.5 - 8.5] 10^9/L; NPTST026-BACTERIUM: 1+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST056-CRP: 26.1 [0 - 0.3] mg/dL; NPTST103-GRANULAR CASTS: 1+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 107): Blood: ? [-1 - 0] UNIT NOT REPORTED; Creatinine: 36.25 [35.36 - 70.72] umol/L; Erythrocytes: 19 [0 - 4] /HPF; Leukocytes: 1 [0 - 5] /HPF; Leukocytes: 8.7 [3.5 - 8.5] 10^9/L; NPTST056-CRP: 28 [0 - 0.3] mg/dL; Protein: ? [-1 - 0] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 112): Creatinine: 38.9 [35.36 - 70.72] umol/L; Leukocytes: 9.7 [3.5 - 8.5] 10^9/L; NPTST056-CRP: 34 [0 - 0.3] mg/dL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	113 (14 DAYS AFTER LAST TREATMENT)
Duration of AE	31 DAYS
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

Event #4: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	OVARY CANCER
Preferred term	卵巣癌
AE Onset Date / Rx Day	[redacted]20[redacted] / 113 (14 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 101): Erythrocyte Sedimentation Rate: 96.2 [0 - 15] mm/h; Leukocytes: 9.8 [3.5 - 8.5] 10^9/L; NPTST015-ANTIGEN OF LEGIONELLA: ? [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST056-CRP: 26.3 [0 - 0.3] mg/dL; NPTST166-PNEUMOCOCCUS: ? [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 105): NPTST039-C3: 153 [69 - 128] mg/dL; NPTST040-C4: 21 [14 - 36] mg/dL; NPTST048-CH50: 67 [30 - 50] U/mL; NPTST105-HAPTOGLOBIN: 466 [19 - 170] mg/dL; [redacted]20[redacted] (RX DAY 107): Erythrocyte Sedimentation Rate: 90.9 [0 - 15] mm/h; Leukocytes: 8.7 [3.5 - 8.5] 10^9/L; NPTST056-CRP: 28 [0 - 0.3] mg/dL; [redacted]20[redacted] (RX DAY 108): Erythrocyte Sedimentation Rate: 114.4 [0 - 15] mm/h; Leukocytes: 8.3 [3.5 - 8.5] 10^9/L; NPTST003-?-D GLUCAN: LESS THAN 6.0 [NOT REPORTED - 11] UNIT NOT REPORTED; NPTST022-ASO: 258 [0 - 200] IU/mL; NPTST041-C7HRP: ? [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST056-CRP: 27.3 [0 - 0.3] mg/dL; NPTST113-HTLV-1: LESS THAN 16 [NOT REPORTED - 16] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 112): Erythrocyte Sedimentation Rate: 103.2 [0 - 15] mm/h; Leukocytes: 9.7 [3.5 - 8.5] 10^9/L; NPTST056-CRP: 34 [0 - 0.3] mg/dL; [redacted]20[redacted] (RX DAY 115): Erythrocytes: 3 [3.7 - 5.1] 10^12/L; Hemoglobin: 80 [113 - 154] g/L; Leukocytes: 11.4 [3.5 - 8.5] 10^9/L; NPTST056-CRP: 35.16 [0 - 0.3] mg/dL; [redacted]20[redacted] (RX DAY 118): Erythrocyte Sedimentation Rate: 112.7 [0 - 15] mm/h; Erythrocytes: 2.7 [3.7 - 5.1] 10^12/L; Hemoglobin: 72 [113 - 154] g/L; Leukocytes: 10.5 [3.5 -

Microbiology

[redacted]20[redacted] (RX DAY 101): BLOOD NPTST008-AEROBIC CULTURE: NEGATIVE; BLOOD NPTST013-ANAEROBIC CUKTURE: NEGATIVE; [redacted]20[redacted] (RX DAY 102): SPUTUM NPTST006-ACID FAST STAIN: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 101): CT SCAN(CHEST?ABDOMINAL): PELVIC TUMOR; [redacted]20[redacted] (RX DAY 107): TRANSVAGINAL ECHO: LEFT OVARIAN:SOLID TUMOR OF 10CM IN DIAMETER,IT IS NOT THE CAUSE OF THIS EVENT; [redacted]20[redacted] (RX DAY 109): ECHOCARDIOGRAPHY: NO ABNORMAL FINDINGS; [redacted]20[redacted] (RX DAY 112): ENDOSCOPY UPPER GASTROINTESTINAL TRACT: OESOPHAGEAL HIATAL HERNIA,SEVERAL FUNDIC GLAND POLYP OF 2MM IN DIAMETER; [redacted]20[redacted] (RX DAY 114): CONTRAST-ENHANCED CT SCAN?CHEST?ABDOMINAL?: THYROID GLAND?LOW DENSITY AREA IN THE LEFT LOBE MULTIPLE NODULAR OPACITIES IN BOTH LUNG FIELDS. INFILTRATES AND PLEURAL EFFUSION WERE SHOWED IN THE RIGHT LUNG. PELVIC NEOPLASM AND SMALL AMOUNT OF; [redacted]20[redacted] (RX DAY 115): MRI(UTERINE,OVARY): SOFT TISSUE INCLUDING SOLID COMPONENT ON THE LEFT SIDE OF UTERUS. LYMPH NODES ENLARGED(BILATERAL ILIAC ARTERY,PARAAORTIC LYMPH NODES) PELVIC SMALL AMOUNT OF ASCITES.; [redacted]20[redacted] (RX DAY 122): HISTOLOGIC DIAGNOSIS: HIGH-GRADE ADENOCARCINOMA(LEFT OVARY) ENDOMETRIOID CARCINOMA,GRADE1,PT1A(UTERUS) NO NEOPLASTTIC CHANGE(RIGHT OVARY AND TUBE) LEFT OBTURATOR LYMPH NODE METASTASIS(+); PERITONEAL CYTOLOGIC EXAMINATIONS: NEGATIVE; TOTAL HYSTERECTOMY, BILATERAL SALPINGO-OOPHORECTOMY, OBTURATOR LYMPH NODES RESECTION, OMENTECTOMY: THE OPERATION ENDED AS SCHEDULED. NO RESIDUAL MACROSCOPIC LESIONS.; TRANSFUSION: 6 UNITS OF CONCENTRATED HUMAN RED BLOOD CELLS WERE TRANSFUSED TO THE SUBJECT FOR ANAEMIA DUE TO OVARIAN CANCER DURING THE SURGERY.; [redacted]20[redacted] (RX DAY 128): TRANSVAGINAL ECHO: NO HEMATOMA

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CAUSE UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

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，尿路感染及び卵巣癌の事象を発現した。

Event 3 及び 4 の臨床経過：

関連する病歴は尋常性乾癬，乾癬性関節炎，鉄欠乏性貧血，月経困難症，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

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

20[redacted] 年 [redacted] 月 [redacted] 日より，被験者は 38°C の発熱が続いていた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左背部痛及び左上臍部に間欠性の疼痛を発現した。医師は尿路感染を疑った。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。CT スキャン検査を行ったところ，骨盤腫瘍が明らかになった。被験者は，悪寒，食欲不振，体重減少，不眠及び貧血を呈していた。20[redacted] 年 [redacted] 月 [redacted] 日，尿検査により改善が認められたが，高熱は続いた。20[redacted] 年 [redacted] 月 [redacted] 日，20[redacted] 年 [redacted] 月 [redacted] 日からの高い炎症反応及び高熱のため，この被験者の治験参加は完全に中止された。20[redacted] 年 [redacted] 月 [redacted] 日，CT スキャン検査が行われ，卵巣癌が疑われた。20[redacted] 年 [redacted] 月 [redacted] 日，子宮全摘術，両側卵管卵巣摘除，大網切除及び閉鎖リンパ節郭清術が行われた。手術所見は，3 cm の子宮類線維症及び 15 cm の卵巣固形腫瘍であった。20[redacted] 年 [redacted] 月 [redacted] 日，手術時に採取された組織検体に基づき，高悪性度腺癌（左卵巣）と，グレード 1 で PT 1A の類内膜癌（子宮）との組織学的診断が下された。右卵巣・卵管には腫瘍性変化は見られなかった。左閉鎖リンパ節転移が認められた。これらの結果から，卵巣癌と診断された。手術は予定どおり終了し，残存顕微鏡病変は認められなかった。治験責任医師はこれらの腫瘍が発熱の原因であったと判断した。術後経過は良好で，被験者は

20[redacted] 年 [redacted] 月 [redacted] 日に退院した。

投与された薬剤は，メロペネム，ソルデム 3A，ロキソプロフェン，ハイアミン，ジクロフェナクナトリウム，献血ノンスロン，セファゾリンナトリウム，クレキサン，セファクロル，エフェドリン，キシロカイン，ブリディオン，ロクロニウム臭化物，フェンタニル，レミフェンタニル，アセリオ，硫酸アトロピン，デキサート，カルチコール，ブドウ糖，ヒューマリン R，ポプスカイン，フィジオ 140，ボルベン，アルブミナー，トリフリード，カルボシステイン，ハイアミン，グリカンチョー液，タゾピペ，セフトリアキソン NA 及びネオシネジンコーワであった。

The patient's past medications include:

LOXONIN for DYSMENORRHEA (20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Urinary tract infection (10046571) (Urinary tract infection (10046571)) [v.21.1] [10046571]

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

2) Ovarian cancer (10033128) (Ovarian cancer (10033128)) [v.21.1] [10033128]

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 URINARY TRACT INFECTION

- **Investigator:** Not applicable

- AbbVie: Not applicable

Event of OVARY CANCER

- Investigator: Cause unknown

- AbbVie: Weak temporal association with little over 3 months of study drug exposure.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ACID FAST STAIN SPUTUM:** NEGATIVE

[redacted] **20[redacted] AFP:** 3.9 NG/ML (normal 0 to 10)

[redacted] **20[redacted] ASO:** 258 IU/mL (normal 0 to 200)

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

[redacted] **20[redacted] BLOOD ANAEROBIC CULTURE:** NEGATIVE

[redacted] **20[redacted] BLOOD C3:** 153 mg/dL (normal 69 to 128)

[redacted] **20[redacted] BLOOD C4:** 21 mg/dL (normal 14 to 36)

[redacted] **20[redacted] BLOOD CH50:** 67 U/ML (normal 30 to 50)

[redacted] **20[redacted] BLOOD URINE:** 2+

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

[redacted] **20[redacted] CA 125:** 68.1 U/ML (normal 0 to 35)

[redacted] **20[redacted] CA 15-3:** 27 U/ML (normal 0 to 27)

[redacted] **20[redacted] CA 19-9:** Less than 1.0

[redacted] **20[redacted] CEA:** 1.5 NG/ML (normal 0 to 5)

[redacted] **20[redacted] CONTRAST-ENHANCED CT SCAN:** THYROID GLAND：LOW DENSITY AREA IN THE LEFT LOBE MULTIPLE NODULAR OPACITIES IN BOTH LUNG FIELDS.　INFILTRATES AND PLEURAL EFFUSION WERE SHOWED IN THE RIGHT LUNG. PELVIC NEOPLASM AND SMALL AMOUNT OF ASCITES WERE FOUND.

[redacted] **20[redacted] CREATININE:** 0.49 10^2mcL (normal 0.4 to 0.8)

[redacted] **20[redacted] CRP:** 26.338 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CRP:** 26.3 mg/dL (normal 0 to 0.3)04 [redacted] 20[redacted] CRP: 28.0 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CRP:** 27.3 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CRP:** 35.155 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CRP:** 29.821 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CRP:** 28.227 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CRP:** 19.984 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CRP:** 5.209 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CRP:** 2.889 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] CT SCAN:** PELVIC TUMOR

[redacted] **20[redacted] ECHOCARDIOGRAPHY:** NO FINDINGS

[redacted] **20[redacted] ENDOSCOPY UPPER GASTROINTESTINAL TRACT:** OESOPHAGEAL HIATAL HERNIA,SEVERAL FUNDIC GLAND POLYP OF 2MM IN DIAMETER

[redacted] **20[redacted] ESR:** 96.2 mm/h (normal 0 to 15)

[redacted] **20[redacted] ESR:** 90.9 mm/h (normal 0 to 15)

[redacted] **20[redacted] ESR:** 114.4 mm/h (normal 0 to 15)

[redacted] **20[redacted] ESR:** 103.2 mm/h (normal 0 to 15)

[redacted] **20[redacted] ESR:** 101.2 mm/h (normal 0 to 15)

[redacted] **20[redacted] ESR:** 112.7 mm/h (normal 0 to 15)

[redacted] **20[redacted] HAPTOGLOBIN:** 466 mg/dL (normal 19 to 170)

[redacted] **20[redacted] HEMOGLOBIN:** 8 G/DL (normal 11.3 to 15.4)

[redacted] **20[redacted] HEMOGLOBIN:** 7.2 G/DL (normal 11.3 to 15.4)

[redacted] **20[redacted] HEMOGLOBIN:** 6.8 G/DL (normal 11.3 to 15.4)

[redacted] **20[redacted] HEMOGLOBIN:** 9.8 G/DL (normal 11.3 to 15.4)

[redacted] **20[redacted] HTLV-1:** LESS THAN 16 (NORMAL LESS THAN 16 TIMES)

[redacted] **20[redacted] MRI (UTERINE, OVARY):** SOFT TISSUE INCLUDING SOLID COMPONENT ON THE LEFT SIDE OF UTERUS. LYMPH NODES ENLARGED (BILATERAL ILIAC ARTERY, PARAORTIC

LYMPH NODES); PELVIC SMALL AMOUNT OF ASCITES

[redacted] **20[redacted] PERITONEAL CYTOLOGIC EXAMINATIONS:** Negative

[redacted] **20[redacted] PROTEIN URINE:** 2+

[redacted] **20[redacted] RED BLOOD CELLS:** 273 10^2/µL (normal 370 to 510)

[redacted] **20[redacted] RED BLOOD CELLS:** 266 10^2/µL (normal 370 to 510)

[redacted] **20[redacted] RED BLOOD CELLS:** 346 10^2/µL (normal 370 to 510)

[redacted] **20[redacted] RED BLOOD CELLS URINE:** 25 /HPF (normal 0 to 4)

[redacted] **20[redacted] TRANSVAGINAL ECHO:** LEFT OVARIAN:SOLID TUMOR OF 10CM IN DIAMETER,IT IS NOT THE CAUSE OF THIS EVENT

[redacted] **20[redacted] TRANSVAGINAL ECHO:** No hematoma in the vaginal stump; small amount of ascites fluid

[redacted] **20[redacted] TRANSVAAL ECHO:** Normal

[redacted] **20[redacted] URINE ANTIGEN OF LEGIONELLA:** NOT REPORTED

[redacted] **20[redacted] URINE BACTERIUM:** 1+

[redacted] **20[redacted] URINE BLOOD:** +/-

[redacted] **20[redacted] URINE PNEUMOCOCCUS:** NOT REPORTED

[redacted] **20[redacted] URINE PROTEIN:** +/-

[redacted] **20[redacted] URINE RBC:** 19 /HPF (normal <4)

[redacted] **20[redacted] URINE WBC:** 1 /HPF (normal 0 to 5)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9800 mcl (normal 35 to 85)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 98 10^2/µL (normal 35 to 85)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 87 10^2/µL (normal 35 to 85)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 83 10^2/µL (normal 35 to 85)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 97 10^2/µL (normal 35 to 85)

[redacted] **20[redacted] WHITE BLOOD CELLS URINE:** 55 /HPF (normal 0 to 5)

[redacted] **20[redacted] B-D GLUCAN:** LESS THAN 6.0 (NORMAL LESS THAN 11 PG/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
間質性肺疾患	X			
気胸	X	X		
汎血球減少症	X	X	X	
ニューモシスチス・イロベチイ肺炎	X			X
サイトメガロウイルス感染	X			X
十二指腸潰瘍	X			

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	5[redacted]	MALE	ASIAN

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: BUFFERIN COMBINATION TABLET	NOT REPORTED
GASTROESOPHAGEAL REFLUX DISEASE	NOT REPORTED
HYPERTENSION	NOT REPORTED
LIVER DISEASE (EXCLUDING HEPATITIS): ALCOHOLIC LIVER DISEASE	NOT REPORTED
OTHER: EDEMA	NOT REPORTED
OTHER: PERIODONTAL DISEASE	NOT REPORTED
OTHER: PLAQUE PSORIASIS	NOT REPORTED
OTHER: PSYCHOSOMATIC DISORDER	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	32.00	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	2 - 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted] / 1	[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted] / 169	[redacted] / 392	224
ABT-494	30MG	ORAL	QD	[redacted] / 393	[redacted] / 632	240

