[redacted] 20[redacted] **EKG:** Sinus Rhythm, Low QRS voltage in chest leads, Nonspecific T Wave abnormality

[redacted] 20[redacted] **GLASCO COMA SCALE:** 3 No units

[redacted] 20[redacted] **GLOBULIN TOTAL:** 2.2 G/DL (normal 2.0 to 4.5)

[redacted] 20[redacted] **GLUCOSE:** 368 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **GLUCOSE:** 181 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **OSMOLALITY CALC:** 301 mosm/kg (normal 270 to 350)

[redacted] 20[redacted] **POTASSIUM:** 3.9 MMOL/L (normal 3.5 to 5.2)

[redacted] 20[redacted] **PROTEIN:** 5.6 G/DL (normal 6.1 to 8.0)

[redacted] 20[redacted] **SCREENING EKG:** T wave abnormality

[redacted] 20[redacted] **SODIUM:** 148 MMOL/L (normal 133 to 146)

[redacted] 20[redacted] **XR ABDOMEN FOR FEEDING TUBE:** NG tube is well advanced into the proximal stomach region - as above. Tip overlies the cardia of the stomach near the GE junction.

[redacted] 20[redacted] **XR CHEST 1 VW- ORGAN DONATION:** No acute abnormality.

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Anaemia: Intermittent.
Lymphocyte count decreased ([redacted]20[redacted]): Intermittent.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
血中クレアチンホスホキナーゼ増加				X
腎結石症	X			

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

Medical History	Onset Year
CORONARY ARTERY DISEASE: NO FURTHER DETAIL	20[redacted]
DIABETES MELLITUS: BORDERLINE DIABETES	20[redacted]
DRUG ALLERGIES/REACTIONS: AZATHIOPRINE	20[redacted]
DRUG ALLERGIES/REACTIONS: MERCAPTOPURINE	20[redacted]
DRUG ALLERGIES/REACTIONS: PENICILLINS	19[redacted]
DRUG ALLERGIES/REACTIONS: REMICADE	20[redacted]
DRUG ALLERGIES/REACTIONS: SULFASALAZINE	20[redacted]
EYE DISEASE/DISORDER: GLAUCOMA	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERLIPIDEMIA: NO FURTHER INFO	20[redacted]
KIDNEY DISORDER: ACUTE RENAL FAILURE	20[redacted]
LEFT SIDED UC	20[redacted]
MYOCARDIAL INFARCTION	20[redacted]
NEPHROLITHIASIS	20[redacted]
OTHER: ADENOMATOUS POLYP IN STOMACH	20[redacted]
OTHER: ADRENAL INSUFFICIENCY	20[redacted]
OTHER: BASAL CELL CARCINOMA	20[redacted]
OTHER: DEHYDRATION	20[redacted]
OTHER: ESOPHAGEAL DYSMOTILITY	20[redacted]
OTHER: FATIGUE	20[redacted]
OTHER: HIATAL HERNIA	20[redacted]
OTHER: HYPOKALEMIA	20[redacted]
OTHER: INFLAMMATORY ARTHRITIS	20[redacted]
OTHER: INTERMITTENT NAUSEA	20[redacted]

OTHER: JOINT PAIN	20[redacted]
OTHER: LIPODERMATOSCLEROSIS	20[redacted]
OTHER: MUSCLE CRAMPS	20[redacted]
OTHER: OBESITY	20[redacted]
OTHER: PULMONARY EMBOLUS	20[redacted]
OTHER: RIGHT SHOULDER PARTIAL ROTATOR CUFF TEAR	20[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: CHRONIC VENOUS STASIS OF LOWER EXTREMITIES	20[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: DEEP VEIN THROMBOSIS	20[redacted]
PNEUMONIA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: RIGHT TOTAL KNEE ARTHROPLASTY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 373	318
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 374		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
WARFARIN	5 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: Q 8 WEEKS	Y-M: 20[redacted]
HYDROCORTISONE	15 mg	OTHER: IN AM	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: Q 8 WEEKS	Y-M: 20[redacted]
CALCIUM FRUCTOBORATE;HYALURONIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted]
HYDROCORTISONE	5 mg	OTHER: EVERY PM	Y-M: 20[redacted] / -354
MESALAZINE	1.2 g	QID	Y: 20[redacted]
MESALAZINE	2.4 g	BID	Y: 20[redacted]
PREDNISONE	5 mg	QD	Y: 20[redacted]
LATANOPROST	1 gtt	QD	Y: 20[redacted]
AZATHIOPRINE	200 mg	QD	Y: 20[redacted]
BUDESONIDE	3 mg	QD	Y: 20[redacted]
MERCAPTOPURINE	100 mg	QD	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]	ONGOING
WARFARIN	5 mg	QD	Y-M: 20[redacted]	ONGOING
HYDROCORTISONE	15 mg	OTHER: IN AM	Y-M: 20[redacted]	Y-M: 20[redacted] / 490
CALCIUM FRUCTOBORATE;HYALURONIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
HYDROCORTISONE	5 mg	OTHER: EVERY PM	Y-M: 20[redacted] / -354	Y-M: 20[redacted] / 490
POTASSIUM CITRATE	20 mEq	BID	Y-M: 20[redacted] / 27	ONGOING
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	1 L	OTHER: ONCE	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 89
FENTANYL	25 ug	OTHER: ONCE	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 89
GENTAMICIN	120 mg	OTHER: ONCE	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 89

OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 89	ONGOING
VANCOMYCIN	1,250 mg	OTHER: ONCE	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 89
NITROFURANTOIN	100 mg	BID	Y-M: 20[redacted] / 90	ONGOING
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 90	ONGOING
HYDROCORTISONE	12.5 mg	OTHER: QOD	Y-M: 20[redacted] / 460	ONGOING
HYDROCORTISONE	15 mg	OTHER: QOD	Y-M: 20[redacted] / 460	ONGOING
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 1128	Y-M: 20[redacted] / 1138
LATANOPROST	1 gtt	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	RIGHT SIDED RENAL STONES
Preferred term	腎結石症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 462 / 89
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	463 / 90
Duration of AE	2 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MEDICAL HISTORY OF KIDNEY STONES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Creatine Phosphokinase (CPK) Elevation

Event Description	ELEVATED CK
Preferred term	血中クレアチンホスホキナーゼ増加
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1470 / 1097
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1548 / 1175
Duration of AE	79 DAYS

Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，右腎結石の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），腎結石症，急性腎不全，深部静脈血栓症，肺塞栓症，境界型糖尿病，高脂血症，肥満，脱水，副腎機能不全，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与462日後＊　，被験者は右腎結石を発現した。投与463日後＊，右腎結石は消失した。

本事象発現前の投与364日後＊　，被験者は右腎結石症（非重篤）を発現した。

投与462日後＊　，被験者は血尿のため入院した。被験者は軽度の右水腎症及び軽度の右腎萎縮を伴う大きな右腎盂結石があった。被験者は腎結石症の病歴があった。同日，被験者は腎結石砕石術を受け，結石が破砕された。被験者は一晩観察された。投与463日後＊　，被験者は退院した。

投与された薬剤は，ゲンタマイシン，バンコマイシン，オキシコドン，macrobid 及びアセトアミノフェンであった。

Causality for ABT-494 (Open Label)

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1)　Renal stone (10038527)　(Nephrolithiasis (10029148))　[v.22.0]　[10038527]

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 (Open Label)

Event of RIGHT SIDED RENAL STONES

- Investigator: Medical history of kidney stones.

- AbbVie: Event is most like related to the past history nephrolithiasis.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X	X		
帯状疱疹				X
術後イレウス	X			

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	19[redacted]
HYPERTENSION	20[redacted]
OTHER: 6-MERCAPTIPERINE ALLERGY	20[redacted]
OTHER: ACNE	20[redacted]
OTHER: CHICKEN POX	19[redacted]
OTHER: CYTOMEGALOVIRUS INFECTION	20[redacted]
OTHER: FATIGUE	20[redacted]
OTHER: FUNGAL INFECTION OF TOENAIL	20[redacted]
OTHER: HEMORRHOIDS	20[redacted]
OTHER: HERPES ZOSTER	20[redacted]
OTHER: INCOMPLETE RIGHT BUNDLE BRANCH BLOCK	20[redacted]
OTHER: INTERMITTENT ELEVATED LIVER ENZYMES	20[redacted]
OTHER: INTERMITTENT HAND WARTS	20[redacted]
OTHER: INTERMITTENT HEADACHES	19[redacted]
OTHER: INTERMITTENT LEG CRAMPS	20[redacted]
OTHER: INTERMITTENT ORAL APHTHOUS ULCERS	20[redacted]
OTHER: MILD SHORTNESS OF BREATH	20[redacted]
OTHER: PRIMARY SCLEROSING CHOLANGITIS	20[redacted]
OTHER: RECTAL POLYPS	20[redacted]
OTHER: SHINGLES	20[redacted]
OTHER: SUN DAMAGE	20[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]
OTHER: WEIGHT LOSS	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 190	134

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: WEEKLY	Y-M: 20[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -309
UREA	40 %	BID	Y-M: 20[redacted] / -153
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -89
CALCIUM;VITAMIN D NOS	800 IU	QD	Y-M: 20[redacted] / -90
LISINOPRIL	10 mg	QD	Y-M: 20[redacted] / -56
MERCAPTOPURINE	50 mg	BID	Y: 19[redacted]
MESALAZINE	2400 mg	QD	Y: 19[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -309	ONGOING
UREA	40 %	BID	Y-M: 20[redacted] / -153	ONGOING
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -89	ONGOING
CALCIUM;VITAMIN D NOS	800 IU	QD	Y-M: 20[redacted] / -90	ONGOING
LISINOPRIL	10 mg	QD	Y-M: 20[redacted] / -56	ONGOING
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 42
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 49
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 56
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 63
VALACICLOVIR	1 g	TID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 67
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 70
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 77
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted] / 78	Y-M: 20[redacted] / 106
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 107	Y-M: 20[redacted] / 117
PREDNISONE	17.5 mg	QD	Y-M: 20[redacted] / 118	Y-M: 20[redacted] / 123
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 124	Y-M: 20[redacted] / 130
PREDNISONE	12.5 mg	QD	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 148
CEFAZOLIN	2 g	OTHER: ONCE	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
CELECOXIB	400 mg	OTHER: ONCE	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
DEXAMETHASONE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
FENTANYL	100 ug	OTHER: ONCE	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
FENTANYL	50 ug	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
GABAPENTIN	600 mg	OTHER: ONCE	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
HEPARIN	5000 IU	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 158
HYDROMORPHONE	0.2 mg	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
MAGNESIUM OXIDE	400 mg	BID	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 151
METRONIDAZOLE	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
MIDAZOLAM	1 mg	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 151
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 163
PHENYLEPHRINE	100 ug	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
PHENYLEPHRINE	200 ug	PRN	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149
PROPOFOL	150 mg	OTHER: ONCE	Y-M: 20[redacted] / 149	Y-M: 20[redacted] / 149

CHLORHEXIDINE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 150 Y-M: 20[redacted] / 163
OXYCODONE	10 mg	PRN	Y-M: 20[redacted] / 150 Y-M: 20[redacted] / 151
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted] / 150 Y-M: 20[redacted] / 161
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 151 Y-M: 20[redacted] / 157
BENZOCAINE;MENTHA X PIPERITA;MENTHOL	1 OTHER: LOZENGE	PRN	Y-M: 20[redacted] / 152 Y-M: 20[redacted] / 152
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	500 mg	PRN	Y-M: 20[redacted] / 152 Y-M: 20[redacted] / 162
PHENOL	1 OTHER: SPRAY	PRN	Y-M: 20[redacted] / 152 Y-M: 20[redacted] / 152
LISINOPRIL	10 mg	QD	Y-M: 20[redacted] / 153 Y-M: 20[redacted] / 163
PANTOPRAZOLE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 154 Y-M: 20[redacted] / 154
IBUPROFEN	600 mg	PRN	Y-M: 20[redacted] / 155 Y-M: 20[redacted] / 163
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 161 Y-M: 20[redacted] / 163
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 162 Y-M: 20[redacted] / 163

Event #1: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER (SHINGLES)ON LEFT ANTERIOR AND LATERAL CHEST WALL IN REGION OF T5.
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 117 / 61
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	130 / 74
Duration of AE	14 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎

AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 190 / 134
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	219 / 163 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	30 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	POST-PROCEDURAL ILEUS
Preferred term	術後イレウス
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 208 / 152 (18 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 154): Chloride: 98 [98 - 107] MMOL/L; [redacted]20[redacted] (RX DAY 156): Chloride: 96 [98 - 107] MMOL/L; [redacted]20[redacted] (RX DAY 158): Chloride: 98 [98 - 107] MMOL/L; [redacted]20[redacted] (RX DAY 161): Chloride: 96 [98 - 107] MMOL/L

Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	216 / 160 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	EVENT PART OF UNDERLYING DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は米国の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，術後イレウス及び潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎及び体重減少であった。

Event 2 及び 3 の臨床経過：

投与190日後＊，被験者は潰瘍性大腸炎の悪化を発現した。投与208日後＊，被験者は術後イレウスを発現した。投与216日後＊，術後イレウスは消失した。投与219日後＊，潰瘍性大腸炎の悪化は消失した。

被験者は，症状の進行を伴う難治性潰瘍性大腸炎のため手術を受けることを選択した。投与205日後＊，被験者は血便増加及び全般的な健康不良のため入院した。同日，被験者は腹腔鏡下直腸結腸全摘術，回腸瘻造設を受けた。投与208日後＊，被験者はイレウスを発現したことが悪心及び嘔吐から明らかとなった。減圧のため鼻腔栄養チューブが数日間設置された。鼻腔栄養チューブが除去され，被験者は経口食を徐々に開始した。投与216日後＊，術後イレウスは消失した。被験者は食事許容となった。投与219日後＊，被験者は臨床的に安定した状態で退院した。

投与された薬剤は，neurontin，ヘパリン，hibiclens，lovenox，dilaudid，イブプロフェン，リシノプリル，酸化マグネシウム，versed，zofran，protonix，フェニレフリン，prednisone，プロポフォール，デカドロン，メトロニダゾール，ancef，benzocaine w/menthol，アセトアミノフェン，ラクトリンゲル及びフェンタニルであった。

Causality for ABT-494 (Open Label)

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1) Postoperative ileus (10054048) (Postoperative ileus (10054048)) [v.21.1] [10054048]

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

2) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.21.1] [10009901]

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 (Open Label)

Event of POST-PROCEDURAL ILEUS

- Investigator: Event part of underlying disease

- AbbVie: Event is more likely related to recent laproscopic total proctocolectomy and ileostomy.

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Ulcerative colitis

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT OF ABDOMEN AND PELVIS:** FLUID-FILLED AND DILATED LOOPS OF PROXIMAL SMALL BOWEL TO OVER 4.0 CM. TRANSITION TO DECOMPRESSED DISTAL SMALL BOWEL IN THE CENTRAL PELVIS SUGGESTIVE OF SOME ELEMENT OF MECHANICAL OBSTRUCTION. THE DISTAL SMALL BOWEL IS DECOMPRESSED BUT SEVERAL LOOPS CONTAIN INTERNAL FLUID.

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes zoster: One dermatome.