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]
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted]
LORAZEPAM	0.5 mg	QD	Y-M: 20[redacted]
DEXAMETHASONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
TACALCITOL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
CELECOXIB	100 mg	BID	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
RISANKIZUMAB	150 mg	OTHER: PSORIATIC ARTHRITIS, M16-244 TRIAL	Y-M: 20[redacted] / -359
AMLODIPINE BESILATE W/AZILSARTAN	22.5 mg	QD	Y-M: 20[redacted] / -265
METHOTREXATE	8 mg	EVERY WEEK	Y-M: 20[redacted] / -104
FOLIC ACID	5 mg	QD	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
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 632
LORAZEPAM	0.5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 641
CELECOXIB	100 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 632
AMLODIPINE BESILATE W/AZILSARTAN	22.5 mg	QD	Y-M: 20[redacted] / -265	Y-M: 20[redacted] / 633
ALCLOMETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 632
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 632
ESFLURBIPROFEN W/MENTHA SPP. OIL	7 OTHER: SHEET	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 633
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 633
SULPERAZON	1 g	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 634
CARBAZOCHROME	50 mg	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 636
TRANEXAMIC ACID	250 mg	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 636
SOLACET F	500 mL	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 637
INSULIN ASPART	3 mL	QD	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 638
I.V. SOLUTIONS	500 mL	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 639
FENTANYL	2-10 mL	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 642
SIVELESTAT	300 mg	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 645
ROCURONIUM	50 mg	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 651
TRAMADOL	25 mg	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 653
BLOOD AND RELATED PRODUCTS	NA OTHER: UNIT	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 657
IRON	100 mg	BID	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 662
MIDAZOLAM	10 mg	PRN	Y-M: 20[redacted] / 633	Y-M: 20[redacted] / 662
HYDROXYZINE	25 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted]

BIAPENEM	0.3 g	PRN	Y-M: 20[redacted]-[redacted] / 634 Y-M: 20[redacted]-[redacted] / 637
METAMIZOLE	500 mg	PRN	Y-M: 20[redacted]-[redacted] / 634 Y-M: 20[redacted]-[redacted] / 639
PENTAZOCINE	15 ng	PRN	Y-M: 20[redacted]-[redacted] / 634 Y-M: 20[redacted]-[redacted] / 641
REMIFENTANIL	2 mg	PRN	Y-M: 20[redacted]-[redacted] / 636 Y-M: 20[redacted]-[redacted] / 636
REMIFENTANIL	4 mg	PRN	Y-M: 20[redacted]-[redacted] / 636 Y-M: 20[redacted]-[redacted] / 636
DEXMEDETOMIDINE	200 mg	PRN	Y-M: 20[redacted]-[redacted] / 636 Y-M: 20[redacted]-[redacted] / 642
METHYLPREDNISOLONE	1 g	QD	Y-M: 20[redacted]-[redacted] / 637 Y-M: 20[redacted]-[redacted] / 639
BACTRIM	15 mL	QD	Y-M: 20[redacted]-[redacted] / 637 Y-M: 20[redacted]-[redacted] / 652
NAFAMOSTAT	NA mg	QD	Y-M: 20[redacted]-[redacted] / 637 Y-M: 20[redacted]-[redacted] / 659
IMMUNOGLOBULIN HUMAN NORMAL	5 g	PRN	Y-M: 20[redacted]-[redacted] / 638 Y-M: 20[redacted]-[redacted] / 642
SODIUM BICARBONATE	20 mL	PRN	Y-M: 20[redacted]-[redacted] / 638 Y-M: 20[redacted]-[redacted] / 642
DIAZEPAM	10 mg	PRN	Y-M: 20[redacted]-[redacted] / 639 Y-M: 20[redacted]-[redacted] / 639
HALOPERIDOL	5 mg	PRN	Y-M: 20[redacted]-[redacted] / 639 Y-M: 20[redacted]-[redacted] / 639
FLUNITRAZEPAM	2 mg	PRN	Y-M: 20[redacted]-[redacted] / 639 Y-M: 20[redacted]-[redacted] / 640
PREDNISOLONE	60 mg	PRN	Y-M: 20[redacted]-[redacted] / 639 Y-M: 20[redacted]-[redacted] / 662
PARACETAMOL	200 mg	QD	Y-M: 20[redacted]-[redacted] / 640 Y-M: 20[redacted]-[redacted] / 641
GLUCOSE	20 mL	PRN	Y-M: 20[redacted]-[redacted] / 640 Y-M: 20[redacted]-[redacted] / 642
INSULIN HUMAN	10 OTHER: UNIT	PRN	Y-M: 20[redacted]-[redacted] / 640 Y-M: 20[redacted]-[redacted] / 642
MICAFUNGIN	NA mg	PRN	Y-M: 20[redacted]-[redacted] / 640 Y-M: 20[redacted]-[redacted] / 644
LEVOFLOXACIN	500 mg	PRN	Y-M: 20[redacted]-[redacted] / 640 Y-M: 20[redacted]-[redacted] / 645
PROPOFOL	500 mg	PRN	Y-M: 20[redacted]-[redacted] / 640 Y-M: 20[redacted]-[redacted] / 659
CALCIUM POLYSTYRENE SULFONATE	50 g	TID	Y-M: 20[redacted]-[redacted] / 641 Y-M: 20[redacted]-[redacted] / 641
SODIUM CHLORIDE	40 mL	PRN	Y-M: 20[redacted]-[redacted] / 642 Y-M: 20[redacted]-[redacted] / 652
MAGNESIUM SULFATE	20 mL	PRN	Y-M: 20[redacted]-[redacted]

			/ 642 / 656
AMINO ACIDS NOS	NA mL	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 642 / 662
ELEMEAL	2 mL	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 642 / 662
LANSOPRAZOLE	30 mg	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 642 / 662
NEUROBION	5 mL	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 642 / 662
NOREPINEPHRINE	3 mg	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 642 / 662
ANTITHROMBIN GAMMA	NA mL	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 643 / 658
ANTIBIOTICS-RESISTANT LACTIC ACID BACTERIAE	1 g	TID	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 643 / 661
GANCICLOVIR	150 mg	QD	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 644 / 652
HEPARIN	5 mL	QD	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 644 / 656
FACTOR XIII (FIBRIN STABILISING FACTOR)	20 mL	QD	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 645 / 650
UNACID	3 g	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 646 / 650
ZINC	25 mg	BID	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 646 / 655
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 648 / 655
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 648 / 655
MORPHINE	10 mg	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 648 / 659
CASPOFUNGIN	70 mg	QD	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 650 / 650
HEPARIN	5 mL	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 650 / 660
VANCOMYCIN	NA g	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 650 / 660
MEROPENEM	NA g	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 650 / 661
CALCIUM GLUCONATE	5 mL	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 651 / 656
BROMHEXINE	4 mg	PRN	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 651 / 659
CASPOFUNGIN	50 mg	QD	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 651 / 661
FILGRASTIM	75 ug	QD	Y-M: 20[redacted] Y-M: 20[redacted]
			/ 652 / 658
CLINDAMYCIN	600 mg	QD	Y-M: 20[redacted] Y-M: 20[redacted]

AMBROXOL	15 mg	TID	/ 653 Y-M: 20[redacted]- / 654 Y-M: 20[redacted]-
ATOVAQUONE	5 mL	QD	/ 653 Y-M: 20[redacted]- / 655 Y-M: 20[redacted]-
SODIUM PHOSPHATE	20 mL	PRN	/ 654 Y-M: 20[redacted]- / 654 Y-M: 20[redacted]-
POTASSIUM	20 mL	PRN	/ 654 Y-M: 20[redacted]- / 662 Y-M: 20[redacted]-
ATOVAQUONE	10 mL	QD	/ 655 Y-M: 20[redacted]- / 659 Y-M: 20[redacted]-

Event #2: Serious Adverse Event

Event Description	INTERSTITIAL PNEUMONIA
Preferred term	間質性肺疾患
AE Onset Date / Rx Day	[redacted]20[redacted] / 633 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 633): Alanine Aminotransferase: 67 [10 - 42] U/L; Aspartate Aminotransferase: 118 [13 - 30] U/L; Blood Urea Nitrogen: 23.74 [2.86 - 7.14] mmol/L; Creatinine: 211.28 [57.46 - 94.59] umol/L; Erythrocytes: 1.8 [4.4 - 5.6] 10^12/L; Hemoglobin: 76 [137 - 468] g/L; Leukocytes: 2.4 [3.3 - 8.6] 10^9/L; NPTST110-HIV-AB: NEGATIVE [NOT REPORTED - 1] UNIT NOT REPORTED; Platelets: 116 [158 - 348] 10^9/L; Potassium: 5.7 [3.6 - 4.8] mmol/L; [redacted]20[redacted] (RX DAY 634): Erythrocytes: 1.7 [4.4 - 5.6] 10^12/L; Hemoglobin: 71 [137 - 168] g/L; Leukocytes: 3.4 [3.3 - 8.6] 10^9/L; Platelets: 103 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 636): NPTST124-KL-6: 880 [105 - 435] U/mL; [redacted]20[redacted] (RX DAY 637): Alanine Aminotransferase: 31 [10 - 42] U/L; Aspartate Aminotransferase: 67 [13 - 30] U/L; Erythrocytes: 2.2 [4.4 - 5.6] 10^12/L; Hematocrit: 0.23 [0.41 - 0.5] fraction of 1; Hemoglobin: 83 [137 - 168] g/L; Leukocytes: 4 [3.3 - 8.6] 10^9/L; Lymphocytes/Leukocytes: 5 [16.5 - 49.5] %; Monocytes/Leukocytes: 2 [2 - 10] %; NPTST003-?-D GLUCAN: 266.2 [0 - 11] mg/L; NPTST004-?-GTP: 82 [13 - 64] U/L; NPTST024-AT?: 88 [83 - 118] %; NPTST083-FBG: 657 [200 - 400] mg/dL; NPTST084-FDP: 70.1 [0 - 5] UNIT NOT REPORTED; NPTST198-TAT: 41.17 [0 - 3] ng/mL; Neutrophils Band Form/Leukocytes: 11 [0.5 - 6.5] %; Neutrophils/Leukocytes: 81 [38 - 74] %; Platelets: 43 [158 - 348] 10^9/L; Platelets: 43 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 638): Aspartate Aminotransferase: 50 [13 - 30] U/L; Blood Urea Nitrogen: 20.56;

Microbiology

[redacted]20[redacted] (RX DAY 633): BLOOD NPTST029-BLOOD CULTURE: NEGATIVE; OTHER RESECTED LUNG TISSUE NPTST104-GROCOTT STAIN: POSITIVE-PNEUMOCYSTIS JIROVECII CYST; OTHER SUCTION SPUTUM NPTST193-SPUTUM CULTURE: POSITIVE-METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS GRAM-NEGATIVE RODS; [redacted]20[redacted] (RX DAY 642): BLOOD NPTST030-BLOOD CULTURES: NEGATIVE; [redacted]20[redacted] (RX DAY 650): OTHER ENDOTRACHEAL TUBE NPTST193-SPUTUM CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 633): CHEST X-RAY: RIGHT PNEUMOTHORAX,INTERSTITIAL PNEUMONIA LUNG CYST; PLAIN CT: GROUND-GLASS OPACITY; THORACOSCOPIC PNEUMONECTOMY (LUNG CYST SURGERY): DRAINAGE; VITAL SIGNS: BLOOD PRESSURE 160/99, SPO2 60%; [redacted]20[redacted] (RX DAY 636): THORACOSCOPIC LUNG SURGERY: DRAINAGE; [redacted]20[redacted] (RX DAY 637): CHEST IMAGE(CHEST CT): SUBCUTANEOUS EMPHYSEMA INCREASES; STEROID PULSE THERAPY WAS PERFORMED: ONGOING; [redacted]20[redacted] (RX DAY 638): HEMATOLOGY CONSULTATION: PLATELET TRANSFUSION TO THROMBOCYTOPENIA. ADMINISTRATION OF IMMUNOGLOBULIN PREPARATIONS FOR SEVERE INFECTIONS.; ST COMBINATION WAS

STARTED CONSIDERING PNEUMOCYSTIS PNEUMONIA.: ONGOING; [redacted]20[redacted] (RX DAY 639): IMMUNOGLOBULIN ADMINISTRATION START: ONGOING; PLATELET TRANSFUSIONS: NOT IMPROVE.; [redacted]20[redacted] (RX DAY 642): VV?VENO VENOUS?-ECMO?EXTRACORPOREAL MEMBRANE OXYGENATION?: ARTIFICIAL RESPIRATION MANAGEMENT; BRAIN CT: CEREBRAL INFARCTION?LEFT POSTERIOR CEREBRAL ARTERY AREA); [redacted]20[redacted] (RX DAY 648): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 650): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 651): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 652): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); TRACHEOSTOMY: ARTIFICIAL RESPIRATION MANAGEMENT; [redacted]20[redacted] (RX DAY 654): LEFT THORACIC DRAINAGE: LEFT PNEUMOTHORAX; [redacted]20[redacted] (RX DAY 662): AUTOPSY IMAGING.: NO NEW FINDINGS WERE OBTAINED.

AE Stopped Rx Day	662 (30 DAYS AFTER LAST TREATMENT)
Duration of AE	30 DAYS
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, LIFE THREATENING

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

Event Description	RIGHT PNEUMOTHORAX
Preferred term	気胸
AE Onset Date / Rx Day	[redacted]20[redacted] / 633 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 633): Alanine Aminotransferase: 67 [10 - 42] U/L; Aspartate Aminotransferase: 118 [13 - 30] U/L; Blood Urea Nitrogen: 23.74 [2.86 - 7.14] mmol/L; Creatinine: 211.28 [57.46 - 94.59] umol/L; Erythrocytes: 1.8 [4.4 - 5.6] 10^12/L; Hemoglobin: 76 [137 - 468] g/L; Leukocytes: 2.4 [3.3 - 8.6] 10^9/L; NPTST110-HIV-AB: NEGATIVE [NOT REPORTED - 1] UNIT NOT REPORTED; Platelets: 116 [158 - 348] 10^9/L; Potassium: 5.7 [3.6 - 4.8] mmol/L; [redacted]20[redacted] (RX DAY 634): Erythrocytes: 1.7 [4.4 - 5.6] 10^12/L; Hemoglobin: 71 [137 - 168] g/L; Leukocytes: 3.4 [3.3 - 8.6] 10^9/L; Platelets: 103 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 636): NPTST124-KL-6: 880 [105 - 435] U/mL; [redacted]20[redacted] (RX DAY 637): Alanine Aminotransferase: 31 [10 - 42] U/L; Aspartate Aminotransferase: 67 [13 - 30] U/L; Erythrocytes: 2.2 [4.4 - 5.6] 10^12/L; Hematocrit: 0.23 [0.41 - 0.5] fraction of 1; Hemoglobin: 83 [137 - 168] g/L; Leukocytes: 4 [3.3 - 8.6] 10^9/L; Lymphocytes/Leukocytes: 5 [16.5 - 49.5] %; Monocytes/Leukocytes: 2 [2 - 10] %; NPTST003-?-D GLUCAN: 266.2 [0 - 11] mg/L; NPTST004-?-GTP: 82 [13 - 64] U/L; NPTST024-AT?: 88 [83 - 118] %; NPTST083-FBG: 657 [200 - 400] mg/dL; NPTST084-FDP: 70.1 [0 - 5] UNIT NOT REPORTED; NPTST198-TAT: 41.17 [0 - 3] ng/mL; Neutrophils Band Form/Leukocytes: 11 [0.5 - 6.5] %; Neutrophils/Leukocytes: 81 [38 - 74] %; Platelets: 43 [158 - 348] 10^9/L; Platelets: 43 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 638): Aspartate Aminotransferase: 50 [13 - 30] U/L; Blood Urea Nitrogen: 20.56;

Microbiology

[redacted]20[redacted] (RX DAY 633): BLOOD NPTST029-BLOOD CULTURE: NEGATIVE; OTHER RESECTED LUNG TISSUE NPTST104-GROCOTT STAIN: POSITIVE-PNEUMOCYSTIS JIROVECII CYST; OTHER SUCTION SPUTUM NPTST193-SPUTUM CULTURE: POSITIVE-METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS GRAM-NEGATIVE RODS; [redacted]20[redacted] (RX DAY 642): BLOOD

NPTST030-BLOOD CULTURES: NEGATIVE; [redacted]20[redacted] (RX DAY 650): OTHER ENDOTRACHEAL TUBE NPTST193-SPUTUM CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 633): CHEST X-RAY: RIGHT PNEUMOTHORAX,INTERSTITIAL PNEUMONIA LUNG CYST; PLAIN CT: GROUND-GLASS OPACITY; THORACOSCOPIC PNEUMONECTOMY (LUNG CYST SURGERY): DRAINAGE; VITAL SIGNS: BLOOD PRESSURE 160/99, SPO2 60%; [redacted]20[redacted] (RX DAY 636): THORACOSCOPIC LUNG SURGERY: DRAINAGE; [redacted]20[redacted] (RX DAY 637): CHEST IMAGE(CHEST CT): SUBCUTANEOUS EMPHYSEMA INCREASES; STEROID PULSE THERAPY WAS PERFORMED: ONGOING; [redacted]20[redacted] (RX DAY 638): HEMATOLOGY CONSULTATION: PLATELET TRANSFUSION TO THROMBOCYTOPENIA. ADMINISTRATION OF IMMUNOGLOBULIN PREPARATIONS FOR SEVERE INFECTIONS.; ST COMBINATION WAS STARTED CONSIDERING PNEUMOCYSTIS PNEUMONIA.: ONGOING; [redacted]20[redacted] (RX DAY 639): IMMUNOGLOBULIN ADMINISTRATION START: ONGOING; PLATELET TRANSFUSIONS: NOT IMPROVE.; [redacted]20[redacted] (RX DAY 642): VV?VENO VENOUS?-ECMO?EXTRACORPOREAL MEMBRANE OXYGENATION?: ARTIFICIAL RESPIRATION MANAGEMENT; BRAIN CT: CEREBRAL INFARCTION?LEFT POSTERIOR CEREBRAL ARTERY AREA); [redacted]20[redacted] (RX DAY 648): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 650): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 651): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 652): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); TRACHEOSTOMY: ARTIFICIAL RESPIRATION MANAGEMENT; [redacted]20[redacted] (RX DAY 654): LEFT THORACIC DRAINAGE: LEFT PNEUMOTHORAX; [redacted]20[redacted] (RX DAY 662): AUTOPSY IMAGING.: NO NEW FINDINGS WERE OBTAINED.