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

Reason for Narrative

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

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

Medical History	Onset Year
DIABETES MELLITUS	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
OSTEOARTHRITIS: RIGHT AND LEFT KNEE ARTHRITIS	19[redacted]
OTHER: 5TH METATARSAL FOOT FRACTURE	20[redacted]
OTHER: HYPERCHOLESTEROLEMIA	20[redacted]
OTHER: LEFT KNEE INJURY	19[redacted]
OTHER: RIGHT KNEE INJURY	19[redacted]
OTHER: SLEEP APNEA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: 5TH METATARSAL REPAIR	20[redacted]
SURGERY: ACL RECONSTRUCTION SURGERY	19[redacted]
SURGERY: LEFT KNEE ARTHROSCOPY	19[redacted]
SURGERY: RIGHT KNEE ARTHROSCOPY	19[redacted]
SURGERY: VASECTOMY	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	ORAL	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted] / 57	[redacted] / 359	303
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted] / 360		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMLODIPINE	10 mg	QD	Y-M: [redacted]
MESALAZINE	2.4 g	QD	Y-M: [redacted]
MESALAZINE	1200 mg	BID	Y-M: [redacted]
MESALAZINE	4.8 g	QD	Y-M: [redacted]
MESALAZINE	750 mg	BID	Y-M: [redacted]
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
PREDNISONE	5 mg	QD	Y-M: [redacted]
PREDNISONE	10 mg	QD	Y-M: [redacted]
PREDNISONE	5 mg	QD	Y-M: [redacted]
TERBINAFINE	250 mg	QD	Y-M: [redacted] / -319
VITAMINS NOS	1 DF	QD	Y: [redacted]
AMLODIPINE	5 mg	QD	Y: [redacted]
ATORVASTATIN	80 mg	QD	Y: [redacted]
FENOFIBRATE	145 mg	QD	Y: [redacted]
BENAZEPRIL	10 mg	BID	Y: [redacted]
CALCIUM	1 DF	QD	Y: [redacted]
IRON	1 DF	QD	Y: [redacted]
METFORMIN	500 mg	BID	Y: [redacted]
PROBIOTICS NOS	1 DF	QD	Y: [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] / 783	ONGOING
AMIODARONE	450 mg	OTHER: IV DRIP	Y-M: 20[redacted] / 783	Y-M: 20[redacted] / 785
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 783	ONGOING
SULFAMETHOXAZOLE;TRIMETHOPRIM	800/160 mg	QD	Y-M: 20[redacted] / 939	Y-M: 20[redacted] / 979
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 979	Y-M: 20[redacted] / 985
MAGNESIUM SULFATE	2 g	OTHER: ONE TIME	Y-M: 20[redacted] / 985	Y-M: 20[redacted] / 985
POTASSIUM	20 mEq	OTHER: ONE TIME	Y-M: 20[redacted] / 985	Y-M: 20[redacted] / 985
SOTALOL	120 mg	QD	Y-M: 20[redacted] / 985	Y-M: 20[redacted] / 1090
MEXILETINE	200 mg	QD	Y-M: 20[redacted] / 1090	ONGOING
VITAMINS NOS	1 DF	QD	Y: 19[redacted]	ONGOING
ATORVASTATIN	80 mg	QD	Y: 20[redacted]	ONGOING
FENOFIBRATE	145 mg	QD	Y: 20[redacted]	ONGOING
CALCIUM	1 DF	QD	Y: 20[redacted]	ONGOING
IRON	1 DF	QD	Y: 20[redacted]	ONGOING
METFORMIN	500 mg	BID	Y: 20[redacted]	ONGOING
PROBIOTICS NOS	1 DF	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Adjudicated Gastrointestinal Perforations

Event Description	PERFORATION OF SIGMOID COLON
Preferred term	大腸穿孔
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1047 / 688
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	1047 / 688
Duration of AE	1 DAY
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ACUTE ANGLE OF SIGMOID COLON
Discontinued Study Drug Due to the Event	NO

SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

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

Event Description	VENTRICULAR TACHYCARDIA
Preferred term	心室性頻脈
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1142 / 783
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	1144 / 785
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ANGINA AND PREMATURE VENTRICULAR CONTRACTIONS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #3: Serious Adverse Event

Event Description	VENTRICULAR TACHYCARDIA
Preferred term	心室性頻脈
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1344 / 985
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	1348 / 989
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ANGINA AND PREMATURE VENTRICULAR CONTRACTIONS
Discontinued Study Drug Due to the Event	NO

SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Event #4: Serious Adverse Event

Event Description	VENTRICULAR TACHYCARDIA
Preferred term	心室性頻脈
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1448 / 1089
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	1451 / 1092
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HISTORY OF VENTRICULAR TACHYCARDIA, HAD MEDICATION SWITCHED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，S 状結腸穿孔の事象を発現した。関連する病歴は，潰瘍性大腸炎，糖尿病，非喫煙者，元煙草使用者（葉巻）及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与1047日後＊ ，被験者は S 状結腸穿孔を発現した。投与1047日後＊ ，S 状結腸穿孔は消失した。

投与1046日後＊ ，被験者は本治験のため結腸内視鏡検査を受けた。投与1047日後＊ ，被験者は腹痛及び胃の膨満のため救急科を受診した。被験者は華氏 100°F の発熱があった。排便は少量，液状であり，血性ではなく，メレナもなかった。X 線検査及び CT 検査により，S 状結腸穿孔が確認された。被験者は試験開腹，S 状結腸切除及び骨盤膿瘍ドレナージを受けた。投与1051日後＊，被験者は退院した。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted])

APRISO for ULCERATIVE COLITIS ([redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Perforation colon (10034407) (Large intestine perforation (10023804)) [v.23.0] [10034407]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, outcome unknown

Alternative Etiology for UPADACITINIB (Open Label)

Event of PERFORATION OF SIGMOID COLON

- Investigator: Acute angle of sigmoid colon.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **COLONOSCOPY:** No inflammation seen (normal mucosa)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，心室性頻脈の事象を発現した。関連する病歴は，高コレステロール血症，高血圧，睡眠時無呼吸，糖尿病，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与1142日後＊，被験者は心室性頻脈を発現した。投与1144日後＊，心室性頻脈は消失した。

投与1142日後＊　，被験者は主治医に浮動性めまいを訴えた。被験者は心電図異常があり，救急治療室へ搬送された。同日，被験者は心室性頻脈のため入院した。被験者は冠血管造影及び経皮的インターベンションを受けた。投与1144日後＊，被験者は退院した。

投与された薬剤は，アミオダロン及びアスピリンであった。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

APRISO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for UPADACITINIB (Open Label)

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1)　Ventricular tachycardia (10047302)　(Ventricular tachycardia (10047302))　[v.23.1]　[10047302]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, outcome unknown

Alternative Etiology for UPADACITINIB (Open Label)

Event of VENTRICULAR TACHYCARDIA

- Investigator: Angina and premature ventricular contractions

- AbbVie: Risk factors include pre-existing hypertension, diabetes, and hypercholesterolemia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CARDIAC BIOMARKERS:** Not available

[redacted] **20[redacted] COLONOSCOPY:** No inflammation seen (normal mucosa)

[redacted] **20[redacted] COLONOSCOPY:** No inflammation seen (normal mucosa)

[redacted] **20[redacted] CORONARY ANGIOGRAM:** Not reported

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

[redacted] **20[redacted] ECG:** Not available

[redacted] **20[redacted] EKG:** Sinus rhythm occasional ectopic ventricular beat ST Depression plus diffuse nonspecific T-abnormality consider subendocardial injury/ischemia

[redacted] **20[redacted] TROPONIN:** 0.03 U/L (normal <0.04)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，心室性頻脈の事象を発現した。関連する病歴は，高コレステロール血症，高血圧，睡眠時無呼吸，潰瘍性大腸炎，糖尿病，非喫煙者，元煙草使用者

（葉巻）及び現飲酒者（1 日 2 杯未満）であった。

Event 3 の臨床経過：

投与1344日後＊ ，被験者は心室性頻脈を発現した。投与1348日後＊ ，心室性頻脈は消失した。

本事象発現前の 投与1142日後＊に，被験者は重篤な心室性頻脈を発現し，投与1144日後＊ に消失した。

投与1344日後＊ ，被験者は失神寸前の状態，動悸及び胸痛を伴う心室性頻脈のため入院した。被験者は頭部ふらふら感，動悸，胸部不快感及びふらつきを訴えた。投与1346日後＊ ，被験者は電気生理試験及び心アブレーションを受けたが心アブレーションは成功しなかった。投与1347日後＊ ，被験者は二腔植込み型除細動器の設置術を受け，合併症はなかった。投与1348日後＊，被験者は退院した。

治験責任医師によると，本事象に関連する危険因子は，肥満，冠動脈疾患，糖尿病及び高脂血症であった。

投与された薬剤はソタロールであった。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted])

APRISO for ULCERATIVE COLITIS ([redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

---

1) Ventricular tachycardia (10047302) (Ventricular tachycardia (10047302)) [v.23.1] [10047302]

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 (Open Label)

Event of VENTRICULAR TACHYCARDIA

- Investigator: Angina and premature ventricular contractions

- AbbVie: Risk factors include pre-existing hypertension, diabetes and hypercholesterolemia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 35.42 kg/m2

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

[redacted] **20[redacted] EKG:** EP Interp, Normal axis, no ectopy Subltle ST depressions V5 and V6 No T wave inversions.