AE Stopped Rx Day	662 (30 DAYS AFTER LAST TREATMENT)
Duration of AE	30 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	A CYST ON THE SURFACE OF THE LUNGS (PRIMARY SIDE) = PRIMARY SPONTANEOUS PNEUMOTHORAX IN WHICH BRA BREV RUPTURES.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, LIFE THREATENING

Event #4: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Death

Event Description	PANCYTOPENIA
Preferred term	汎血球減少症
AE Onset Date / Rx Day	[redacted]20[redacted] / 637 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 633): Alanine Aminotransferase: 67 [10 - 42] U/L; Aspartate Aminotransferase: 118 [13 - 30] U/L; Blood Urea Nitrogen: 23.74 [2.86 - 7.14] mmol/L; Creatinine: 211.28 [57.46 - 94.59] umol/L; Erythrocytes: 1.8 [4.4 - 5.6] 10^12/L; Hemoglobin: 76 [137 - 468] g/L; Leukocytes: 2.4 [3.3 - 8.6] 10^9/L; NPTST110-HIV-AB: NEGATIVE [NOT REPORTED - 1] UNIT NOT REPORTED; Platelets: 116 [158 - 348] 10^9/L; Potassium: 5.7 [3.6 - 4.8] mmol/L; [redacted]20[redacted] (RX DAY 634): Erythrocytes: 1.7 [4.4 - 5.6] 10^12/L; Hemoglobin: 71 [137 - 168] g/L; Leukocytes: 3.4 [3.3 - 8.6] 10^9/L; Platelets: 103 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 636): NPTST124-KL-6: 880 [105 - 435] U/mL; [redacted]20[redacted] (RX DAY 637): Alanine Aminotransferase: 31 [10 - 42] U/L; Aspartate Aminotransferase: 67 [13 - 30] U/L; Erythrocytes: 2.2 [4.4 - 5.6] 10^12/L; Hematocrit: 0.23 [0.41 - 0.5] fraction of 1; Hemoglobin: 83 [137 - 168] g/L; Leukocytes: 4 [3.3 - 8.6]

10^9/L; Lymphocytes/Leukocytes: 5 [16.5 - 49.5] %; Monocytes/Leukocytes: 2 [2 - 10] %; NPTST003-?-D GLUCAN: 266.2 [0 - 11] mg/L; NPTST004-?-GTP: 82 [13 - 64] U/L; NPTST024-AT?: 88 [83 - 118] %; NPTST083-FBG: 657 [200 - 400] mg/dL; NPTST084-FDP: 70.1 [0 - 5] UNIT NOT REPORTED; NPTST198-TAT: 41.17 [0 - 3] ng/mL; Neutrophils Band Form/Leukocytes: 11 [0.5 - 6.5] %; Neutrophils/Leukocytes: 81 [38 - 74] %; Platelets: 43 [158 - 348] 10^9/L; Platelets: 43 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 638): Aspartate Aminotransferase: 50 [13 - 30] U/L; Blood Urea Nitrogen: 20.56;

Microbiology

[redacted]20[redacted] (RX DAY 633): BLOOD NPTST029-BLOOD CULTURE: NEGATIVE; OTHER RESECTED LUNG TISSUE NPTST104-GROCOTT STAIN: POSITIVE-PNEUMOCYSTIS JIROVECII CYST; OTHER SUCTION SPUTUM NPTST193-SPUTUM CULTURE: POSITIVE-METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS GRAM-NEGATIVE RODS; [redacted]20[redacted] (RX DAY 642): BLOOD NPTST030-BLOOD CULTURES: NEGATIVE; [redacted]20[redacted] (RX DAY 650): OTHER ENDOTRACHEAL TUBE NPTST193-SPUTUM CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 633): CHEST X-RAY: RIGHT PNEUMOTHORAX,INTERSTITIAL PNEUMONIA LUNG CYST; PLAIN CT: GROUND-GLASS OPACITY; THORACOSCOPIC PNEUMONECTOMY (LUNG CYST SURGERY): DRAINAGE; VITAL SIGNS: BLOOD PRESSURE 160/99, SPO2 60%; [redacted]20[redacted] (RX DAY 636): THORACOSCOPIC LUNG SURGERY: DRAINAGE; [redacted]20[redacted] (RX DAY 637): CHEST IMAGE(CHEST CT): SUBCUTANEOUS EMPHYSEMA INCREASES; STEROID PULSE THERAPY WAS PERFORMED: ONGOING; [redacted]20[redacted] (RX DAY 638): HEMATOLOGY CONSULTATION: PLATELET TRANSFUSION TO THROMBOCYTOPENIA. ADMINISTRATION OF IMMUNOGLOBULIN PREPARATIONS FOR SEVERE INFECTIONS.; ST COMBINATION WAS STARTED CONSIDERING PNEUMOCYSTIS PNEUMONIA.: ONGOING; [redacted]20[redacted] (RX DAY 639): IMMUNOGLOBULIN ADMINISTRATION START: ONGOING; PLATELET TRANSFUSIONS: NOT IMPROVE.; [redacted]20[redacted] (RX DAY 642): VV?VENO VENOUS?-ECMO?EXTRACORPOREAL MEMBRANE OXYGENATION?: ARTIFICIAL RESPIRATION MANAGEMENT; BRAIN CT: CEREBRAL INFARCTION?LEFT POSTERIOR CEREBRAL ARTERY AREA); [redacted]20[redacted] (RX DAY 648): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 650): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 651): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 652): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); TRACHEOSTOMY: ARTIFICIAL RESPIRATION MANAGEMENT; [redacted]20[redacted] (RX DAY 654): LEFT THORACIC DRAINAGE: LEFT PNEUMOTHORAX; [redacted]20[redacted] (RX DAY 662): AUTOPSY IMAGING.: NO NEW FINDINGS WERE OBTAINED.

AE Stopped Rx Day	662 (30 DAYS AFTER LAST TREATMENT)
Duration of AE	26 DAYS
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, RESULTS IN DEATH

Event #5: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	PNEUMOCYSTIS PNEUMONIA
Preferred term	ニューモシスチス・イロベチイ肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 637 (5 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 633): Alanine Aminotransferase: 67 [10 - 42] U/L; Aspartate Aminotransferase: 118 [13 - 30] U/L; Blood Urea Nitrogen: 23.74 [2.86 - 7.14] mmol/L; Creatinine: 211.28 [57.46 - 94.59] umol/L; Erythrocytes: 1.8 [4.4 - 5.6] 10^12/L; Hemoglobin: 76 [137 - 468] g/L; Leukocytes: 2.4 [3.3 - 8.6] 10^9/L; NPTST110-HIV-AB: NEGATIVE [NOT REPORTED - 1] UNIT NOT REPORTED; Platelets: 116 [158 - 348] 10^9/L; Potassium: 5.7 [3.6 - 4.8] mmol/L; [redacted]20[redacted] (RX DAY 634): Erythrocytes: 1.7 [4.4 - 5.6] 10^12/L; Hemoglobin: 71 [137 - 168] g/L; Leukocytes: 3.4 [3.3 - 8.6] 10^9/L; Platelets: 103 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 636): NPTST124-KL-6: 880 [105 - 435] U/mL; [redacted]20[redacted] (RX DAY 637): Alanine Aminotransferase: 31 [10 - 42] U/L; Aspartate Aminotransferase: 67 [13 - 30] U/L; Erythrocytes: 2.2 [4.4 - 5.6] 10^12/L; Hematocrit: 0.23 [0.41 - 0.5] fraction of 1; Hemoglobin: 83 [137 - 168] g/L; Leukocytes: 4 [3.3 - 8.6] 10^9/L; Lymphocytes/Leukocytes: 5 [16.5 - 49.5] %; Monocytes/Leukocytes: 2 [2 - 10] %; NPTST003-?-D GLUCAN: 266.2 [0 - 11] mg/L; NPTST004-?-GTP: 82 [13 - 64] U/L; NPTST024-AT?: 88 [83 - 118] %; NPTST083-FBG: 657 [200 - 400] mg/dL; NPTST084-FDP: 70.1 [0 - 5] UNIT NOT REPORTED; NPTST198-TAT: 41.17 [0 - 3] ng/mL; Neutrophils Band Form/Leukocytes: 11 [0.5 - 6.5] %; Neutrophils/Leukocytes: 81 [38 - 74] %; Platelets: 43 [158 - 348] 10^9/L; Platelets: 43 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 638): Aspartate Aminotransferase: 50 [13 - 30] U/L; Blood Urea Nitrogen: 20.56;

Microbiology

[redacted]20[redacted] (RX DAY 633): BLOOD NPTST029-BLOOD CULTURE: NEGATIVE; OTHER RESECTED LUNG TISSUE NPTST104-GROCOTT STAIN: POSITIVE-PNEUMOCYSTIS JIROVECII CYST; OTHER SUCTION SPUTUM NPTST193-SPUTUM CULTURE: POSITIVE-METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS GRAM-NEGATIVE RODS; [redacted]20[redacted] (RX DAY 642): BLOOD NPTST030-BLOOD CULTURES: NEGATIVE; [redacted]20[redacted] (RX DAY 650): OTHER ENDOTRACHEAL TUBE NPTST193-SPUTUM CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 633): CHEST X-RAY: RIGHT PNEUMOTHORAX,INTERSTITIAL PNEUMONIA LUNG CYST; PLAIN CT: GROUND-GLASS OPACITY; THORACOSCOPIC PNEUMONECTOMY (LUNG CYST SURGERY): DRAINAGE; VITAL SIGNS: BLOOD PRESSURE 160/99, SPO2 60%; [redacted]20[redacted] (RX DAY 636): THORACOSCOPIC LUNG SURGERY: DRAINAGE; [redacted]20[redacted] (RX DAY 637): CHEST IMAGE(CHEST CT): SUBCUTANEOUS EMPHYSEMA INCREASES; STEROID PULSE THERAPY WAS PERFORMED: ONGOING; [redacted]20[redacted] (RX DAY 638): HEMATOLOGY CONSULTATION: PLATELET TRANSFUSION TO THROMBOCYTOPENIA. ADMINISTRATION OF IMMUNOGLOBULIN PREPARATIONS FOR SEVERE INFECTIONS.; ST COMBINATION WAS STARTED CONSIDERING PNEUMOCYSTIS PNEUMONIA.: ONGOING; [redacted]20[redacted] (RX DAY 639): IMMUNOGLOBULIN ADMINISTRATION START: ONGOING; PLATELET TRANSFUSIONS: NOT IMPROVE.; [redacted]20[redacted] (RX DAY 642): VV?VENO VENOUS?-ECMO?EXTRACORPOREAL MEMBRANE OXYGENATION?: ARTIFICIAL RESPIRATION MANAGEMENT; BRAIN CT: CEREBRAL INFARCTION?LEFT POSTERIOR CEREBRAL ARTERY AREA); [redacted]20[redacted] (RX DAY 648): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 650): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 651): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 652): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); TRACHEOSTOMY: ARTIFICIAL RESPIRATION MANAGEMENT; [redacted]20[redacted] (RX DAY 654): LEFT THORACIC DRAINAGE: LEFT PNEUMOTHORAX; [redacted]20[redacted] (RX DAY 662): AUTOPSY IMAGING.: NO NEW FINDINGS WERE OBTAINED.

AE Stopped Rx Day	662 (30 DAYS AFTER LAST TREATMENT)
Duration of AE	26 DAYS
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, LIFE THREATENING

Event #6: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	CYTOMEGALOVIRUS INFECTION
Preferred term	サイトメガロウイルス感染
AE Onset Date / Rx Day	[redacted]20[redacted] / 640 (8 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	662 (30 DAYS AFTER LAST TREATMENT)
Duration of AE	23 DAYS
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

Event #8: Serious Adverse Event

Event Description	DUODENAL ULCER
Preferred term	十二指腸潰瘍
AE Onset Date / Rx Day	[redacted]20[redacted] / 648 (16 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 633): Alanine Aminotransferase: 67 [10 - 42] U/L; Aspartate Aminotransferase: 118 [13 - 30] U/L; Blood Urea Nitrogen: 23.74 [2.86 - 7.14] mmol/L; Creatinine: 211.28 [57.46 - 94.59] umol/L; Erythrocytes: 1.8 [4.4 - 5.6] 10^12/L; Hemoglobin: 76 [137 - 468] g/L; Leukocytes: 2.4 [3.3 - 8.6] 10^9/L; NPTST110-HIV-AB: NEGATIVE [NOT REPORTED - 1] UNIT NOT REPORTED; Platelets: 116 [158 - 348] 10^9/L; Potassium: 5.7 [3.6 - 4.8] mmol/L; [redacted]20[redacted] (RX DAY 634): Erythrocytes: 1.7 [4.4 - 5.6] 10^12/L; Hemoglobin: 71 [137 - 168] g/L; Leukocytes: 3.4 [3.3 - 8.6] 10^9/L; Platelets: 103 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 636): NPTST124-KL-6: 880 [105 - 435] U/mL; [redacted]20[redacted] (RX DAY 637): Alanine Aminotransferase: 31 [10 - 42] U/L; Aspartate Aminotransferase: 67 [13 - 30] U/L; Erythrocytes: 2.2 [4.4 - 5.6]

10^12/L; Hematocrit: 0.23 [0.41 - 0.5] fraction of 1; Hemoglobin: 83 [137 - 168] g/L; Leukocytes: 4 [3.3 - 8.6] 10^9/L; Lymphocytes/Leukocytes: 5 [16.5 - 49.5] %; Monocytes/Leukocytes: 2 [2 - 10] %; NPTST003-?-D GLUCAN: 266.2 [0 - 11] mg/L; NPTST004-?-GTP: 82 [13 - 64] U/L; NPTST024-AT?: 88 [83 - 118] %; NPTST083-FBG: 657 [200 - 400] mg/dL; NPTST084-FDP: 70.1 [0 - 5] UNIT NOT REPORTED; NPTST198-TAT: 41.17 [0 - 3] ng/mL; Neutrophils Band Form/Leukocytes: 11 [0.5 - 6.5] %; Neutrophils/Leukocytes: 81 [38 - 74] %; Platelets: 43 [158 - 348] 10^9/L; Platelets: 43 [158 - 348] 10^9/L; [redacted]20[redacted] (RX DAY 638): Aspartate Aminotransferase: 50 [13 - 30] U/L; Blood Urea Nitrogen: 20.56;

Microbiology

[redacted]20[redacted] (RX DAY 633): BLOOD NPTST029-BLOOD CULTURE: NEGATIVE; OTHER RESECTED LUNG TISSUE NPTST104-GROCOTT STAIN: POSITIVE-PNEUMOCYSTIS JIROVECII CYST; OTHER SUCTION SPUTUM NPTST193-SPUTUM CULTURE: POSITIVE-METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS GRAM-NEGATIVE RODS; [redacted]20[redacted] (RX DAY 642): BLOOD NPTST030-BLOOD CULTURES: NEGATIVE; [redacted]20[redacted] (RX DAY 650): OTHER ENDOTRACHEAL TUBE NPTST193-SPUTUM CULTURE: POSITIVE-STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 633): CHEST X-RAY: RIGHT PNEUMOTHORAX,INTERSTITIAL PNEUMONIA LUNG CYST; PLAIN CT: GROUND-GLASS OPACITY; THORACOSCOPIC PNEUMONECTOMY (LUNG CYST SURGERY): DRAINAGE; VITAL SIGNS: BLOOD PRESSURE 160/99, SPO2 60%; [redacted]20[redacted] (RX DAY 636): THORACOSCOPIC LUNG SURGERY: DRAINAGE; [redacted]20[redacted] (RX DAY 637): CHEST IMAGE(CHEST CT): SUBCUTANEOUS EMPHYSEMA INCREASES; STEROID PULSE THERAPY WAS PERFORMED: ONGOING; [redacted]20[redacted] (RX DAY 638): HEMATOLOGY CONSULTATION: PLATELET TRANSFUSION TO THROMBOCYTOPENIA. ADMINISTRATION OF IMMUNOGLOBULIN PREPARATIONS FOR SEVERE INFECTIONS.; ST COMBINATION WAS STARTED CONSIDERING PNEUMOCYSTIS PNEUMONIA.: ONGOING; [redacted]20[redacted] (RX DAY 639): IMMUNOGLOBULIN ADMINISTRATION START: ONGOING; PLATELET TRANSFUSIONS: NOT IMPROVE.; [redacted]20[redacted] (RX DAY 642): VV?VENO VENOUS?-ECMO?EXTRACORPOREAL MEMBRANE OXYGENATION?: ARTIFICIAL RESPIRATION MANAGEMENT; BRAIN CT: CEREBRAL INFARCTION?LEFT POSTERIOR CEREBRAL ARTERY AREA); [redacted]20[redacted] (RX DAY 648): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 650): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 651): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); [redacted]20[redacted] (RX DAY 652): GASTROLNTESTINAL FIBERSCOPE: DUODENAL ULCER (MULTIPLE); TRACHEOSTOMY: ARTIFICIAL RESPIRATION MANAGEMENT; [redacted]20[redacted] (RX DAY 654): LEFT THORACIC DRAINAGE: LEFT PNEUMOTHORAX; [redacted]20[redacted] (RX DAY 662): AUTOPSY IMAGING.: NO NEW FINDINGS WERE OBTAINED.

AE Stopped Rx Day	662 (30 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
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, LIFE THREATENING

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

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，致死的な汎血球減少症，ニューモシスチス肺炎，間質性肺炎，右気胸，サイトメガロウイルス感染及び十二指腸潰瘍の事象を発現した。

Event 1～5 及び 7 の臨床経過：

関連する病歴は乾癬性関節炎，胃食道逆流性疾患，心身症，アルコール性肝疾患，浮腫，高血圧，局面型乾癬，現紙巻タバコ喫煙者（1 日 1 箱を 32 年間）及び元飲酒者（1 日 2～4 杯）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は間質性肺炎及び右気胸を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は汎血球減少症及びニューモシスチス肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はサイトメガロウイルス感染を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は十二指腸潰瘍を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。死因は汎血球減少症と報告された。剖検が実施された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は高血圧のため内科医を受診した。被験者は体調が悪そうであり，顔面蒼白及び労作時呼吸困難を伴っていた。また，血圧が高値で，酸素飽和度が低値であった。胸部 X 線検査が行われ，右気胸が認められた。内科医は治療として右第 1 肋間穿刺による脱気を行った。脱気後，被験者は救急サービスを介して病院に搬送され，同日入院した。

入院後，HIV 検査が行われ，結果は陰性であった。右気胸に変化は見られず，肺瘻が認められた。肺瘻はコントロール不能であった。その後，分離肺換気が行われた。換気により右気胸の回復が認められたが，気漏は持続していた。肺瘻閉鎖術が緊急に行われた。その後，CT 検査が行われ，すりガラス陰影が認められたことから間質性肺炎が明らかとなった。また，肺嚢胞（X 線画像で発覚）に対する緊急胸腔鏡下肺全摘除と，継続的な胸腔ドレナージが行われた。

20[redacted] 年 [redacted] 月 [redacted] 日，再度，胸腔鏡下肺手術とドレナージが行われた。ドレーン挿入に起因すると思われる右肺損傷に対する肺縫縮術が行われた。肺縫縮術後，外科医は人工呼吸器のウィーニングを試みたが，酸素飽和度が低下した。被験者は ICU に入院となり，そこでも換気補助が必要な状態であった。20[redacted] 年 [redacted] 月 [redacted] 日，間質性肺炎に対し，ステロイドパルス療法が行われ，

バクトラミンの静脈内投与が開始された。また，血液検査で KL-6 及び β-D-グルカンの増加が認められたことからニューモシスチス肺炎が疑われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は播種性血管内凝固（非重篤）を発現した。同日，血液専門医による診察が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，右肺切除部の検体から気腫性嚢胞及びニューモシスチス・イロベチイが検出された。右肺ドレナージ及び左肺機能低下のため，換気が継続された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，ニューモシスチス肺炎による持続的な炎症反応を伴う ARDS を発症した。被験者は心肺バイパス装置に繋がれた。同日，脳 CT 検査により塞栓性が疑われる急性脳梗塞（非重篤）が明らかとなり，ヘパリンが投与された。20[redacted] 年 [redacted] 月 [redacted] 日，サイトメガロウイルス性抗原血症に対するデノシン静脈内投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，血便が認められ，消化管ファイバースコープ（GIF）で十二指腸潰瘍が見つかった。出血点のクリッピングにより止血が達成されたが，別の部位で新たな出血が起こった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左気胸を発症し，左胸腔ドレナージが行われた。両肺に持続的な気漏が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，Bactrim（スルファメトキサゾール・トリメトプリム合剤）及びデノシンに起因する汎血球減少症より，骨髄抑制が示唆された。これらの 2 剤は中止された。また，連日にわたって血小板輸血が行われた。血小板輸血にもかかわらず，血小板数は 80,000/mL を上回ることはなかった。20[redacted] 年 [redacted] 月 [redacted] 日，この被験者に対する治療は限界と判断されたため，血小板輸血は家族の同意の下に中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は死亡した。実施された剖検は画像診断のみであった。

入院前に CMV の血清学的検査は行われなかった。さらに，被験者が症状を呈していなかったため，入院前及び入院中に EBV 及びパルボウイルス B19 の血清学的検査も行われなかった。

医療記録によると，20[redacted] 年 [redacted] 月に，CMV の再検査が行われ，結果は陽性であった。20[redacted] 年 [redacted] 月 [redacted] 日，メレナが認められ，ヘパリンが減量された。20[redacted] 年 [redacted] 月 [redacted] 日，GIF が行われ，十二指腸潰瘍が認められたため，露出血管をクリッピングした。20[redacted] 年 [redacted] 月 [redacted] 日，十二指腸潰瘍が再び出血し，再 GIF が行われ，緊急クリッピングが必要となった。20[redacted] 年 [redacted] 月 [redacted] 日，GIF が再度行われ，別の部位からの出血が認められたため，その出血部位をクリッピングした。同日，気管切開が行われた。

退院時サマリーによると，複数回の輸血が行われた。十二指腸潰瘍からの胃腸出血が複数回発生し，露出血管をクリッピングするために GIF が行われた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はメレ

ナを発現した。

投与された薬剤は，免疫グロブリン，酸素，bactrim（スルファメトキサゾール・トリメトプリム合剤），クエン酸第一鉄ナトリウム，バクトラミン，ダラシン-S，サムチレール，ソル・メルコート，グラン，フィブロガミン P，デノシン，濃厚血小板（10 単位），カンサイダス，ヘパリン，血液，DHPG，タケキャブ，レバミピド，アンヒバ，レミフェンタニル，アドナ，トランサミン，グロベニン I，プレドニン，クラビット，ファンガード，タケプロン，モルヒネ塩酸塩，スルバシリン，バンコマイシン，クエン酸第一鉄ナトリウム及びメロペネムであった。

The patient's past medications include:

BONALFA for PSORIASIS ([redacted])

DIFLAL for PSORIATIC ARTHROPATHY ([redacted])

METHADERM for PSORIATIC ARTHROPATHY ([redacted])

LOCOID for ARTHROPATHIC PSORIASIS ([redacted])

RISANKIZUMAB for PSORIATIC ARTHRITIS ([redacted])

RHEUMATREX for ARTHROPATHIC PSORIASIS ([redacted])

HIRUDOID for PSORIASIS ([redacted])

BUFFERIN COMBINATION for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Pancytopenia (10033661) (Pancytopenia (10033661)) [v.22.0] [10033661]

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

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

Dechallenge: Not Applicable

2) Pneumocystis pneumonia (10035661) (Pneumocystis jirovecii pneumonia (10073755)) [v.22.0] [10035661]

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

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

Dechallenge: Not Applicable

3) Interstitial pneumonia (10022617) (Interstitial lung disease (10022611)) [v.22.0] [10022617]

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

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

Dechallenge: Unknown

4) Pneumothorax (10035759) (Pneumothorax (10035759)) [v.22.0] [10035759]

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

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

Dechallenge: Unknown

5) Cytomegalovirus infection (10011831) (Cytomegalovirus infection (10011831)) [v.22.0] [10011831]

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

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

Dechallenge: Not Applicable

6) Duodenal ulcer (10013836) (Duodenal ulcer (10013836)) [v.22.0] [10013836]

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 PANCYTOPENIA

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing alcoholic liver disease and underlying systemic inflammatory disease.

Event of PNEUMOCYSTIS PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Event of INTERSTITIAL PNEUMONIA

- Investigator: Not applicable

- AbbVie: Event is more likely related to current, extensive smoking history of one pack a day for 32 years.

Event of RIGHT PNEUMOTHORAX

- Investigator: A cyst on the surface of the lungs (primary side) = primary spontaneous pneumothorax in which Bra Brev ruptures.

- AbbVie: Risk factors include concurrent interstitial pneumonia and current cigarette smoker (1 PPD for 32 years).

Event of CYTOMEGALOVIRUS INFECTION

- Investigator: Not Applicable

- AbbVie: risk factors include recent hospitalization, recent surgeries, and recent use of steroid pulse therapy.

Event of DUODENAL ULCER

- Investigator: Not applicable.

- AbbVie: Risk factors include concomitant heparin treatment, disseminated intravascular coagulation, acute critical illness, and current, extensive smoking history of one pack per day for 32 years.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ALANINE AMINO TRANSFERASE:** 67 U/L (normal 10 to 42)

[redacted] 20[redacted] **ANTI-HEP B SURFACE AG2 QUAL:** negative

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 118 U/L (normal 13 to 30)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 50 U/L (normal 13 to 30)

[redacted] 20[redacted] **B-D GLUCAN:** 266.2 PG/ML (normal 0 to 11.0)

[redacted] 20[redacted] **BANDS %:** 11 % (normal 0.5 to 6.5)

[redacted] 20[redacted] **BANDS %:** 1.0 % (normal 0.5 to 6.5)

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

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

[redacted] 20[redacted] **BLOOD PRESSURE:** 160/90 mmHg

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 66.5 mg/dL (normal 8 to 20.0)

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 57.6 mg/dL (normal 8 to 20.0)

[redacted] 20[redacted] **BRAIN CT:** Low density area is well-defined from Left occipital lobe to mesial temporal lobe and left posterior limb of internal capsule. Diagnosed as cerebral infraction at the sub acute stage or the later stage. There is no detectable bleeding. Cerebral infarction (left posterior cerebral artery area)

[redacted] 20[redacted] **CHEST CT:** Subcutaneous emphysema increases.

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

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

[redacted] 20[redacted] **CHEST X-RAY:** Right pneumothorax, interstitial pneumonia

[redacted] 20[redacted] **CREATININE (BLOOD):** 2.39 mg/dL (normal 0.65 to 1.07)

[redacted] 20[redacted] **CREATININE (BLOOD):** 2.37 mg/dL (normal 0.65 to 1.07)

[redacted] 20[redacted] **CRP:** 31.59 mg/dL (normal 0.0 to 0.14)

[redacted] 20[redacted] **CT:** Ground-glass opacity.

[redacted] 20[redacted] **CYTOMEGALOVIRUS ANTIGENEMIA:** 8 NA (normal 0 to 0)

[redacted] 20[redacted] **CYTOMEGALOVIRUS TEST:** 6 NA (normal 0 to 0)

[redacted] 20[redacted] **EOSINOPHILS %:** 7.0 % (normal 0.0 to 8.5)

[redacted] 20[redacted] **ERYTHROBLAST:** 7.0 % (normal 0 to 0)

[redacted] **20[redacted] Gastrointestinal Fiberscope:** Duodenal ulcer (multiple): A1 stage was observed, visible vessels were clipped.

[redacted] **20[redacted] Gastrointestinal Fiberscope:** Duodenal ulcer (multiple).

[redacted] **20[redacted] Gastrointestinal Fiberscope:** Duodenal ulcer (multiple). Bleeding started again and was clipped

[redacted] **20[redacted] Gastrointestinal Fiberscope:** Duodenal ulcer (multiple).The bleeding was detected from the different part and the bleeding part was clipped.

[redacted] **20[redacted] HEMOGLOBIN:** 7.6 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] HEMOGLOBIN:** 7.1 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] HEMOGLOBIN:** 8.2 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] HEMOGLOBIN:** 7.6 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] HEP B SURFACE AG:** negative

[redacted] **20[redacted] HEPATITIS B CORE TOTAL:** negative

[redacted] **20[redacted] HEPATITIS C VIRUS ANTIBODY-QT:** negative

[redacted] **20[redacted] HGB:** 9.6 G/DL (normal 12.7 to 18.1)

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

[redacted] **20[redacted] KL-6:** 880 U/ML (normal 105 to 435)

[redacted] **20[redacted]LUNG PATHOLOGY:** THORACOSCOPIC PNEUMONECTOMY: Bulla and Pneumocystis jirovecii cyst were found from the right-lung resected specimen.

[redacted] **20[redacted] LYMPHOCYTES %:** 5.0 % (normal 16.5 to 49.5)

[redacted] **20[redacted] LYMPHOCYTES %:** 26.0 % (normal 16.5 to 49.5)

[redacted] **20[redacted] LYMPHOCYTES %:** 1.0 % (normal 16.5 to 49.5)

[redacted] **20[redacted] MONOCYTE %:** 7.0 % (normal 2.0 to 10.0)

[redacted] **20[redacted] MONOCYTES %:** 2.0 % (normal 2.0 to 10.0)

[redacted] **20[redacted] NEUTORPHILS %:** 58.0 % (normal 38.0 to 74.0)

[redacted] **20[redacted] NEUTROPHILS %:** 81.0 % (normal 38.0 to 74.0)

[redacted] **20[redacted] PLATELET COUNT:** 116 X10**3/MCL (normal 158 to 348)

[redacted] **20[redacted] PLATELET COUNT:** 103 X10**3/MCL (normal 158 to 348)

[redacted] **20[redacted] PLATELET COUNT:** 30 X10**3/MCL (normal 158 to 348)

[redacted] **20[redacted] PLATELET COUNT:** 21 X10**3/MCL (normal 158 to 348)

[redacted] **20[redacted] PLATELET COUNT:** 91 X10**3/MCL (normal 158 to 348)

[redacted] **20[redacted] PLATELET COUNT:** 5 X10**3/MCL (normal 158 to 348)

[redacted] **20[redacted] POTASSIUM:** 5.7 MMOL/L (normal 3.6 to 4.8)

[redacted] **20[redacted] RBC MORPH:** Anisocytosis Polychromatophilia

[redacted] **20[redacted] RED BLOOD CELLS:** 1.81 X10**6/MCL (normal 4.35 to 5.55)

[redacted] **20[redacted] RED BLOOD CELLS:** 2.25 X10**6/MCL (normal 4.35 to 5.55)

[redacted] **20[redacted] RED BLOOD CELLS:** 2.49 X10**6/MCL (normal 4.35 to 5.55)

[redacted] **20[redacted] SPO2:** 60 %

[redacted] **20[redacted] SPUTUM CULTURE:** Suction: Positive - Methicillin-susceptible Staphylococcus aureus gram-negative Rods

[redacted] **20[redacted] SPUTUM CULTURE:** Endotracheal tube: Positive - Staphylococcus aureus

[redacted] **20[redacted] WHITE BLOOD CELL COUNT:** 2.36 X10**3/MCL (normal 3.80 to 10.70)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 2.35 X10**3/MCL (normal 3.30 to 8.60)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3.43 X10**3/MCL (normal 3.30 to 8.60)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 6.46 X10**3/MCL (normal 3.30 to 8.60)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 0.73 X10**3/MCL (normal 3.30 to 8.60)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 0.55 X10**3/MCL (normal 3.30 to 8.60)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 0.28 X10**3/MCL (normal 3.30 to 8.60)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
ABT-494 30 mg QD	4[redacted]	MALE	ASIAN