[redacted] **20[redacted] EP STUDY WITH CARDIAC ABLATION:** Recurrent ventricular tachycardia in need of ICD implantation
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，心室性頻脈の事象を発現した。関連する病歴は，高コレステロール血症，高血圧，潰瘍性大腸炎（左側），糖尿病及び現飲酒者（1 日 2 杯未満）であった。

Event 4 の臨床経過：

投与1448日後＊，被験者は心室性頻脈を発現した。投与1451日後＊，心室性頻脈は消失した。

本事象の発現前に，被験者は2回の心室性頻脈（投与の約38ヵ月後＊及び投与の約44ヵ月後＊に1回ずつ）の後，投与の約44ヵ月後＊に自動植込み型除細動器を装着していた。

投与1448日後＊，被験者は自動植込み型除細動器の抜去に伴う浮動性めまい及び胸痛を訴え，救急治療室を受診した。被験者はペースメーカーの問診を受けた。入院中はソタロールが中止された。投与1451日後＊，被験者は退院した。

治験責任医師によると，被験者には心室性頻脈の既往の危険因子があった。

投与された薬剤は，メキシレチン及びアミオダロンであった。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

APRISO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for UPADACITINIB (Open Label)

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1) Ventricular tachycardia (10047302) (Ventricular tachycardia (10047302)) [v.24.0] [10047302]

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 (Open Label)

Event of VENTRICULAR TACHYCARDIA

- Investigator: History of Ventricular Tachycardia; had medication switched

- AbbVie: Risk factors include pre-existing hypertension, diabetes and hypercholesterolemia. Additionally, subject has had multiple episodes of ventricular tachycardia leading to dual chamber ICD implantation in [redacted] 20[redacted].

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 36.9 kg/m2

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
不安	X			
うつ病	X			
企図的過量投与	X			
自殺念慮	X			

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

Medical History	Onset Year
DIABETES MELLITUS: BORDERLINE	NOT REPORTED
EXTENSIVE UC/PANCOLITIS	20[redacted]
MIGRAINE HEADACHE	20[redacted]
OTHER: BIPOLAR	NOT REPORTED
OTHER: DRUG ALLERGY TO ASOCOL	20[redacted]
OTHER: DRUG ALLERGY TO ASPIRIN	20[redacted]
OTHER: DRUG ALLERGY TO CODINE	20[redacted]
OTHER: DRUG ALLERGY TO REMICADE	20[redacted]
OTHER: DRUG ALLERGY TO TRAMADOL	20[redacted]
OTHER: NEUROPATHY	20[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: HIGH CHOLESTEROL	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.5 PACK	1	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 54	54
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 55	[redacted] / 418	364
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted] / 419	[redacted] / 643	225

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
GABAPENTIN	300 mg	QD	Y-M: [redacted]
MESALAZINE	1600 mg	BID	Y-M: [redacted]
MESALAZINE	800 mg	BID	Y-M: [redacted]
PARACETAMOL	1000 mg	OTHER: Q8 HRS PRN	Y-M: [redacted] / -306
RIZATRIPTAN	10 mg	PRN	Y-M: [redacted] / -286
ZOLPIDEM	5 mg	QD	Y-M: [redacted] / -248
ONDANSETRON	4 mg	TID	Y-M: [redacted] / -35
OXYCODONE;PARACETAMOL	5-325 mg	OTHER: 1 TAB Q6HRS X3DAYS PRN	Y-M: [redacted] / -35
GALCANEZUMAB	120 OTHER: MG/ML	OTHER: QMTH	Y-M: [redacted] / -44
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	5.86 g	OTHER: ONCE	Y-M: [redacted] / -1
SIMVASTATIN	20 mg	QD	Y: [redacted]
TOPIRAMATE	200 mg	BID	Y: [redacted]
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y: [redacted]
FLUPHENAZINE	25 mg	OTHER: Q MONTHLY	Y: [redacted]
VENLAFAXINE	75 mg	QD	Y: [redacted]
BENZATROPINE	1 mg	QD	Y: [redacted]
GOLIMUMAB	100 mg	OTHER: QMONTH	Y: [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
GABAPENTIN	300 mg	QD	Y-M: 20[redacted]	ONGOING
PARACETAMOL	1000 mg	OTHER: Q8 HRS PRN	Y-M: 20[redacted] / -306	ONGOING
RIZATRIPTAN	10 mg	PRN	Y-M: 20[redacted] / -286	ONGOING
ZOLPIDEM	5 mg	QD	Y-M: 20[redacted] / -248	ONGOING
ONDANSETRON	4 mg	TID	Y-M: 20[redacted] / -35	ONGOING
OXYCODONE;PARACETAMOL	5-325 mg	OTHER: 1 TAB Q6HRS X3DAYS PRN	Y-M: 20[redacted] / -35	ONGOING
GALCANEZUMAB	120 OTHER: MG/ML	OTHER: QMTH	Y-M: 20[redacted] / -44	ONGOING
MACROGOL 3350;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	5.86 g	OTHER: ONCE	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 56
SIMVASTATIN	20 mg	QD	Y: 20[redacted]	ONGOING
TOPIRAMATE	200 mg	BID	Y: 20[redacted]	ONGOING
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING
FLUPHENAZINE	25 mg	OTHER: Q MONTHLY	Y: 20[redacted]	ONGOING
VENLAFAXINE	75 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 73
BENZATROPINE	1 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION
Preferred term	不安，うつ病，企図的過量投与，自殺念慮
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 484 / 66
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 67): NPTST015-ACETAMINOPHEN LEVEL: 140.10 [10 - 30] UG/ML; NPTST015-ACETAMINOPHEN LEVEL: 77.80 [10 - 30] UG/ML

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	491 / 73
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	SUBJECT STATED THAT SHE WAS HAVING FAMILY PROBLEMS AND BOYFRIEND PROBLEMS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，アセトアミノフェンの企図的過量投与，うつ病の悪化，不安の悪化及び自殺念慮の事象を発現した。関連する病歴は，高コレステロール，潰瘍性大腸炎，元喫煙者（1 日 0.5 箱を 1 年間），双極性，境界型糖尿病及び片頭痛であった。

Event 1 の臨床経過：

投与484日後＊　，被験者はアセトアミノフェンの企図的過量投与，うつ病の悪化，不安の悪化及び自殺念慮を発現した。投与491日後＊　，アセトアミノフェンの企図的過量投与，うつ病の悪化，不安の悪化及び自殺念慮は消失した。

投与484日後＊　　，被験者は入院した。被験者は観察のため問題行動フロアに入院した。入院中，被験者はグループミーティング及び精神科医とのプライベートセッションに出席し，よりよい対処技能，生活のストレス要因の特定及びそれらに対する対処方法を学習した。コロンビア自殺重症度評価尺度（C-SSRS）は 17 であった。投与薬剤は変更されなかった。被験者は人・場所・時間・状況について意識清明で見当識が保たれていると報告された。悪寒，発熱又は息切れは報告されなかった。心電図検査が実施され，正常洞調律であった。被験者は，疼痛を 10 段階中 5 と評価し，上腹部及び下腹部の両方の正中線部に発生しており，恒常的な鈍痛であると述べた。投与491日後＊，被験者は退院した。

治験責任医師によると，被験者は家族及び男友達の問題を抱えていると述べていた。

Causality for UPADACITINIB (Open Label)

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1) Active suicidal ideation (10071456) (Suicidal ideation (10042458)) [v.22.1] [10071456]

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

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

Dechallenge: Not Applicable

2) Anxiety aggravated (10048339) (Anxiety (10002855)) [v.22.1] [10048339]

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

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

Dechallenge: Not Applicable

3) Intentional overdose (10022523) (Intentional overdose (10022523)) [v.22.1] [10022523]

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

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

Dechallenge: Not Applicable

4) Depression aggravated (10012379) (Depression (10012378)) [v.22.1] [10012379]

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 (Open Label)

Event of INTENTIONAL OVERDOSE WITH ACETAMINOPHEN, INCREASED DEPRESSION, INCREASED ANXIETY, ACTIVE SUICIDAL IDEATION

- Investigator: Subject stated that she was having family problems and boyfriend problems.