Medical History	Onset Year
HYPERTENSION	19[redacted]
OTHER: PSORIASIS VULGARIS	20[redacted]
OTHER: INFECTIOUS ATHEROMA	20[redacted]
OTHER: HEMATURIA	20[redacted]
OTHER: OBESITY	20[redacted]
OTHER: BASEMENT MEMBRANE THINNING DISEASE, KIDNEY	20[redacted]
OTHER: LOWER LIMB EDEMA	20[redacted]
OTHER: LUMBER SPINAL STENOSIS-L4	20[redacted]
OTHER: OBESITY-RELATED NEPHROPATHY	20[redacted]
OTHER: PSORIATIC SPONDYLITIS	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	26	
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	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 35	35

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	QD	Y-M: 20[redacted]
METHOTREXATE	6 mg	EVERY WEEK	Y-M: 20[redacted]
CLOBETASOL	NA OTHER: NA	BID	Y-M: 20[redacted]
TACALCITOL	NA OTHER: NA	BID	Y-M: 20[redacted]
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted]
TILDRAKIZUMAB	200 mL	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
DIFLUPREDNATE	NA OTHER: NA	QD	Y-M: 20[redacted]
BETAMETHASONE	NA OTHER: NA	BID	Y-M: 20[redacted]
DIFLUPREDNATE	NA OTHER: NA	BID	Y-M: 20[redacted]
INFLIXIMAB	100 mL	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
OLMESARTAN	30 mg	QD	Y-M: 20[redacted]
PREGABALIN	50 mg	BID	Y-M: 20[redacted] / -308
SODIUM CHLORIDE	250 mL	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted] / -76

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 38
METHOTREXATE	6 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 38
OLMESARTAN	30 mg	QD	Y-M: 20[redacted]	ONGOING
HYOSCINE	10 mg	PRN	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 31
LAC-B GRANULAR POWDER N	1 g	TID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 31
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 31
METOCLOPRAMIDE	5 mg	TID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 31
PARACETAMOL	200 mg	PRN	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 31
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 31
SOLITA-T1	500 mL	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 29
FOSFOMYCIN	500 mg	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 41
ELECTROLYTES NOS	500 mL	PRN	Y-M: 20[redacted] /	Y-M: 20[redacted] / 41

LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted]-[redacted] 31 / Y-M: 20[redacted]-[redacted] / 41
SODIUM BICARBONATE	500 mL	PRN	Y-M: 20[redacted]-[redacted] 31 / Y-M: 20[redacted]-[redacted] / 41
VITAMEDIN	1 OTHER: VIAL	PRN	Y-M: 20[redacted]-[redacted] 31 / Y-M: 20[redacted]-[redacted] / 41
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted]-[redacted] 31 / Y-M: 20[redacted]-[redacted] / 45
OMEPRAZOLE	20 mg	PRN	Y-M: 20[redacted]-[redacted] 31 / Y-M: 20[redacted]-[redacted] / 41
PARACETAMOL	400 mg	TID	Y-M: 20[redacted]-[redacted] 34 / Y-M: 20[redacted]-[redacted] / 41
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted]-[redacted] 37 / Y-M: 20[redacted]-[redacted] / 41
GANCICLOVIR	500 mg	BID	Y-M: 20[redacted]-[redacted] 38 / Y-M: 20[redacted]-[redacted] / 56
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted]-[redacted] 43 / Y-M: 20[redacted]-[redacted] / 92
NUTRIENTS NOS	250 mL	QD	Y-M: 20[redacted]-[redacted] 45 / Y-M: 20[redacted]-[redacted] / 57
NUTRIENTS NOS	250 mL	QD	Y-M: 20[redacted]-[redacted] 56 / Y-M: 20[redacted]-[redacted] / 58
HYDROCORTISONE	NA OTHER: NA	BID	Y-M: 20[redacted]-[redacted] 56 / Y-M: 20[redacted]-[redacted] / 87
IRON	50 mg	QD	Y-M: 20[redacted]-[redacted] 58 / ONGOING
DAIVOBET	NA OTHER: NA	QD	Y-M: 20[redacted]-[redacted] 64 / Y-M: 20[redacted]-[redacted] / 87

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

Event Description SMALL INTESTINAL ULCER
Preferred term 小腸潰瘍
AE Onset Date / Rx Day [redacted]20[redacted] / 31
Age at AE Onset 4[redacted]
Laboratory Testing
[redacted]20[redacted] (RX DAY 35): Hemoglobin: 77 [137 - 168] g/L; [redacted]20[redacted] (RX DAY 42): Alanine Aminotransferase: 33 [10 - 20] U/L; Albumin: 24 [41 - 51] g/L; Aspartate Aminotransferase: 28 [13 - 30] U/L; Bilirubin: 17.1 [6.84 - 25.66] umol/L; Blood Urea Nitrogen: 12.07 [2.86 - 7.14] mmol/L; Creatinine: 93.71 [57.46 - 94.59] umol/L; Erythrocytes: 1.5 [4.4 - 5.6] 10^12/L; Hemoglobin: 44 [137 - 168] g/L; Leukocytes: 22.8 [3.3 - 8.6] 10^9/L; NPTST056-CRP: 3.93 [0 - 0.14] mg/dL; NPTST078-EGFR: 60.3 [60 - 120] mL/min/1.73m2; NPTST085-FE: 44 [40 - 188] ug/dL; NPTST086-FERRITIN: 194.4 [50 - 200] ng/mL; NPTST130-LDH: 152 [124 - 222] U/L; NPTST186-RETICULOCYTE: 10.7 [8 - 22] %; NPTST201-TIBC: 243 [253 - 365] ug/dL; NPTST204-TRANSFERRIN: 193 [199 - 318] mg/dL; NPTST213-UNSATURATED IRON BINDING CAPACI: 199 [111 - 255] ug/dL; Platelets: 382 [158 - 348] 10^9/L; Protein: 43 [66 - 81] g/L
Microbiology
NOT REPORTED
SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 42): CT?16.19.29.OCTOBER2018?ABDOMEN, PELVIS?: NO PERFORATION OF DIGESTIVE TRACT. [redacted]20[redacted].IMPROVEMENT TREND; GASTRO-INTESTINAL FIBERSCOPY (GIF) [redacted]20[redacted]: WITHOUT IMPROVING THE ULCER. [redacted]20[redacted]THE ULCER IS PARTIALLY SCARRED.; HISTOLOGICAL EXAMINATION FOR CMV SCRUTINY.: NEGATIVE

AE Stopped Rx Day	92 (57 DAYS AFTER LAST TREATMENT)
Duration of AE	62 DAYS
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, LIFE THREATENING

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は日本の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，小腸潰瘍の事象を発現した。

Event 1 の臨床経過：

関連する病歴は高血圧，尋常性乾癬，乾癬性関節炎，血尿，肥満，現紙巻タバコ喫煙者（1 日 1 箱を 26 年間）及び禁酒であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は小腸潰瘍を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，小腸潰瘍は消失した。

本事象発現前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は嘔吐及び腹痛を呈し，胃腸炎（非重篤）と診断された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は上腹部痛，貧血，白血球増加，低アルブミン血症，胃腸出血及びメレナで入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は他院に転院となり，CT 検査及び消化管ファイバースコープが行われた。ファイバースコープにより，十二指腸下行部から肛門側にかけて複数の穿孔性潰瘍が検出された。十二指腸下行部では筋層が露出しており，肛門にスコープを挿入することができなかった。デノシンの静脈内投与が行われた。被験者は 20[redacted] 年 [redacted] 月 [redacted] 日に食事を開始した。20[redacted] 年 [redacted] 月 [redacted] 日，消化管ファイバースコープが再度行われ，潰瘍の軽快と部

分的な瘢痕形成が認められた。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が完全に中止された。

投与された薬剤は，デノシン，ホスミシン，ビカーボン，ビタメジン，クラビット，アセリオ，オメプラゾール，カロナール，レバミピド及びソリタ-T であった。

Causality for UPADACITINIB (Blinded)

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1) Small intestine ulcer (10041133) (Small intestine ulcer (10041133)) [v.22.0] [10041133]

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 SMALL INTESTINAL ULCER

- Investigator: Not applicable

- AbbVie: Risk factors include current smoking status and concomitant therapy with Metolate.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 2.4 G/DL (normal 4.1 to 5.1)

[redacted] **20[redacted] BUN:** 33.8 mg/dL (normal 8 to 20)

[redacted] **20[redacted] CREATININE:** 1.06 mg/dL (normal 0.65 to 1.07)

[redacted] **20[redacted] CRP:** 3.93 mg/dL (normal 0 to 0.14)

[redacted] **20[redacted] ENDOSCOPY:** the Intestinal wall was very thin

[redacted] **20[redacted] FE:** 44 MCG/DL (normal 40 to 188)

[redacted] **20[redacted] FERRITIN:** 194.4 NG/ML (normal 50 to 200)

[redacted] **20[redacted] GASTRO-INTESTINAL FIBROSCOPY:** Multiple punched ulcers were detected from the descending portion of the duodenum to the anal side. The decending portion of duodenum have muscle layer exposure, the scope could not be inserted into anus.

[redacted] **20[redacted] GASTRO-INTESTINAL FIBROSCOPY:** improving ulcer, partial scarring

[redacted] **20[redacted] HB:** 7.7 G/DL

[redacted] **20[redacted] HB:** 4 G/DL

[redacted] **20[redacted] HEMOGLOBIN:** 7.7 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] HGB:** 4.4 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] RBC:** 1.45 X10**6/MCL (normal 4.35 to 5.55)

[redacted] **20[redacted] RETICULOCYTE:** 10.7 % (normal 8 to 22)

[redacted] **20[redacted] TIBC:** 243 MCG/DL (normal 253 to 365)

[redacted] **20[redacted] TOTAL PROTEIN:** 4.3 G/DL (normal 6.6 to 8.1)

[redacted] **20[redacted] TRANSFERRIN:** 193 mg/dL (normal 199 to 318)

[redacted] **20[redacted] UNSATURATED IRON BINDING CAPACITY:** 199 MCG/DL (normal 111 to 255)

[redacted] **20[redacted] WBC:** Over 20,000

[redacted] **20[redacted] WBC:** 22.78 X10**3/MCL (normal 3.30 to 8.60)

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

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 15 mg QD	4[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: PLAQUE PSORIASIS	NOT REPORTED
OTHER: GASTRIC ULCER	20[redacted]
PANCREATITIS: ACUTE PANCREATITIS	20[redacted]
OTHER: DIABETES MELLITUS	20[redacted]
TUBERCULOSIS: LATENT TUBERCULOSIS	20[redacted]
DIABETES MELLITUS: WORSENINNG OF DIABETES MELLITUS	20[redacted]
OTHER: RETINOPATHY	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.75 PACK	31.10	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	CURRENT	0.75 SESSIONS	0.40	
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 392	224
ABT-494	15MG	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]
INSULIN ASPART W/INSULIN DEGLUDEC	9-20 OTHER: UNITS	BID	Y-M: 20[redacted]
MIGLITOL	75 mg	TID	Y-M: 20[redacted]
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
LOXOPROFEN	60 mg	BID	Y-M: 20[redacted]
METHOTREXATE	6 mg	EVERY WEEK	Y-M: 20[redacted]
REBAMIPIDE	100 mg	BID	Y-M: 20[redacted]
ISONIAZID	100 mg	TID	Y-M: 20[redacted]
INFLIXIMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
SODIUM CHLORIDE	250 mL	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
SECUKINUMAB	300 mg	OTHER: ONCE A MONTH	Y-M: 20[redacted]
ADALIMUMAB	40 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
REBAMIPIDE	100 mg	BID	Y-M: 20[redacted] / -315
INSULIN ASPART	2-6 OTHER: UNITS	QD	Y-M: 20[redacted] / -238
METHOTREXATE	8 mg	EVERY WEEK	Y-M: 20[redacted] / -91

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
MIGLITOL	75 mg	TID	Y-M: 20[redacted]	Not reported.
INSULIN ASPART W/INSULIN DEGLUDEC	9-20 OTHER: UNITS	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 307
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]	Not reported.
LOXOPROFEN	60 mg	BID	Y-M: 20[redacted]	Not reported.
REBAMIPIDE	100 mg	BID	Y-M: 20[redacted] / -315	Y-M: 20[redacted] / 308
INSULIN ASPART	2-6 OTHER: UNITS	QD	Y-M: 20[redacted] / -238	Not reported.
METHOTREXATE	8 mg	EVERY WEEK	Y-M: 20[redacted] / -91	Not reported.
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 216	Not reported.
REBAMIPIDE	100 mg	QD	Y-M: 20[redacted] / 307	Not reported.
GLUCOSE	10 g	PRN	Y-M: 20[redacted] /	Y-M: 20[redacted] /

MIGLITOL	75 mg	TID	Y-M: 20[redacted]-[redacted] / 307	Y-M: 20[redacted]-[redacted] / 310
INSULIN DEGLUDEC	4 OTHER: UNIT	QD	Y-M: 20[redacted]-[redacted] / 307	Not reported.
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted]-[redacted] / 308	Y-M: 20[redacted]-[redacted] / 315
			Y-M: 20[redacted]-[redacted] / 318	Y-M: 20[redacted]-[redacted] / 321

Event #1: Serious Adverse Event

Event Description	WORSENING OF DIABETES MELLITUS
Preferred term	糖尿病
AE Onset Date / Rx Day	[redacted]20[redacted] / 281
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 281): Glucose: 16.93 [4.05 - 6.05] mmol/L; [redacted]20[redacted] (RX DAY 308): Glucose: 4.05 [4.05 - 6.05] mmol/L; [redacted]20[redacted] (RX DAY 365): Glucose: 19.7 [4.05 - 6.05] mmol/L; [redacted]20[redacted] (RX DAY 393): Glucose: 16.26 [4.05 - 6.05] mmol/L; [redacted]20[redacted] (RX DAY 442): Glucose: 10.1 [4.05 - 6.05] mmol/L; [redacted]20[redacted] (RX DAY 470): Glucose: 18.04 [4.05 - 6.05] mmol/L; [redacted]20[redacted] (RX DAY 477): Glucose: 19.59 [4.05 - 6.05] mmol/L; [redacted]20[redacted] (RX DAY 497): Glucose: 4.27 [4.05 - 6.05] mmol/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THERE IS NO CAUSAL RELATIONSHIP BECAUSE IT IS AGGRAVATED BY POOR CONTROL OF BLOOD GLUCOSE.
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: M15-554

治験責任医師からの報告。本被験者は日本の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，糖尿病の悪化の事象を発現した。

Event 1 の臨床経過：

関連する病歴は糖尿病，潜伏結核，乾癬性関節炎，元紙巻タバコ喫煙者（1 日 0.75 箱を 31.10 年間），糖尿病の悪化，血糖値コントロール目的の入院，局面型乾癬，現電子タバコ使用者（1 日 0.75 回を 0.40 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，被験者は糖尿病の悪化を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は血糖値コントロール不良のため入院した。随伴症状は頭痛及び高血糖症であった。インスリンの用量調節を行ったところ，血糖値がコントロールされた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。本事象発現前の使用薬剤や生活習慣の変更は報告されなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は再教育のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，血糖値は再び正常化し，教育は終了した。

投与された薬剤は，ミグリトール及びトレシーバであった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Diabetes mellitus aggravated (10012603) (Diabetes mellitus (10012601)) [v.22.1] [10012603]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF DIABETES MELLITUS

- Investigator: THERE IS NO CAUSAL RELATIONSHIP BECAUSE IT IS AGGRAVATED BY POOR CONTROL OF BLOOD GLUCOSE.

- AbbVie: Event is more likely related to pre-existing diabetes mellitus. Additionally, the subject was hospitalized prior to study drug administration for blood glucose control purposes ([redacted] 20[redacted]).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD GLUCOSE:** 305 mg/dL (normal 73 to 109)

[redacted] **20[redacted] BLOOD GLUCOSE:** 73 mg/dL (normal 73 to 109)

[redacted] **20[redacted] BLOOD GLUCOSE:** 77 mg/dL (normal 73 to 109)

[redacted] **20[redacted] GLUCOSE:** 355 mg/dL (normal 73 to 109)

[redacted] **20[redacted] GLUCOSE:** 293 mg/dL (normal 73 to 109)

[redacted] **20[redacted] GLUCOSE:** 353 mg/dL (normal 73 to 109)

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
顔面麻痺	X			
ウイルス性胃腸炎	X			X
喘息	X	X		

Treatment Group	Age at Study Start	Sex	Race
Placebo/ABT-494 30 mg QD	4[redacted]	FEMALE	ASIAN

Medical History	Onset Year
OTHER: PASORIASIS VULGARIS	19[redacted]
DEGENERATIVE DISC DISEASE: LUMBAGO HERNIA	19
ASTHMA: BRONCHIAL ASTHEMA	20
OTHER: GENETIAL ITCHING FEMALE	20
OTHER: CHRONIC URTICARIA	20
EYE DISEASE/DISORDER: BILATERAL MYOPIA	20
DIABETES MELLITUS	20
OBESITY	20
ANEMIA: IRON DEFICIENCY ANEMIA	20
OTHER: FATTY LIVER	20
OTHER: TOE AND NAIL TINEA	20
TUBERCULOSIS: LATENT TUBERCULOSIS	20
OTHER: CELLULITIS	20
OTHER: FURUNCULOSIS	20
OTHER: BACTERIAL GASTROENTERITIS	20
HYPERTENSION	20
MIGRAINE HEADACHE	20

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	18	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
PLACEBO		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 169	[redacted]20[redacted] / 385	217
ABT-494	30MG	ORAL	QD	[redacted]20[redacted] / 386	[redacted]20[redacted] / 768	383

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ANERON	1 OTHER: CAPSULE	PRN	Y-M: 20[redacted]
FEMININA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
TOCOPHEROL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
TRAVELMIN	1 OTHER: TABLET	PRN	Y-M: 20[redacted]
TRIAMCINOLONE	2.5 mL	QD	Y-M: 20[redacted]
METHOTREXATE	12 mg	EVERY WEEK	Y-M: 20[redacted]
CELECOXIB	200 mg	BID	Y-M: 20[redacted]
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted]
DICLOFENAC	25 mg	PRN	Y-M: 20[redacted]
ISONIAZID	100 mg	TID	Y-M: 20[redacted]
PYRIDOXAL	10 mg	TID	Y-M: 20[redacted]
ADALIMUMAB	80 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
METHOTREXATE	12 mg	EVERY WEEK	Y-M: 20[redacted]
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
OLOPATADINE	10 mg	BID	Y-M: 20[redacted]
CELECOXIB	200 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
TACALCITOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
MOILIP	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
DIFLUCORTOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
KETOPROFEN	1 OTHER: PATCH	QD	Y-M: 20[redacted]
IGURATIMOD	25 mg	QD	Y-M: 20[redacted]
IGURATIMOD	25 mg	BID	Y-M: 20[redacted]
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted]
EXENATIDE	2 mg	EVERY WEEK	Y-M: 20[redacted]
METFORMIN	250 mg	BID	Y-M: 20[redacted]
DAPAGLIFLOZIN	5 mg	QD	Y-M: 20[redacted]

IRON	105 mg	QD	Y-M: 20[redacted] / -315
HEPARINOID	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -196
TELMISARTAN	40 mg	QD	Y-M: 20[redacted] / -134
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / -71
INDOMETACIN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -70
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -35

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ANERON	1 OTHER: CAPSULE	PRN	Y-M: 20[redacted]	ONGOING
FEMININA	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
TOCOPHEROL	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
TRAVELMIN	1 OTHER: TABLET	PRN	Y-M: 20[redacted]	ONGOING
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 428
ISONIAZID	100 mg	TID	Y-M: 20[redacted]	ONGOING
PYRIDOXAL	10 mg	TID	Y-M: 20[redacted]	ONGOING
METHOTREXATE	12 mg	EVERY WEEK	Y-M: 20[redacted]	ONGOING
FOLIC ACID	5 mg	QD	Y-M: 20[redacted]	ONGOING
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 428
CELECOXIB	200 mg	BID	Y-M: 20[redacted]	ONGOING
MOILIP	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]	ONGOING
IGURATIMOD	25 mg	BID	Y-M: 20[redacted]	ONGOING
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted]	ONGOING
METFORMIN	250 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 597
DAPAGLIFLOZIN	5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 597
IRON	105 mg	QD	Y-M: 20[redacted] / -315	ONGOING
TELMISARTAN	40 mg	QD	Y-M: 20[redacted] / -134	ONGOING
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / -71	ONGOING
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -35	ONGOING
OLOPATADINE	5 mg	QD	Y-M: 20[redacted] / 2	ONGOING
PROCATEROL	1 OTHER: INHALATION	PRN	Y-M: 20[redacted] / 36	ONGOING

BILASTINE	20 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 428
DIPHENHYDRAMINE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 113	ONGOING
FUSIDIC ACID	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 483
BREO ELLIPTA	1 OTHER: INHALATION	QD	Y-M: 20[redacted] / 141	ONGOING
ROHTO	1 OTHER: DROPS	PRN	Y-M: 20[redacted] / 212	Y-M: 20[redacted] / 799
POVIDONE-IODINE	1 OTHER: GARGLE	PRN	Y-M: 20[redacted] / 351	Y-M: 20[redacted] / 574
MYDRIN P	0.3 mL	OTHER: ONCE	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 429
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 434
ADENOSINE	40 mg	QD	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 436
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 436
MECOBALAMIN	1 mL	QD	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 436
PREDNISOLONE	80 mg	QD	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 436
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 439
ADENOSINE	1 g	TID	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 456
HYALURONIC ACID	1 OTHER: DROPS	TID	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 456
MECOBALAMIN	500 ug	TID	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 456
BROTIZOLAM	0.25 mg	PRN	Y-M: 20[redacted] / 431	Y-M: 20[redacted] / 439
LANSOPRAZOLE	30 mg	QD	Y-M: 20[redacted] / 440	ONGOING
CETIRIZINE	10 mg	QD	Y-M: 20[redacted] / 440	Y-M: 20[redacted] / 483
BILASTINE	20 mg	QD	Y-M: 20[redacted] / 440	Y-M: 20[redacted] / 597
NADIFLOXACIN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 449	Y-M: 20[redacted] / 454
LIRANAFTATE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 457	ONGOING
CLOBETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 457	Y-M: 20[redacted] / 489
BENFOTIAMINE	25 mg	QD	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 770

VIDARABINE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 569	Y-M: 20[redacted] / 580
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 570	Y-M: 20[redacted] / 576
GUALENIC ACID	1 OTHER: GARGLE	PRN	Y-M: 20[redacted] / 575	Y-M: 20[redacted] / 615
FUSIDIC ACID	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 576	Y-M: 20[redacted] / 582
CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 597	Y-M: 20[redacted] / 597
HYOSCINE	1 mL	OTHER: ONCE	Y-M: 20[redacted] / 597	Y-M: 20[redacted] / 597
BIO-THREE	1 OTHER: TABLETS	TID	Y-M: 20[redacted] / 597	Y-M: 20[redacted] / 598
LOPERAMIDE	1 OTHER: CAPSULES	BID	Y-M: 20[redacted] / 597	Y-M: 20[redacted] / 598
INSULIN HUMAN	5 IU	QD	Y-M: 20[redacted] / 598	Y-M: 20[redacted] / 598
INSULIN HUMAN	5 IU	BID	Y-M: 20[redacted] / 599	Y-M: 20[redacted] / 602
TERBINAFINE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 599	Y-M: 20[redacted] / 615
CLOSTRIDIUM BUTYRICUM	1 OTHER: TABLETS	TID	Y-M: 20[redacted] / 602	Y-M: 20[redacted] / 604
INSULIN HUMAN	5 IU	QD	Y-M: 20[redacted] / 603	Y-M: 20[redacted] / 603
BILASTINE	20 mg	QD	Y-M: 20[redacted] / 606	ONGOING
PARACETAMOL	400 mg	QD	Y-M: 20[redacted] / 606	Y-M: 20[redacted] / 606
BROTIZOLAM	0.25 mg	PRN	Y-M: 20[redacted] / 607	ONGOING
SENNOSIDE A+B	24 mg	OTHER: ONCE	Y-M: 20[redacted] / 608	Y-M: 20[redacted] / 608
INDIGO CARMINE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / 609	Y-M: 20[redacted] / 609
LIDOCAINE	10 g	OTHER: ONCE	Y-M: 20[redacted] / 609	Y-M: 20[redacted] / 609
MIDAZOLAM	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 609	Y-M: 20[redacted] / 609
MUBEN	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 609	Y-M: 20[redacted] / 609
DAPAGLIFLOZIN	5 mg	QD	Y-M: 20[redacted] / 611	ONGOING
METFORMIN	250 mg	BID	Y-M: 20[redacted] / 611	ONGOING
ROSUVASTATIN	7.5 mg	QD	Y-M: 20[redacted] /	Y-M: 20[redacted] /

NERIPROCT	2 OTHER: PIECES	BID	Y-M: 20[redacted]-[redacted] / 611	Y-M: 20[redacted]-[redacted] / 615
GLYCEROL	60 mL	TID	Y-M: 20[redacted]-[redacted] / 612	Y-M: 20[redacted]-[redacted] / 618
LIDOCAINE	10 g	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 613	Y-M: 20[redacted]-[redacted] / 613
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted]-[redacted] / 613	ONGOING
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted] / 616	ONGOING
MYDRIN P	0.3 mL	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 638	Y-M: 20[redacted]-[redacted] / 763
KLIOGEST	1 OTHER: PATCH	OTHER: 2 TIME PER WEEK	Y-M: 20[redacted]-[redacted] / 763	ONGOING
PLACENTA	2 mL	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 766	Y-M: 20[redacted]-[redacted] / 766
AMBROXOL	15 mg	TID	Y-M: 20[redacted]-[redacted] / 766	Y-M: 20[redacted]-[redacted] / 769
CAFFEINE	60 mg	TID	Y-M: 20[redacted]-[redacted] / 766	Y-M: 20[redacted]-[redacted] / 769
PARACETAMOL	150 mg	TID	Y-M: 20[redacted]-[redacted] / 766	Y-M: 20[redacted]-[redacted] / 769
PROMETHAZINE	13.5 mg	TID	Y-M: 20[redacted]-[redacted] / 766	Y-M: 20[redacted]-[redacted] / 769
SALICYLAMIDE	270 mg	TID	Y-M: 20[redacted]-[redacted] / 766	Y-M: 20[redacted]-[redacted] / 769
SALBUTAMOL	0.3 mL	QD	Y-M: 20[redacted]-[redacted] / 769	Y-M: 20[redacted]-[redacted] / 770
SALBUTAMOL	0.5 mL	QD	Y-M: 20[redacted]-[redacted] / 770	Y-M: 20[redacted]-[redacted] / 770
PARACETAMOL	400 mg	QD	Y-M: 20[redacted]-[redacted] / 771	Y-M: 20[redacted]-[redacted] / 771
SALBUTAMOL	0.3 mL	QID	Y-M: 20[redacted]-[redacted] / 771	Y-M: 20[redacted]-[redacted] / 774
DEXTROMETHORPHAN	15 mg	TID	Y-M: 20[redacted]-[redacted] / 771	Y-M: 20[redacted]-[redacted] / 782
SALBUTAMOL	0.3 mL	QD	Y-M: 20[redacted]-[redacted] / 775	Y-M: 20[redacted]-[redacted] / 775

Event #1: Serious Adverse Event

Event Description	LEFT FACIAL NERVE PALSY
Preferred term	顔面麻痺
AE Onset Date / Rx Day	[redacted]20[redacted] / 428
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 429): Basophils/Leukocytes: 0.3 [0 - 2.5] %; Eosinophils/Leukocytes: 2.2 [0 - 8.5] %;

Leukocytes: 10.9 [3.3 - 8.6] 10^9/L; Lymphocytes/Leukocytes: 26.5 [16.5 - 49.5] %; Monocytes/Leukocytes: 5.5 [2 - 10] %; NPTST038-C-REACTIVE PROTEIN: 0.97 [NOT REPORTED - 0.3] mg/dL; NPTST106-HBA1C: 6.3 [4.6 - 6.2] %; NPTST111-HSV-IGG: 80.0 [NOT REPORTED - 1.9] UNIT NOT REPORTED; NPTST112-HSV-IGM: 0.17 [NOT REPORTED - 0.79] UNIT NOT REPORTED; NPTST223-VZV IGG: 13.3 [NOT REPORTED - 1.9] UNIT NOT REPORTED; NPTST224-VZV-IGM: 0.12 [NOT REPORTED - 0.79] UNIT NOT REPORTED; Neutrophils/Leukocytes: 65.5 [38.5 - 80.5] %; [redacted]20[redacted] (RX DAY 437): Basophils/Leukocytes: 0.3 [0 - 2.5] %; Eosinophils/Leukocytes: 1.9 [0 - 8.5] %; Leukocytes: 10.3 [3.3 - 8.6] 10^9/L; Lymphocytes/Leukocytes: 27.9 [16.5 - 49.5] %; Monocytes/Leukocytes: 6.9 [2 - 10] %; NPTST106-HBA1C: 6.4 [4.6 - 6.2] %; Neutrophils/Leukocytes: 63 [38.5 - 80.5] %

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Rx Day	457
Duration of AE	30 DAYS
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

Event #2: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	VIRAL ENTERITIS
Preferred term	ウイルス性胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 597
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 597): Leukocytes: 12.5 [3.3 - 8.6] 10^9/L; [redacted]20[redacted] (RX DAY 598): Leukocytes: 9.2 [3.3 - 8.6] 10^9/L; NPTST038-C-REACTIVE PROTEIN: 14.64 [NOT REPORTED - 0.3] mg/dL; NPTST109-HEMOGLOBIN A1C: 6.3 [4.6 - 6.2] %; [redacted]20[redacted] (RX DAY 602): Leukocytes: 7 [3.3 - 8.6] 10^9/L; NPTST038-C-REACTIVE PROTEIN: 2.66 [NOT REPORTED - 0.3] mg/dL; [redacted]20[redacted] (RX DAY 609): Leukocytes: 7.6 [3.3 - 8.6] 10^9/L; NPTST038-C-REACTIVE PROTEIN: 0.66 [NOT REPORTED - 0.3] mg/dL; [redacted]20[redacted] (RX DAY 612): Leukocytes: 9 [3.3 - 8.6] 10^9/L; NPTST038-C-REACTIVE PROTEIN: 0.50 [NOT REPORTED - 0.3] mg/dL; [redacted]20[redacted] (RX DAY 613): Leukocytes: 7.5 [3.3 - 8.6] 10^9/L; NPTST038-C-REACTIVE PROTEIN: 0.47 [NOT REPORTED - 0.3] mg/dL

Microbiology

[redacted]20[redacted] (RX DAY 598): STOOL NPTST144-MICROBIOLOGY EXAMINATION: NEGATIVE; URINE NPTST144-MICROBIOLOGY EXAMINATION: POSITIVE-ESCHERICHIA COLI; BLOOD NPTST144-MICROBIOLOGY EXAMINATION: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 597): BODY TEMPERATURE: 38.0 C; [redacted]20[redacted] (RX DAY 598): BLOOD PRESSURE: 110/62; BODY TEMPERATURE: 37.5?C; CT (ABDOMINAL): NO ABNORMALITY; PULSE: 104; [redacted]20[redacted] (RX DAY 605): BODY PRESSURE: 124/75; BODY TEMPERATURE: 36.5 C; PULSE: 66; [redacted]20[redacted] (RX DAY 609): COLONOSCOPY: COLORECTAL POLYPS(ADENOMA),SIGMOID COLON DIVERTICULUM; [redacted]20[redacted] (RX DAY 613): COLONOSCOPY: HEMORRHOID

AE Stopped Rx Day	615

Duration of AE	19 DAYS
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

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

Event Description	WORSENING OF BRONCHIAL ASTHEMA
Preferred term	喘息
AE Onset Date / Rx Day	[redacted]20[redacted] / 769 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 769): NPTST038-C-REACTIVE PROTEIN: 4.86 [NOT REPORTED - 0.3] mg/dL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 769): BODY PRESSURE: 149/108; BODY TEMPERATURE: 36.5; PULSE: 95; RESPIRATORY RATE: 30; SPO2: 97; X-RAY(CHEST): NO ABNORMALITY; [redacted]20[redacted] (RX DAY 770): BODY PRESSURE: 151/93; BODY TEMPERATURE: 36.6; ECG: NO ABNORMALITY; PULSE: 101; RESPIRATORY RATE: 24; SPO2: 98; X-RAY(CHEST): NO ABNORMALITY; [redacted]20[redacted] (RX DAY 771): BODY PRESSURE: 125/84; BODY TEMPERATURE: 36.7; PULSE: 80; RESPIRATORY RATE: 16; SPO2: 97; [redacted]20[redacted] (RX DAY 774): BODY PRESSURE: 138/83; BODY TEMPERATURE: 36.7; PULSE: 79; RESPIRATORY RATE: 18; SPO2: 98

AE Stopped Rx Day	775 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	7 DAYS
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DUE TO COMMON COLD
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: M15-554

治験責任医師からの報告。本被験者は日本の4[redacted]歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左顔面神経麻痺の事象を発現した。