- AbbVie: event is more likely related to pre-existing bipolar disorder. Additionally, per PI subject was having family and boyfriend problems.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ACETAMINOPHEN LEVEL:** 140.10 MCG/ML (normal 10.0 to 30.0)

[redacted] **20[redacted] ACETAMINOPHEN LEVEL:** 77.80 MCG/ML (normal 10.0 to 30.0)

[redacted] **20[redacted] BLOOD PRESSURE:** 121/87mmHg

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

[redacted] **20[redacted] HEART RATE:** 102 bpm

[redacted] **20[redacted] PAIN SCALE:** 5/10

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

[redacted] **20[redacted] SP02 (ROOM AIR):** 100 %

[redacted] **20[redacted] TEMPERATURE (ORAL):** 98.3 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
COVID-19	X			X
帯状疱疹				X

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

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: AZATHIOPRINE	20[redacted]
DRUG ALLERGIES/REACTIONS: DOXYCYCLINE	20[redacted]
DRUG ALLERGIES/REACTIONS: PREDNISONE - HYPERGLYCEMIA	20[redacted]
DRUG ALLERGIES/REACTIONS: SULFA	20[redacted]
DRUG ALLERGIES/REACTIONS: TACROLIMUS - MIGRAINES AND VOMITING	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: ATTENTION DEFICIT HYPERACTIVITY DISORDER	20[redacted]
OTHER: AUTO-IMMUNE ENTEROPATHY - ENTIRE SMALL BOWEL	20[redacted]
OTHER: AUTOIMMUNE ENTEROPATHY (DUODENUM ONLY)	20[redacted]
OTHER: LOW TESTOSTERONE	20[redacted]
OTHER: MIGRAINES	20[redacted]
OTHER: PREDNISONE -ECCHYMOSIS/EXCORIATIONS ON EXTREMITIES SINCE BEING ON LONG TERM STEROID USE.	20[redacted]
OTHER: SEASONAL ALLERGIES	19[redacted]

Prior Procedures	Procedure Year
SURGERY: CHOLEYCYSTECTOMY	20[redacted]
SURGERY: LEFT ROTATOR CUFF	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	FORMER			
CIGARETTES	NEVER			
CIGARS	CURRENT			

PIPES NEVER

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 166	110
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 167		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1.2 g	BID	Y-M: 20[redacted]-[redacted]
AMFETAMINE;DEXAMFETAMINE	20 mg	OTHER: QD PRN	Y-M: 20[redacted]-[redacted]
FEXOFENADINE;PSEUDOEPHEDRINE	ONE OTHER: ONE CAPSULE	OTHER: QD PRN	Y-M: 20[redacted]-[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]-[redacted]
CICLESONIDE	50 OTHER: MCG	OTHER: QD PRN	Y-M: 20[redacted]-[redacted]
DICYCLOVERINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]-[redacted]
TACROLIMUS	1.5 mg	BID	Y-M: 20[redacted]-[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	OTHER OTHER: NEEDLES PLACED	OTHER: EVERY 2 WEEKS	Y-M: 20[redacted]-[redacted]
DICYCLOVERINE	20 mg	PRN	Y-M: 20[redacted]-[redacted] / -178
LOPERAMIDE	5 mg	OTHER: BID PRN	Y-M: 20[redacted]-[redacted] / -178
IRON	325 mg	TID	Y-M: 20[redacted]-[redacted] / -14

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AMFETAMINE;DEXAMFETAMINE	20 mg	OTHER: QD PRN	Y-M: 20[redacted]-[redacted]	ONGOING

FEXOFENADINE;PSEUDOEPHEDRINE	ONE OTHER: ONE CAPSULE	OTHER: QD PRN	Y-M: 20[redacted]	ONGOING
DICYCLOVERINE	20 mg	PRN	Y-M: 20[redacted] / -178	ONGOING
LOPERAMIDE	5 mg	OTHER: BID PRN	Y-M: 20[redacted] / -178	ONGOING
BALSALAZIDE	3000 mg	BID	Y-M: 20[redacted] / 674	ONGOING
GABAPENTIN	UNK OTHER: UNK	OTHER: UNK	Y-M: 20[redacted] / 1058	Y-M: 20[redacted] / 1066
HYDROCODONE;PARACETAMOL	UNK OTHER: UNK	OTHER: UNK	Y-M: 20[redacted] / 1058	Y-M: 20[redacted] / 1066
LIDOCAINE	UNK OTHER: UNK	OTHER: UNK	Y-M: 20[redacted] / 1058	Y-M: 20[redacted] / 1066
METHYLPREDNISOLONE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 1058	Y-M: 20[redacted] / 1058
VALACICLOVIR	1 g	TID	Y-M: 20[redacted] / 1058	Y-M: 20[redacted] / 1064
MESALAZINE	4G/60ML OTHER: G/ML	OTHER: QOD	Y-M: 20[redacted] / 1432	ONGOING
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 1501	Y-M: 20[redacted] / 1506
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / 1501	Y-M: 20[redacted] / 1506
CORTICOSTEROIDS FOR SYSTEMIC USE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y: 20[redacted] / 793	Not reported

Event #1: Event of Interest - Herpes Zoster

Event Description	SHINGLES
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1224 / 1058
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1232 / 1066
Duration of AE	9 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	COVID 19 INFECTION
Preferred term	COVID-19
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1667 / 1501
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PER SUBI, PATIENT DEVELOPED COVID 19 DUE TO EXPOSURE TO COVID 19 INFECTION AND BEING UNVACCINATED DESPITE RECOMMENDATIONS.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，COVID-19 の感染症の事例を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者，現飲酒者（1 日 2 杯未満），現煙草使用者（葉巻）及び噛みタバコの元喫煙者であった。

Event 2 の臨床経過：

投与1667日後＊，被験者は COVID-19 の感染症を発現した。

投与1685日後＊，被験者は息切れのために入院した。

投与された薬剤は，ソル・メドロール，アジスロマイシン及びメチルプレドニゾロンであった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for AUTOIMMUNE ENTEROPATHY ([redacted] 20[redacted] - [redacted] 20[redacted])

CANASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for AUTOIMMUNE ENTEROPATHY ([redacted] 20[redacted] - [redacted] 20[redacted])

TACROLIMUS for AUTOIMMUNE ENTEROPATHY ([redacted] 20[redacted] - [redacted] 20[redacted])

METAMUCIL for EXACERBATION OF UC (LOOSE STOOLS) and EXACERBATION OF UC ([redacted] 20[redacted] - [redacted] 20[redacted])

SULFA for UNKNOWN INDICATION

DOXYCYCLINE for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1) COVID-19 (10084268) (COVID-19 (10084268)) [v.24.1] [10084268]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Open Label)

Event of COVID 19 INFECTION

- Investigator: Per sub-investigator, patient developed COVID-19 due to COVID-19 infection and being unvaccinated despite recommendations.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 23 kg/m2

[redacted] **20[redacted] BODY WEIGHT:** 7[redacted] KG

[redacted] **20[redacted] COVID-19 TEST:** Positive

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes zoster: One dermatome. Study drug interrupted.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
不安定狭心症	X			X
冠動脈疾患				X
帯状疱疹				X

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

Medical History	Onset Year
CORONARY ARTERY DISEASE: MID RIGHT CORONARY ARTERY, DISTAL RIGHT CORONARY ARTERY, PROXIMAL DESCENDING ARTERY, PROXIMAL CIRCUMFLEX AND MID CIRCUMFLEX	20[redacted]
CORONARY ARTERY DISEASE: MULTIPLE ARTERIES	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HYPERLIPIDEMIA: ELEVATED CHOLESTEROL	20[redacted]
HYPERTENSION	20[redacted]
MYOCARDIAL INFARCTION	20[redacted]
OTHER: ANXIETY	20[redacted]
OTHER: CARDIAC STENTS	20[redacted]
OTHER: CARDIAC STENTS	20[redacted]
OTHER: CARDIAC STENTS	20[redacted]
OTHER: DIVERTICULOSIS	19[redacted]
OTHER: DYSPHAGIA	20[redacted]
OTHER: ERECTILE DYSFUNCTION	20[redacted]
OTHER: INTOLERANCE TO ENTOCORT	20[redacted]
OTHER: INTOLERANCE TO PREDNISONE	20[redacted]
OTHER: OBESITY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	19[redacted]
SURGERY: HERNIORRHAPHY	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	ORAL	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 57	[redacted] / 364	308
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted] / 365	[redacted] / 1548	1184

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]
MESALAZINE	1.2 g	QD	Y-M: 20[redacted]
ALPRAZOLAM	0.5 mg	PRN	Y-M: 20[redacted]
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]
MESALAZINE	1.2 g	QD	Y-M: 20[redacted]
LOPERAMIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISONE	5 mg	OTHER: ON AND OFF BETWEEN THE DATES LISTED DUE TO FLARES	Y-M: 20[redacted]
BALSALAZIDE	750 mg	TID	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY 10 DAYS	Y-M: 20[redacted]
DICYCLOVERINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]