Event 1 の臨床経過：

関連する病歴は尋常性乾癬，元喫煙者（1 日 1 箱を 18 年間），糖尿病，肥満，潜伏結核，乾癬性関節炎，高血圧，片頭痛及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左顔面神経麻痺を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，左顔面神経麻痺は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日の事象発現前，口唇単純ヘルペスの再燃（非重篤）が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は左眼の流涙を自覚した。左眼は完全に閉じることができなかった。また被験者は，口唇左側があまり動かないことに気づいた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は皮膚科医を受診した。そのとき，顔面の痛みはまったくなかった。帯状疱疹を示唆する皮膚発疹もなかった。被験者は耳鼻咽喉科医を受診し，左顔面神経麻痺と診断された。被験者は，柳原法による顔面麻痺評価で，40 点中 7 点と評価された。聴覚障害は報告されなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はステロイド注入のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，症状は改善した。被験者は，柳原法により，40 点中 21 点と評価された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は耳鼻咽喉科及び皮膚科を受診し，舌不快感を訴えた。顔面神経麻痺は軽快したと報告された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，柳原法により，40 点中 40 点と評価された。被験者は回復したと判断された。検査結果から原因ウイルスは特定されなかった。

投与された薬剤は，ファモチジン，アデホス-L，バラシクロビル，メチコバール，アデホスコーワ，ヒアレイン，プレドニン及びヒアルロン酸 NA であった。

The patient's past medications include:

DICLOFENAC NA for PSORIATIC ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

LIDOMEX KOWA for PSORIASIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

BYDUREON for DIABETES MELLITUS ([redacted] 20[redacted] - [redacted] 20[redacted])

HEPARINOID for PSORIASIS (■ ■ 20■ - ■ ■ 20■)

INTEBAN for PSORIATIC ARTHRITIS (■ ■■ 20■ - ■ ■■ 20■)

FAMVIR for HERPES SIMPLEX REACTIVATION(LIP) (■ ■ 20■ - ■ ■ 20■)

Causality for ABT-494 (Blinded)

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1) Facial palsy (10016060) (Facial paralysis (10016062)) [v.22.0] [10016060]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of LEFT FACIAL NERVE PALSY

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

■ ■■ **20■ C REACTIVE PROTEIN:** 0.97 mg/dL (normal <0.3)

■ ■■ **20■ ELECTRONEUROGRAPHY:** 36.6%- Compound muscle action potential (CMAP) of affected side

■ ■■ **20■ HSV IGM:** 0.17 no unit (normal <0.79)

■ ■■ **20■ HSV-IGG:** 80.0 no unit (normal <1.9)

■ ■■ **20■ VZV IGG:** 13.3 no unit (normal <1.9)

■ ■■ **20■ VZV IGM:** 0.12 no unit (normal <0.79)

■ ■■ **20■ WHITE BLOOD CELLS:** 10.93 X10**3/MCL (normal 3.3 to 8.6)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は日本の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，ウイルス性小腸炎の事象を発現した。

Event 2 の臨床経過：

関連する病歴は尋常性乾癬，元喫煙者（1 日 1 箱を 18 年間），糖尿病，肥満，細菌性胃腸炎及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はウイルス性小腸炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，ウイルス性小腸炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は悪心及び下痢（水様便が 1 日 5～6 回）を来した。被験者は内科を受診し，ブスコパン及びソルデム 3A を投与された。ロペミン及びビオスリーが処方され，その後，被験者は帰宅した。来院時には発熱はなかったが，夜間に 38°C の発熱を来した。20[redacted] 年 [redacted] 月 [redacted] 日，悪心及び下痢（水様便が 1 日 10 回）が続いた。被験者は内科を再受診し，急性胃腸炎（ウイルス性小腸炎の疑い）のため，同日入院した。被験者は左腰部痛及び腹痛も訴えた。絶食及び点滴が開始された。被験者は下痢の原因と考えられる食物を思いつかなかった。20[redacted] 年 [redacted] 月 [redacted] 日，水様便は 1 日 3 回に減少し，悪心はなく，さらなる左腰部痛もなかった。20[redacted] 年 [redacted] 月 [redacted] 日，「泥状」便が 1 日 1～3 回認められた。臨床検査値は改善し，被験者は食事を開始した。20[redacted] 年 [redacted] 月 [redacted] 日，悪心及び腹痛を伴う「泥状」便が 1 回認められた。20[redacted] 年 [redacted] 月 [redacted] 日，微生物学的検査の結果は陰性であったが，被験者は依然として悪心及び腹痛を呈していたため，ウイルス性小腸炎と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，便は正常で，悪心や腹痛も伴っていなかった。20[redacted] 年 [redacted] 月 [redacted] 日，結腸内視鏡検査が行われた。大腸ポリープ（腺腫，非重篤）及び S 状結腸憩室（非重篤）との診断が下された。20[redacted] 年 [redacted] 月 [redacted] 日，便中に血液が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，結腸内視鏡検査で直腸痔核（非重篤）が明らかとなった。便中の血液は痔核からの出血ではないかと考えられた。これについては経過観察を行うこととなった。20[redacted] 年 [redacted] 月 [redacted] 日，ウイルス性小腸炎は消失したと判断され，被験者は退院した。20[redacted] 年 [redacted] 月 [redacted] 日，治験責任医師は被験者に電話し，被験者の状態はもう問題ないと伝えた。治験薬の投与が再開された。

投与された薬剤は，ロペミン，ビオスリー，ヒューマリン R，ミヤ BM，ブスコパン及びソルデム 3A であった。

Causality for UPADACITINIB (Blinded)

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1) Viral gastroenteritis (10047445) (Gastroenteritis viral (10017918)) [v.22.0] [10047445]

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 VIRAL ENTERITIS

- Investigator: Not applicable

- AbbVie: Event is common in the general population.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **BLOOD CULTURE:** negative

[redacted] **BLOOD PRESSURE:** 110/62 mmHg

[redacted] **BLOOD PRESSURE:** 124/75 mmHg

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

[redacted] **BODY TEMPERATURE:** 37.5 Degrees C

[redacted] **BODY TEMPERATURE:** 36.5 Degrees C

[redacted] **C REACTIVE PROTEIN:** 14.64 mg/dL (normal <0.30)

[redacted] **C REACTIVE PROTEIN:** 2.66 mg/dL (normal <0.30)

[redacted] **20[redacted] C REACTIVE PROTEIN:** 0.47 mg/dL (normal <0.30)

[redacted] **20[redacted] COLONOSCOPY:** colorectal polyps (adenoma) and sigmoid colon diverticulum

[redacted] **20[redacted] COLONOSCOPY:** hemorrhoids in rectum

[redacted] **20[redacted] CT ABDOMEN:** no abnormality

[redacted] **20[redacted] HEART RATE:** 104 bpm

[redacted] **20[redacted] HEMOGLOBIN A1C:** 6.3 % (normal 4.6 to 6.2)

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

[redacted] **20[redacted] URINE CULTURE:** positive: Escherichia coli

[redacted] **20[redacted] WBC:** 12.53 10^3/ul (normal 3.30 to 8.60)

[redacted] **20[redacted] WBC:** 9.23 10^3/ul (normal 3.30 to 8.60)

[redacted] **20[redacted] WBC:** 7.46 10^3/ul (normal 3.30 to 8.60)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は日本の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，気管支喘息の悪化の事象を発現した。

Event 3 の臨床経過：
関連する病歴は尋常性乾癬，喘息，元紙巻タバコ喫煙者（1 日 1 箱を 18 年間），糖尿病，肥満，鉄欠乏性貧血，潜伏結核，乾癬性関節炎，喘息発作，片頭痛及び現飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ABT-494 の盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は気管支喘息の悪化を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，気管支喘息の悪化は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は感冒症状を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は疲労，咳嗽，頻呼吸及び咽喉痛で病院を受診した。被験者の胸部 X 線検査は正常であった。被験者は感冒のために喘息が悪化し，治験薬投与が中断された。被験者は薬物療法による治療を受け，喘鳴は改善した。被験者は喘息発作に対し別の薬を処方され，帰宅した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は再び喘息の症状を発現し病院を受診した。再度の胸部 X 線検査及び心電図検査は正常であった。被験者の呼吸状態は仰臥位で悪化した。被験者はその後，喘息のコントロールのため入院した。被験者の喘息発作は軽度と説明された。被験者は再度薬物療法

による治療を受けた。喘息発作と同様に感冒も緩和された。気管支喘息の悪化は消失した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。治験責任医師の判断では，被験者は糖尿病を合併しており，治験参加後に感染症を繰り返していたため，感染の危険性が高かった。そのため，治験責任医師は治験薬の中止を決定した。

投与された薬剤は，メプチン，レルベアエリプタ及びベネトリンであった。

Causality for UPADACITINIB (Blinded)
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1) Asthma aggravated (10003554) (Asthma (10003553))[v.23.0] [10003554]

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 BRONCHIAL ASTHEMA

- Investigator: Due to common cold.

- AbbVie: Risk factors include the subject's pre-existing asthma, obesity (BMI 43.4) and concurrent common cold.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** 149/108 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 151/93 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 125/84 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** 138/83 mmHg

[redacted] **20[redacted] BODY TEMPERATURE:** 36.5 Degrees C

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

[redacted] **20[redacted] BODY TEMPERATURE:** 36.7 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 36.7 Degrees C

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 4.86 mg/dL (normal <=0.30)

[redacted] **20[redacted] CHEST X-RAY:** NO ABNORMALITY

[redacted] **20[redacted] CHEST X-RAY:** NO ABNORMALITY

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

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

[redacted] **20[redacted] PULSE:** 95 /min

[redacted] **20[redacted] PULSE:** 101 /min

[redacted] **20[redacted] PULSE:** 80 /min

[redacted] **20[redacted] PULSE:** 79 /min

[redacted] **20[redacted] RESPIRATIONS:** 30 /min

[redacted] **20[redacted] RESPIRATIONS:** 24 /min

[redacted] **20[redacted] RESPIRATIONS:** 16 /min

[redacted] **20[redacted] RESPIRATION:** 18 /min

[redacted] **20[redacted] SP02:** 98 %

[redacted] **20[redacted] SPO2:** 97 %

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

[redacted] **20[redacted] SPO2:** 97 %

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
ウイルス性胃腸炎	X			X
乾癬性関節症	X			

Treatment Group	Age at Study Start	Sex	Race
ABT-494 15 mg QD	3[redacted]	MALE	ASIAN

Medical History	Onset Year
OTHER: PSORIASIS VULGARIS	20[redacted]
OTHER: POLLINOSIS	20
DIABETES MELLITUS	20
LIVER DISEASE (EXCLUDING HEPATITIS): FATTY LIVER	20
HYPERLIPIDEMIA: HYPERCHOLESTEROLEMIA	20
SEIZURE DISORDER/CONVULSIONS: CONTROLLED BY MEDICATION	20
OTHER: PIGMENTED NEVUS RESECTION	20
SLEEP APNEA	20

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.5 PACK	15	
CIGARS	NEVER			
E-CIGARETTES	CURRENT	0 SESSIONS	3	
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 170	170
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 171	[redacted]20[redacted] / 392	222
ABT-494	15MG	ORAL	QD	[redacted]20[redacted] / 393	/	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
TACALCITOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
VALISONE-G	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
DICLOFENAC	37.5 mg	BID	Y-M: 20[redacted]
METHOTREXATE	8 mg	EVERY WEEK	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
LIRAGLUTIDE	0.9 mg	QD	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted]
INFLIXIMAB	550 mg	OTHER: EVERY8WEEK	Y-M: 20[redacted]
BEZAFIBRATE	200 mg	QD	Y-M: 20[redacted]
METFORMIN	500 mg	TID	Y-M: 20[redacted]
DAIVOBET	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
ADALIMUMAB	80 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
LEVETIRACETAM	1000 mg	BID	Y-M: 20[redacted] / -256
BEPOTASTINE	10 mg	BID	Y-M: 20[redacted] / -245
BETAMETHASONE BUTYRATE PROPIONATE W/MAXACALCI	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -245
LOXOPROFEN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -245
MAXACALCITOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -245
MAXACALCITOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -235
INSULIN DEGLUDEC	6 IU	QD	Y-M: 20[redacted] / -182
CELECOXIB	200 mg	BID	Y-M: 20[redacted] / -126
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -123
LACOSAMIDE	50 mg	BID	Y-M: 20[redacted] / -112
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted] / -112
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted]

			/ -90
FLURBIPROFEN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -33
LANSOPRAZOLE	15 mg	QD	Y-M: 20[redacted] / -33
HEPARINOID	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -32

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
LIRAGLUTIDE	0.9 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 365
BEZAFIBRATE	200 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 844
METFORMIN	500 mg	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 844
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / -123	Y-M: 20[redacted] / 360
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted] / -112	Not reported.
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -90	Y-M: 20[redacted] / 359
FLURBIPROFEN	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -33	Not reported.
LANSOPRAZOLE	15 mg	QD	Y-M: 20[redacted] / -33	Not reported.
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 15	Not reported.
ESCITALOPRAM	20 mg	QD	Y-M: 20[redacted] / 61	Not reported.
LEVETIRACETAM	2000 mg	QD	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 555
CLOBETASOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 113	Not reported.
INSULIN DEGLUDEC	12 IU	QD	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 365
LACOSAMIDE	100 mg	QD	Y-M: 20[redacted] / 255	Y-M: 20[redacted] / 760
LACOSAMIDE	50 mg	QD	Y-M: 20[redacted] / 255	Y-M: 20[redacted] / 760
CELECOXIB	200 mg	PRN	Y-M: 20[redacted] / 262	Not reported.
URSODEOXYCHOLIC ACID	100 mg	BID	Y-M: 20[redacted] / 311	Y-M: 20[redacted] / 844
LAMOTRIGINE	5 mg	BID	Y-M: 20[redacted] / 345	Y-M: 20[redacted] / 358
LAMOTRIGINE	10 mg	BID	Y-M: 20[redacted] / 359	Y-M: 20[redacted] / 380

LACTOMIN	1 OTHER: TABLET	OTHER: ONCE	Y-M: 20[redacted] / 364	Y-M: 20[redacted] / 364
EUFUSOL	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
SODIUM CHLORIDE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
SULTAMICILLIN	3 g	TID	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
INSULIN HUMAN	2 IU	BID	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 367
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 368
INSULIN LISPRO	2 IU	OTHER: ONCE	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 367
INSULIN LISPRO	6 IU	OTHER: ONCE	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 367
UNACID	3 g	QID	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 368
INSULIN DEGLUDEC	9-12 IU	QD	Y-M: 20[redacted] / 368	Not reported.
INSULIN LISPRO	2 IU	OTHER: ONCE	Y-M: 20[redacted] / 368	Y-M: 20[redacted] / 368
LIRAGLUTIDE	0.9 mg	QD	Y-M: 20[redacted] / 369	Not reported.
INSULIN LISPRO	2 IU	OTHER: ONCE	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
UNACID	3 g	TID	Y-M: 20[redacted] / 369	Y-M: 20[redacted] / 369
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / 380	Not reported.
FOLIC ACID	10 mg	EVERY WEEK	Y-M: 20[redacted] / 382	Not reported.
LEVETIRACETAM	1000 mg	QD	Y-M: 20[redacted] / 599	Not reported.
LAMOTRIGINE	200 mg	BID	Y-M: 20[redacted] / 649	Y-M: 20[redacted] / 760
LAMOTRIGINE	200 mg	BID	Y-M: 20[redacted] / 761	Not reported.
LACOSAMIDE	150 mg	QD	Y-M: 20[redacted] / 761	Y-M: 20[redacted] / 830
LACOSAMIDE	50 mg	QD	Y-M: 20[redacted] / 761	Y-M: 20[redacted] / 830
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 794	Y-M: 20[redacted] / 801
LACOSAMIDE	200 mg	QD	Y-M: 20[redacted] / 831	Not reported.
LACOSAMIDE	50 mg	QD	Y-M: 20[redacted] / 831	Not reported.

SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / 844	Y-M: 20[redacted] / 844
INSULIN LISPRO	2 IU	PRN	Y-M: 20[redacted] / 844	Y-M: 20[redacted] / 846
CEFAZOLIN	1 g	BID	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
DESFLURANE	4%	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
DICLOFENAC	25 mg	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
FENTANYL	100 OTHER: ?G	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
FENTANYL	150 OTHER: ?G	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
FLURBIPROFEN	50 mg	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
PROPOFOL	150 mg	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
REMIFENTANIL	0.5 mg	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
ROCURONIUM	70 mg	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
SUGAMMADEX	200 mg	PRN	Y-M: 20[redacted] / 845	Y-M: 20[redacted] / 845
BEZAFIBRATE	200 mg	QD	Y-M: 20[redacted] / 846	Not reported.
URSODEOXYCHOLIC ACID	100 mg	BID	Y-M: 20[redacted] / 846	Not reported.
CEFAZOLIN	1 g	TID	Y-M: 20[redacted] / 846	Y-M: 20[redacted] / 846
UNSPECIFIED HERBAL	2.7 g	TID	Y-M: 20[redacted] / 846	Y-M: 20[redacted] / 858
INSULIN LISPRO	4 IU	PRN	Y-M: 20[redacted] / 847	Y-M: 20[redacted] / 847
SUVOREXANT	20 mg	PRN	Y-M: 20[redacted] / 855	Y-M: 20[redacted] / 856
METFORMIN	500 mg	TID	Y-M: 20[redacted] / 857	Y-M: 20[redacted] / 858

Event #1: Serious Adverse Event, Study Specific Adverse Events of Interest

Event Description	VIRAL GASTROENTEROCOLITIS
Preferred term	ウイルス性胃腸炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 366
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 366): Alanine Aminotransferase: 63 [10 - 42] U/L; Aspartate Aminotransferase: 61 [13 - 30] U/L; Leukocytes: 8.7 [3.3 - 8.6] 10^9/L; NPTST056-CRP: 0.04 [0 - 0.14] mg/dL; NPTST068-CULTURE INSPECTION TEST: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST068-CULTURE INSPECTION TEST: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST078-EGFR: 84.6 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST220-VIROLOGY INSPECTION: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 367): Alanine Aminotransferase: 50 [10 - 42] U/L; Aspartate Aminotransferase: 47 [13 - 30] U/L; Leukocytes: 4.6 [3.3 - 8.6] 10^9/L; NPTST056-CRP: 2.23 [0 - 0.14] mg/dL; NPTST078-EGFR: 70.7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 369): Alanine Aminotransferase: 50 [10 - 42] U/L; Aspartate Aminotransferase: 46 [13 - 30] U/L; Leukocytes: 4.8 [3.3 - 8.6] 10^9/L; NPTST056-CRP: 0.62 [0 - 0.14] mg/dL; NPTST078-EGFR: 81.4 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 374): Alanine Aminotransferase: 73 [10 - 42] U/L; Aspartate Aminotransferase: 47 [13 - 30] U/L; Leukocytes: 5.6 [3.3 - 8.6] 10^9/L; NPTST056-CRP: 0.21 [0 - 0.14] mg/dL; NPTST078-EGFR: 98.7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 366): CHEST CT: NO ABNORMAL CHANGE; CHEST X-RAY: NO ABNORMAL CHANG.; PLEVIS CT: NO ABNORMAL CHANGE; TEMPERATURE: 38.7?; [redacted]20[redacted] (RX DAY 367): TEMPERATURE: 36.8?

AE Stopped Rx Day	374
Duration of AE	9 DAYS
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	WORSENING OF PSORIATIC ARTHRITIS
Preferred term	乾癬性関節症
AE Onset Date / Rx Day	[redacted]20[redacted] / 724
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 845): SURGERY(SWAN-NECK DEFORMITY ARTHRODESIS): THE SYMPTOMS

WERE ALLEVIATED.; X-RAY(TOE): PIN WAS SUCCESSFULLY FIXED.; [redacted]20[redacted] (RX DAY 852): X-RAY(TOE): PIN WAS SUCCESSFULLY FIXED.; [redacted]20[redacted] (RX DAY 857): X-RAY(TOE): PIN WAS SUCCESSFULLY FIXED.

AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THIS EVENT IS CAUSED BY PROGRESSION OF THE PRIMARY DISEASE,THE CAUSAL RELATIONSHIP BETWEEN THE EVENT AND THE STUDY DRUG WAS ASSESSED AS UNRELATED.
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: M15-554

治験責任医師からの報告。本被験者は日本の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，ウイルス性胃腸炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は糖尿病，現喫煙者（1 日 0.5 箱を 15 年間）及び元飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted]年[redacted]月[redacted]日，ABT-494 の盲検投与が開始された。

20[redacted]年[redacted]月[redacted]日，被験者はウイルス性胃腸炎を発現した。20[redacted]年[redacted]月[redacted]日，ウイルス性胃腸炎は消失した。

20[redacted]年[redacted]月[redacted]日，被験者は咽喉痛，咳嗽及び下痢を呈した。20[redacted]年[redacted]月[redacted]日，被験者は発熱，からだのゆれ及び悪寒で入院した。抗生物質の静脈内投与が行われた。20[redacted]年[redacted]月[redacted]日，発熱は消失し，被験者の全身状態は改善した。20[redacted]年[redacted]月[redacted]日，被験者は退院した。

投与された薬剤は，スルバシリン，ヴィーン-F，生理食塩液，ヒューマリン R，ヒューマログ，ビクトーザ，トレシーバ，ビオフェルミン及びカロナールであった。

The patient's past medications include:

LOXONIN TAPE for PSORIATIC ARTHRITIS ([redacted])

TALION for PSORIASIS VULGARIS ([redacted])

Causality for ABT-494 (Blinded)

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1) Viral gastroenteritis (10047445) (Gastroenteritis viral (10017918)) [v.21.1] [10047445]

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 VIRAL GASTROENTEROCOLITIS

- Investigator: Not applicable

- AbbVie: Event is common in the general population

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ALANINE AMINO TRANSFERASE:** 73 IU/L (normal 10 to 42)

[redacted] **ALANINE AMINOTRANSFERASE:** 63 U/L (normal 10 to 42)

[redacted] **ALKALINE AMINO PHOSPHATASE:** 50 U/L (normal 10 to 30)

[redacted] **ASPARTATE AMINO TRANSFERASE:** 61 IU/L (normal 13 to 30)

[redacted] **ASPARTATE AMINO TRANSFERASE:** 46 IU/L (normal 13 to 30)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 47 IU/L (normal 13 to 30)

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

[redacted] **20[redacted] BODY TEMP:** 38.6 Degrees C

[redacted] **20[redacted] BODY TEMP:** 36.8 Degrees C

[redacted] **20[redacted] CHEST X-RAY:** No Abnormal change

[redacted] **20[redacted] CRP:** 0.04 mg/dL (normal 0 to 0.14)

[redacted] **20[redacted] CRP:** 2.23 mg/dL (normal 0 to 0.14)

[redacted] **20[redacted] CRP:** 0.62 mg/dL (normal 0 to 0.14)

[redacted] **20[redacted] CRP:** 0.21 mg/dL (normal 0 to 0.14)

[redacted] **20[redacted] CT CHEST:** No Abnormal change

[redacted] **20[redacted] CT PELVIS:** No Abnormal change

[redacted] **20[redacted] EGFR:** 84.6 No units

[redacted] **20[redacted] EGFR:** 70.7 No units

[redacted] **20[redacted] EGFR:** 81.4 No units

[redacted] **20[redacted] EGFR:** 98.7 No units

[redacted] **20[redacted] NASAL MUSCUS VIROLOGY INSPECTION:** Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.74 X10**3/MCL (normal 3.3 to 8.6)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.76 X10**3/MCL (normal 3.3 to 8.6)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.56 X10**3/MCL (normal 3.3 to 8.6)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-554

治験責任医師からの報告。本被験者は日本の 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，乾癬性関節炎の悪化の事象を発現した。

Event 2 の臨床経過：
関連する病歴は尋常性乾癬，乾癬性関節炎，花粉症，色素性母斑切除術，現喫煙者（1 日 0.5 本を 15 年間）及び元飲酒者（1 日 2 杯未満）であった。

被験者は，最初の 24 週間，本治験の盲検プラセボ対照期に組み入れられていた。20[redacted] 年 [redacted] 月 [redacted] 日，ウパダシチニブの盲検投与が開始された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は乾癬性関節炎の悪化を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は足趾の疼痛が増強し手術が必要となった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はスワンネック変形に対し関節固定術を受けた。被験者は再度 X 線検査を受け，ピンが正しい位置にあることが確認され，被験者の症状は緩和した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は抜糸し退院した。

投与された薬剤は，ボンフェナックであった。

The patient's past medications include:

VOLTAREN SR for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

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

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

LOXONIN TAPE for PSORIATIC ARTHRITIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Psoriatic arthritis aggravated (10037161) (Psoriatic arthropathy (10037162)) [v.23.0] [10037161]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF PSORIATIC ARTHRITIS

- Investigator: This event is caused by progression of the primary disease, the causal relationship between the event and the study drug was assessed as unrelated.

- AbbVie: Event is more likely due to the subject's pre-existing psoriatic arthritis.

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		X

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

Medical History	Onset Year
TUBERCULOSIS: TUBERCULOSIS IN CHILDHOOD(ACTIVE TB)	19[redacted]
OTHER: PSORIASIS VULGARIS	19
DEGENERATIVE DISC DISEASE: LUMBER HERNIA	19
EYE DISEASE/DISORDER: UVEITIS	20
OTHER: HYPERURICEMIA	20
OTHER: INSOMUNIA	20

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	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	30MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 118	118

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ALLOPURINOL	100 mg	QD	Y-M: 20[redacted]
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted]
FLUOROMETHOLONE	1 OTHER: APPLICATION	TID	Y-M: 20[redacted]
CERTOLIZUMAB PEGOL	200 mg	EVERY 2 WEEKS	Y-M: 20[redacted]
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]
METHOTREXATE	8 mg	EVERY WEEK	Y-M: 20[redacted]
DEXAMETHASONE	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -365
DIPHENHYDRAMINE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -365
DIFLUPREDNATE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -197
CALCIPOTRIOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -169
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / -155
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -85
ISONIAZID	100 mg	TID	Y-M: 20[redacted] / -23
PYRIDOXAL	10 mg	TID	Y-M: 20[redacted] / -23
LOXOPROFEN	60 mg	TID	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
ALLOPURINOL	100 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 149
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted]	ONGOING
FOLIC ACID	5 mg	EVERY WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 115
METHOTREXATE	10 mg	EVERY WEEK	Y-M: 20[redacted] / -85	Y-M: 20[redacted] / 119
ISONIAZID	100 mg	TID	Y-M: 20[redacted] / -23	Y-M: 20[redacted] / 140
PYRIDOXAL	10 mg	TID	Y-M: 20[redacted] / -23	Y-M: 20[redacted] / 140
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / -21	Y-M: 20[redacted] / 141
LANSOPRAZOLE	15 mg	QD	Y-M: 20[redacted] / 1	ONGOING
LULICONAZOLE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 168
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 121
PARACETAMOL	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 122
SODIUM CHLORIDE	10 mL	QD	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 123
METHYLPREDNISOLONE	1000 mg	QD	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 124
BACTRIM	3 OTHER: TABLETS	TID	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 125
HEPARIN	10 mL	QD	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 125
MEROPENEM	0.5 g	TID	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 127
CALCIUM POLYSTYRENE SULFONATE	25 g	TID	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 126
INSULIN LISPRO	2 IU	PRN	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 126
INSULIN LISPRO	4 IU	PRN	Y-M: 20[redacted] / 123	Y-M: 20[redacted] / 127
BACTRIM	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 126
PREDNISOLONE	10-30 mg	TID	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 128
ALENDRONIC ACID	35 mg	EVERY WEEK	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 152

ALFACALCIDOL	0.5 ug	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 125 155
BACTRIM	1 OTHER: TABLET	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 127 134
PREDNISOLONE	20-15 mg	BID	Y-M: 20[redacted] / Y-M: 20[redacted] / 129 132
PREDNISOLONE	20-5 mg	BID	Y-M: 20[redacted] / Y-M: 20[redacted] / 133 135
AMPHOTERICIN B	1 OTHER: APPLICATION	QID	Y-M: 20[redacted] / Y-M: 20[redacted] / 134 142
HEPARINOID	1 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / ONGOING 135
XYLOCAINE-EPINEPHRINE	5 mL	OTHER: ONCE	Y-M: 20[redacted] / Y-M: 20[redacted] / 135 135
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 135 141
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 136 141
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / ONGOING 142
PREDNISOLONE	7.5 mg	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 142 148
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted] / Y-M: 20[redacted] / 149 155

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

Event Description	DRUG INDUCED PNEUMONIA
Preferred term	肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 118
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 122): URINE NPTST002- LEGIONELLA PNEUMOPHILA ANTIGEN: NEGATIVE; BLOOD NPTST005-?D GLUCAN: NEGATIVE; BLOOD NPTST029-BLOOD CULTURE: NEGATIVE; BLOOD NPTST073-CYTOMEGALOVIRUS ANTIGEN: NEGATIVE; OTHER NASAL MUCUS NPTST117-INFLUENZA TEST: NEGATIVE; SPUTUM NPTST148-MYCOBACTERIUM TUBERCULOSIS: NEGATIVE; OTHER THROAT SWAB NPTST163-PHARYNX MYCOPLASMA: NEGATIVE; URINE NPTST167-PNEUMOCOCCUS THEA ANTIGEN: NEGATIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 122): CT: PNEUMONITIS; X-RAY: PNEUMONITIS; [redacted]20[redacted] (RX DAY 128): CHEST CT: IMPROVEMENT OF PNEUMONIA.; [redacted]20[redacted] (RX DAY 141): CHEST X-RAY: IMPROVEMENT; [redacted]20[redacted] (RX DAY 148): CHEST X-RAY: IMPROVEMENT; [redacted]20[redacted] (RX DAY 155): CHEST X-RAY: IMPROVEMENT; [redacted]20[redacted] (RX DAY 169): CHEST X-RAY: IMPROVEMENT

AE Stopped Rx Day	169 (51 DAYS AFTER LAST TREATMENT)
Duration of AE	52 DAYS

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: M15-554

治験責任医師からの報告。本被験者は日本の 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，薬剤誘発性肺炎の事象を発現した。

Event 1 の臨床経過：

関連する病歴は小児期の結核，尋常性乾癬，乾癬性関節炎，ぶどう膜炎，非喫煙者及び非飲酒者であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は薬剤誘発性肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，薬剤誘発性肺炎は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は，咽喉痛を伴う悪寒戦慄，咳嗽，発熱，鼻分泌物及び労作時呼吸困難を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は 38°C の発熱を来し，咳嗽が続いた。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 39°C の発熱で来院した。同日，被験者は入院し，肺臓炎と診断された。20[redacted] 年 [redacted] 月 [redacted] 日，コンピュータ断層撮影（CT）検査及び胸部 X 線検査が行われ，肺臓炎が明らかになった。血液培養とレジオネラ及び肺炎球菌の尿中抗原検査の結果は陰性であった。20[redacted] 年 [redacted] 月 [redacted] 日，薬剤誘発性肺炎が強く疑われた。20[redacted] 年 [redacted] 月 [redacted] 日，胸部 CT 検査が行われ，肺炎の軽快が確認された。20[redacted] 年 [redacted] 月 [redacted] 日，臨床所見は改善し，自覚症状も消失した。同日，被験者は退院した。

ステロイド療法下にて再度胸部 X 線検査が行われ，軽快が確認された。20[redacted] 年 [redacted] 月 [redacted] 日，ステロイド療法が中止され，胸部 X 線検査により著明な変化は認められなかった。被験者に症状はなく，本事象は消失したと判断された。

投与された薬剤は，ジスロマック，メロペネム，メチルプレドニゾロンコハク酸エステルナトリウム，プレドニン，カロナール及びダイフェンであった。

The patient's past medications include:

PROPETO for PSORIASIS VULGARIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Blinded)

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1) Pneumonia (10035664) (Pneumonia (10035664)) [v.21.1] [10035664]

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 ABT-494 (Blinded)

Event of DRUG INDUCED PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] CHEST CT:** Improvement of pneumonia

[redacted] **20[redacted] CHEST X-RAY:** Calcification of paratracheal lymph node

[redacted] **20[redacted] CHEST X-RAY:** Improved (on steroid therapy)

[redacted] **20[redacted] CHEST X-RAY:** Improved (on steroid therapy)

[redacted] **20[redacted] CHEST X-RAY:** Improved (steroid therapy stopped)

[redacted] **20[redacted] CHEST X-RAY:** No remarkable change (off steroid therapy)

[redacted] **20[redacted] CT:** PNEUMONITS

[redacted] **20[redacted] CXR:** PNEUMONITIS

[redacted] **20[redacted] CYTOMEGALOVIRUS ANTIGEN BLOOD:** Negative

[redacted] **20[redacted] INFLUENZA TEST (NASAL MUCUS):** Negative

[redacted] **20[redacted] LEGIONELLA PNEUMOPHILA ANTIGEN URINE:** Negative

[redacted] **20[redacted] MYCOBACTERIUM TUBERCULOSIS SPUTUM:** Negative

[redacted] **20[redacted] PHARYNX MYCOPLASMA (THROAT SWAB):** Negative

[redacted] **20[redacted] PNEUMOCUCCUS THEA ANTIGEN URINE:** Negative

[redacted] **20[redacted] B-D GLUCAN BLOOD:** Negative