BLINDED THERAPY	90 mg	OTHER: USTEKINUMAB V. PLACEBO EVERY 8 OR 12 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	10 mg/kg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]
LISINOPRIL	5 mg	QD	Y-M: 20[redacted]
HYDROCODONE;PARACETAMOL	10/325 mg	OTHER: 1 TABLET Q 4 HOURS PRN	Y-M: 20[redacted] / -4
SILDENAFIL	100 mg	PRN	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 541
LISINOPRIL	5 mg	QD	Y-M: 20[redacted]	ONGOING
HYDROCODONE;PARACETAMOL	10/325 mg	OTHER: 1 TABLET Q 4 HOURS PRN	Y-M: 20[redacted] / -4	Y-M: 20[redacted] / 371
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 251
ISOSORBIDE MONONITRATE	30 mg	QD	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 256
METOPROLOL	25 mg	QD	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 256
CIPROFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 269
ATROPINE	0.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
FENTANYL	12.5 OTHER: MCG	OTHER: THREE TIMES	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
FENTANYL	50 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
GLYCERYL TRINITRATE	200 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
HEPARIN	4000 OTHER: UNITS	OTHER: 2 TIMES	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
HEPARIN	5000 OTHER: UNITS	OTHER: 2 TIMES	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
HYDROMORPHONE	1 mg	OTHER: 3 TIMES	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
IOPAMIDOL	325 mg	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
LIDOCAINE	1 mL	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
PHENYLEPHRINE	40 OTHER: MCG	OTHER: 2 TIMES	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
TICAGRELOR	180 mg	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
TIROFIBAN	10.9 mg	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260

VERAPAMIL	2500 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
TICAGRELOR	90 mg	BID	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 272
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 273	ONGOING
TRAMADOL	50 mg	QD	Y-M: 20[redacted] / 325	Y-M: 20[redacted] / 327
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 333
LIDOCAINE	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
PROPOFOL	350 mg	OTHER: ONCE	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
SILDENAFIL	50 mg	PRN	Y-M: 20[redacted] / 363	Y-M: 20[redacted] / 826
ATORVASTATIN	80 mg	QD	Y-M: 20[redacted] / 644	ONGOING
SODIUM PHOSPHATE	1 OTHER: BOTTLE	OTHER: TWICE	Y-M: 20[redacted] / 680	Y-M: 20[redacted] / 680
PARACETAMOL	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 728	Y-M: 20[redacted] / 728
LORATADINE	10 mg	PRN	Y-M: 20[redacted] / 744	Y-M: 20[redacted] / 744
TADALAFIL	5 mg	QD	Y-M: 20[redacted] / 826	Y-M: 20[redacted] / 910
VALACICLOVIR	1 g	BID	Y-M: 20[redacted] / 834	Y-M: 20[redacted] / 839
VARICELLA ZOSTER VACCINE	1 OTHER: INJECTION	OTHER: ONCE	Y-M: 20[redacted] / 848	Y-M: 20[redacted] / 848
FEXOFENADINE	180 mg	PRN	Y-M: 20[redacted] / 882	Y-M: 20[redacted] / 1062
SODIUM PHOSPHATE	1 OTHER: BOTTLE	OTHER: TWICE	Y-M: 20[redacted] / 1009	Y-M: 20[redacted] / 1009
SILDENAFIL	100 mg	PRN	Y: 20[redacted]	Y-M: 20[redacted] / 256

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

Event Description	UNSTABLE ANGINA
Preferred term	不安定狭心症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 620 / 256
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 261): Erythrocytes: 3.7 [4.05 - 5.64] 10^12/L; Glucose: 5.5507 [3.607955 - 5.495193] MMOL/L; Hemoglobin: 119 [135 - 175] G/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	625 / 261
Duration of AE	6 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNDERLYING CORONARY ARTERY DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Event #2: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 679 / 315
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	700 / 336
Duration of AE	22 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Event of Interest - Adjudicated Cardiovascular events

Event Description	WORSENING CORONARY ARTERY DISEASE
Preferred term	冠動脈疾患
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1039 / 675
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]#

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，不安定狭心症の事象を発現した。関連する病歴は，潰瘍性大腸炎，心臓ステント，冠動脈疾患，心筋梗塞，コレステロール上昇，高血圧，非喫煙者及び少量の現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与620日後＊　，被験者は不安定狭心症を発現した。投与625日後＊　，不安定狭心症は消失した。

本事象発現前，被験者は投与の約16ヵ月後＊にうっ血性心不全（非重篤），投与の約17ヵ月後＊に尿路感染（非重篤）を発現した。

本事象発現前，被験者は胸部不快感があり，活動レベルがかなり低かった。投与624日後＊　，被験者は不安定狭心症による胸部圧迫感により入院した。被験者は，安静時疼痛，浮腫，起座呼吸及び発作性夜間呼吸困難（PND）を否定した。被験者はベータ受容体遮断薬及び硝酸塩の投与により改善しなかった。投与624日後＊　，被験者は薬剤溶出性ステント留置を伴う心カテーテル検査，薬剤溶出性ステント留置を伴う右冠動造影及び薬剤溶出性ステント留置を伴う左冠動造影を受けた。

経皮的インターベンション左前下行枝，経皮的インターベンション中間枝，経皮的インターベンション回旋枝近位部，経皮的インターベンション右冠動脈近位部，経皮的インターベンション右冠動脈中央部が行われた。インターベンションには PTCA 冠動脈ステント留置，カッティングバルーン血管形成を含んでいた。合併症は発現しなかった。投与625日後＊　，被験者は退院し，退院時に心不全の症状は完全に消失していた。

被験者の NYHA スコアは III（日常生活以下の身体活動であっても症状がみられるため，身体活動に高度制限がある。安静時にのみ症状がない）であった。

投与された薬剤は，ヘパリン，versed，neosynephrine，チカグレロル，アトロピン，ニトログリセリン，ベラパミル，isovue 370，一硝酸イソソルビド，シプロフロキサシン，aggrastat 及びコハク酸メトプロロールであった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Unstable angina (10046251) (Angina unstable (10002388)) [v.22.0] [10046251]

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 (Open Label)

Event of UNSTABLE ANGINA

- Investigator: Underlying coronary artery disease.

- AbbVie: Event is more likely related to pre-existing history of coronary artery disease and myocardial infarction. Elevated cholesterol and hypertension are additional risk factors.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** 160/100

[redacted] **20[redacted] BODY TEMPERATURE:** 36.8 Degrees C

[redacted] **20[redacted] BUN:** 12 mg/dL (normal 6 to 24)

[redacted] **20[redacted] CALCIUM:** 9.1 mg/dL (normal 8.7 to 10.2)

[redacted] **20[redacted] CARDIAC CATHETERIZATION:** Proximal LAD: Proximal curcumflex: 80% stensosis Ramus intermedius: 90%stenosis Proximal RCA: 90% stenosis Mid-RCA: 85% stenosis

[redacted] **20[redacted] CL:** 106 mmol/L (normal 97 to 108)

[redacted] **20[redacted] CO2:** 27 mmol/L (normal 20 to 32)

[redacted] **20[redacted] CREATININE:** 0.80 mg/dL (normal 0.76 to 1.27)

[redacted] **20[redacted] ECG:** Normal sinus rhythm, inferior infarct (age undetermined)

[redacted] **20[redacted] GLUCOSE:** 100 mg/dL (normal 65 to 99)

[redacted] **20[redacted] HEART RATE:** 72 bpm

[redacted] **20[redacted] HEMOGLOBIN:** 11.9 G/DL (normal 13.5 to 17.5)

[redacted] **20[redacted] NA:** 140 mmol/L (normal 136 to 146)

[redacted] **20[redacted] POTASSIUM:** 4.4 mmol/L (normal 3.7 to 5.4)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.70 million/mcl (normal 4.05 to 5.64)

[redacted] **20[redacted] RESPIRATORY RATE:** 16 BPM

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Coronary artery disease: Exertional angina.
Herpes zoster: One dermatome. Study drug interrupted.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19 肺炎	X			X

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: ALLERGIES	20[redacted]
OTHER: ANXIETY	19[redacted]
OTHER: CANKER SORES - MOUTH	20[redacted]
OTHER: HAY FEVER	20[redacted]
OTHER: HIATAL HERNIA	20[redacted]
OTHER: SINUS DRAINAGE	20[redacted]
OTHER: SPINAL STENOSIS (C7 -T1)	20[redacted]
OTHER: TINNITUS (BILATERAL EARS)	20[redacted]
PEPTIC ULCER DISEASE: SUPERFICIAL GASTRIC ULCERS	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 420	363
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 421		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
ETHINYLESTRADIOL;NORETHISTERONE	1 OTHER: TABLET	QD	Y-M: 20[redacted]
ESCITALOPRAM	20 mg	QD	Y-M: 20[redacted]
MESALAZINE	3.6 g	QD	Y-M: 20[redacted]
PLANTAGO OVATA	1 OTHER: TBL	QD	Y-M: 20[redacted]
PROBIOTICS NOS	10 BILLION CELLS OTHER: 1 CAPSULE	QD	Y-M: 20[redacted]
MESALAZINE	1600 mg	TID	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
DICYCLOVERINE	20 mg	OTHER: Q 6 HOURS; PRN	Y-M: 20[redacted]
MESALAZINE	1.2 g	TID	Y-M: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
MESALAZINE	1600 mg	TID	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
PARACETAMOL	325 mg	PRN	Y-M: 20[redacted]
MOMETASONE	1 METERED DOSE IN EACH NOSTRIL OTHER: MICROGRAMS	QD	Y-M: 20[redacted] / -332

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
ETHINYLESTRADIOL;NORETHISTERONE	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 719
ESCITALOPRAM	20 mg	QD	Y-M: 20[redacted]	ONGOING
DICYCLOVERINE	20 mg	OTHER: Q 6 HOURS; PRN	Y-M: 20[redacted]	ONGOING
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 719
PARACETAMOL	325 mg	PRN	Y-M: 20[redacted]	ONGOING

MOMETASONE	1 METERED DOSE IN EACH NOSTRIL OTHER: MICROGRAMS	QD	Y-M: 20[redacted] / -332	Y-M: 20[redacted] / 719
FLUTICASONE	50MCG/SPRAY OTHER: MCG/SPRAY	PRN	Y-M: 20[redacted] / 704	ONGOING
BENZONATATE	100 mg	TID	Y-M: 20[redacted] / 719	ONGOING
CODEINE;GUAIFENESIN	10-100/5ML mg	PRN	Y-M: 20[redacted] / 719	ONGOING
FLUTICASONE	50 OTHER: MCG	QD	Y-M: 20[redacted] / 719	ONGOING
ONDANSETRON	4 mg	TID	Y-M: 20[redacted] / 719	ONGOING
OXYCODONE;PARACETAMOL	5-325 mg	OTHER: TID FOR THREE DAYS	Y-M: 20[redacted] / 719	Y-M: 20[redacted] / 722
VERAPAMIL	120 mg	QD	Y-M: 20[redacted] / 719	Y-M: 20[redacted] / 721

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

Event Description	COVID-19 PNEUMONIA
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1128 / 708
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 717): Calcium: 2.021031 [2.120835 - 2.520051] MMOL/L; Chloride: 95 [98 - 112] MMOL/L; Leukocytes: 3.9 [4 - 10] 10^9/L; Lymphocytes: 0.6 [0.8 - 5] 10^9/L; Sodium: 132 [135 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 718): NPTST108-CRP: 4.8 [NOT REPORTED - 0.5] mg/dL

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	1139 / 719
Duration of AE	12 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID-19 INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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，COVID-19 肺炎の事象を発現した。関連する病歴は，裂孔ヘルニア，潰瘍性大腸炎，副鼻腔ドレナージ，枯草熱，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与1128日後＊，被験者は COVID-19 肺炎を発現した。投与1139日後＊　，COVID-19 肺炎は消失した。

投与1128日後＊，被験者は COVID-19 検査で陽性であった。

投与1137日後＊　，被験者は，COVID-19 検査で陽性となってから悪化した労作時呼吸困難，筋肉痛，咳嗽，悪心及び嘔吐で救急治療室を受診した。同日，被験者は症状安定化のために入院し，デキサメタゾンを静脈内投与された。被験者の状態は改善した。投与1139日後＊　，被験者は退院した。

投与された薬剤は，benzonatate，オンダンセトロン，オキシコドン・アセトアミノフェン合剤，デキサメタゾン及びグアイフェネシン・コデイン合剤であった。

The patient's past medications include:

MESALAMINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METAMUCIL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ASACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

LIALDA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 PNEUMONIA

- Investigator: Covid-19 Infection

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 24.5 kg/m2

[redacted] **20[redacted] CALCIUM:** 8.1 MEQ/L (normal 8.5 to 10.1)

[redacted] **20[redacted] CHEST XRAY:** CARDIAC SIZE WITHIN NORMAL LIMITS; MILD BILATERAL AIRSPACE, RIGHT MORE THAN LEFT; NO SIGNIFICANT PLEURAL EFFUSION; NO PNEUMOTHORAX

[redacted] **20[redacted] CHLORIDE:** 95 MEQ/L (normal 98 to 112)

[redacted] **20[redacted] CRP:** 4.8 mg/dL (normal <0.5)

[redacted] **20[redacted] CT ANGIO CHEST WO AND /OR W CONTRAST:** MILD TO MODERATE PATCHY AND CONFLUENT BILATERAL GROUNDGLASS OPACITIES CONSISTENT WITH MULTIFOCAL PNEUMONIA AND COMPATIBLE WITH HISTORY OF COVID 19 INFECTION. NO EVIDENCE OF ACUTE PULMONARY EMBOLISM.

[redacted] **20[redacted] ECG 12 LEAD:** NORMAL SINUS RHYTHM; NONSPECIFIC T WAVE ABNORMALITY WHEN COMPARED WITH ECG OF [redacted]20[redacted]; NONSPECIFIC T WAVE ABNORMALITY WORSE IN ANTERIOR-LATERAL LEADS.

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 0.6 K/UL (normal 0.8 to 5.0)

[redacted] 20[redacted] **SARS-COV-2 TEST:** Nasopharyngeal swab- Positive

[redacted] 20[redacted] **SODIUM:** 132 MEQ/L (normal 135 to 144)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.9 K/UL (normal 4.0 to 10)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19 肺炎	X			X
肺塞栓症	X	X		

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

Medical History	Onset Year
ANTERIOR PERIANAL ABSCESS	20[redacted]
ANTERIOR PERIANAL FISTULA	20[redacted]
EXTENSIVE UC/PANCOLITIS	19[redacted]
GOUT	20[redacted]
SEASONAL ALLERGIES	20[redacted]
SHIGELLA POSITIVE STOOL SAMPLE	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: ANTERIOR PERIANAL ABSCESS INCISION AND DRAINAGE	20[redacted]
PRIOR PROCEDURES: VASECTOMY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 57	57
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	[redacted] / 58	[redacted] / 114	57
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted] / 115	[redacted] / 484	370
M14-533 ABT-494 (LTE)	30 mg	ORAL	QD	[redacted] / 485	[redacted] / 904	420

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	160 mg	OTHER: ONCE	Y-M: 20[redacted]
ADALIMUMAB	80 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	QD	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
MIRIKIZUMAB	300 mg	OTHER: Q MONTH	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
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 414	Y-M: 20[redacted] / 428
AZITHROMYCIN	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 422	Y-M: 20[redacted] / 422
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 422	Y-M: 20[redacted] / 424
OXYGEN	8 L	OTHER: CONTINUOUS	Y-M: 20[redacted] / 422	Y-M: 20[redacted] / 430
ASCORBIC ACID	1500 mg	QD	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 452
COLECALCIFEROL	5000 IU	QD	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 452
DEXAMETHASONE	10 mg	BID	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 435
DEXAMETHASONE	6 mg	OTHER: ONCE	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 423
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 429
GUAIFENESIN	600 mg	BID	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 452
LACTOBACILLUS ACIDOPHILUS	1 OTHER: CAPLET	QD	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 452
OXYGEN	15 L	OTHER: CONTINUOUS	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 448
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 452

REMDESIVIR	200 mg	QD	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 427
SALBUTAMOL	180 ug	PRN	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 452
ZINC	220 mg	QD	Y-M: 20[redacted] / 423	Y-M: 20[redacted] / 452
BARICITINIB	4 mg	QD	Y-M: 20[redacted] / 424	Y-M: 20[redacted] / 430
FORMOTEROL;MOMETASONE	2 OTHER: PUFFS	PRN	Y-M: 20[redacted] / 424	Y-M: 20[redacted] / 452
TIOTROPIUM	18 ug	QD	Y-M: 20[redacted] / 424	Y-M: 20[redacted] / 452
LORAZEPAM	1 mg	PRN	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 452
CEFEPIME	2 g	BID	Y-M: 20[redacted] / 428	Y-M: 20[redacted] / 435
IBUPROFEN	800 mg	PRN	Y-M: 20[redacted] / 428	Y-M: 20[redacted] / 452
ENOXAPARIN	70 mg	BID	Y-M: 20[redacted] / 430	Y-M: 20[redacted] / 452
METHYLPREDNISOLONE	40 mg	BID	Y-M: 20[redacted] / 430	Y-M: 20[redacted] / 452
CITALOPRAM	20 mg	QD	Y-M: 20[redacted] / 432	Not reported
HYDROXYZINE	50 mg	QD	Y-M: 20[redacted] / 443	Y-M: 20[redacted] / 452
OXYGEN	4 L	OTHER: CONTINUOUS	Y-M: 20[redacted] / 452	Y-M: 20[redacted] / 477
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 452	Y-M: 20[redacted] / 452

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

Event Description	COVID-19 PNEUMONIA
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 906 / 422 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 422): NPTST103-COVID-19 NAA: POSITIVE [NOT REPORTED - NOT REPORTED] 099,NA; NPTST115-D-DIMER: 1.22 [0.1 - 0.5] MG/L; [redacted]20[redacted] (RX DAY 423): Leukocytes: 5.7 [4.5 - 11] 10^9/L; NPTST055-BNP: 18 [100 - 400] 099,PG/ML; NPTST096-CO2: 26 [23 - 29] MEQ/L; NPTST115-D-DIMER: 1.32 [0.4 - 0.5] MG/L; NPTST115-D-DIMER: 1.32 [0.1 - 0.5] MG/L; Neutrophils/Leukocytes: 86.3 [45 - 75] %; [redacted]20[redacted] (RX DAY 428): NPTST108-CRP: 6.07 [0 - 0.5] MG/DL; NPTST115-D-DIMER: 5.20 [0.1 - 0.5] MG/L; NPTST142-FERRITIN: 336 [22 - 275] NG/ML

Microbiology

[redacted]20[redacted] (RX DAY 428): BLOOD NPTST052-BLOOD CULTURE: Negative-NO GROWTH IN 5 DAYS

AE Stopped Initial Rx Day / Rx Day	936 / 452 (32 DAYS AFTER LAST TREATMENT)
Duration of AE	31 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID- 19 INFECTION

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

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

Event Description	BILATERAL PULMONARY EMBOLISMS
Preferred term	肺塞栓症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 914 / 430 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 423): NPTST115-D-DIMER: 1.32 [0.23 - 0.5] 099,UG/ML; NPTST115-D-DIMER: 1.32 [0.23 - 0.5] 099,UG/ML; [redacted]20[redacted] (RX DAY 424): NPTST096-CO2: 28 [23 - 29] MEQ/L; NPTST096-CO2: 28 [23 - 29] MEQ/L; [redacted]20[redacted] (RX DAY 430): NPTST115-D-DIMER: 5.20 [0.1 - 0.5] MG/L; NPTST115-D-DIMER: 5.20 [0.1 - 0.5] MG/L; [redacted]20[redacted] (RX DAY 431): NPTST096-CO2: 28 [23 - 29] MEQ/L; NPTST096-CO2: 28 [23 - 29] MEQ/L; [redacted]20[redacted] (RX DAY 432): NPTST096-CO2: 31 [23 - 29] MEQ/L; NPTST096-CO2: 31 [23 - 29] MEQ/L; NPTST108-CRP: 3.79 [0 - 0.5] MG/DL; NPTST108-CRP: 3.79 [0 - 0.5] MG/DL; NPTST115-D-DIMER: 5.20 [0.1 - 0.5] MG/L; NPTST115-D-DIMER: 5.20 [0.1 - 0.5] MG/L; NPTST142-FERRITIN: 649 [22 - 275] NG/ML; NPTST142-FERRITIN: 649 [22 - 275] NG/ML; [redacted]20[redacted] (RX DAY 433): NPTST096-CO2: 33 [23 - 29] MEQ/L; NPTST096-CO2: 33 [23 - 29] MEQ/L; [redacted]20[redacted] (RX DAY 440): NPTST096-CO2: 35 [23 - 29] MEQ/L; NPTST096-CO2: 35 [23 - 29] MEQ/L; [redacted]20[redacted] (RX DAY 443): NPTST096-CO2: 36 [23 - 29] MEQ/L; NPTST096-CO2: 36 [23 - 29] MEQ/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	936 / 452 (32 DAYS AFTER LAST TREATMENT)
Duration of AE	23 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID -19 VIRUS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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，COVID-19 肺炎及び両側性肺塞栓症の事象を発現した。関連する病歴は，潰瘍性大腸炎，前方肛門周囲膿瘍，前方肛門周囲膿瘍切開及びドレナージ，前方肛門周囲瘻，赤痢菌陽性便検体，噛みタバコの現使用者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 及び 2 の臨床経過：

投与906日後＊　，被験者は COVID-19 肺炎を発現した。投与914日後＊　，被験者は両側性肺塞栓症を発現した。投与936日後＊，COVID-19 肺炎及び両側性肺塞栓症は消失した。

治験責任医師によると，投与898日後＊　に，被験者に先行の重篤な事象として COVID-19 のウイルス感染が認められ，同日に治験薬の投与を中断した。

投与904日後＊，被験者は治験実施計画書の規定により，完全に治験を中止した。

投与906日後＊　，被験者は発熱，疲労，筋肉痛，息切れ，及び酸素飽和度低下を発症した。被験者は酸素補給を受けた状態で救急治療室へ運び込まれ，入院した。被験者は治療を受け，検査及び診断法を受けた。投与907日後＊　，酸素マスクによる酸素補給 15 L の状態で，被験者の酸素飽和度は 85%であった。被験者は，酸素補給 15 L で非再呼吸式マスクを装着され，酸素飽和度は 94%に改善した。

投与909日後＊　　，被験者の CT スキャン検査では，肺塞栓症は否定された。投与912日後＊，被験者は一晩，101°F の発熱を呈した。被験者に白血球数増加が認められた。被験者の血液及び尿培養が終了し，いずれも陰性であった。被験者にセフェピムの投与を開始した。投与914日後＊　，被験者は，酸素マスクによる酸素補給 15 L の状態にある間に，息切れの悪化，不安及び頻呼吸を発現し始めた。下肢超音波検査の再検査では陰性であったが，胸部 CT スキャン検査の再検査では，複数の小さな両側性の肺塞栓症が認められた。被験者は，非再呼吸式マスクによる酸素補給 15 L を継続し，鼻カニューレによる 15 L の高流量の酸素投与を追加した。Lovenox，ativan，ヒドロキシジン及び citalopram の投与を開始した。被験者の呼吸状態は改善した。被験者は，呼吸器科専門医及びすべての副専門医により退院を許可された。投与936日後＊　，被験者は，鼻カニューレによる酸素補給 4 L を受けた状態で退院した。

治験責任医師によると，被験者の危険因子に含まれるもの：40 歳超の年齢，炎症性腸疾患，長期にわたる運動抑制，最近の入院，低血圧及び息切れ。

投与された薬剤は，酸素，セフトリアキソン，ジスロマック，コレカルシフェロール，アスコルビン酸，デキサメタゾン，mucinex，亜鉛，ソル・メドロール，lovenox，protonix，レムデ

シビル，サルブタモール，セフェピム，dulera，チオトロピウム，バリシチニブ，ロラゼパム，イブプロフェン，citalopram，エリキュース，prednisone 及びラクトミンであった。

The patient's past medications include:

HUMIRA for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

MIRIKIZUMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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

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

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

Dechallenge: Not Applicable

2) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.24.0] [10037377]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 PNEUMONIA

- Investigator: COVID- 19 INFECTION

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

Event of BILATERAL PULMONARY EMBOLISM

- Investigator: COVID-19 VIRUS

- AbbVie: Risk factors include concurrent COVID 19 infection, and complicated hospitalization course.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 3.33 G/DL (normal 3.4 to 5.4)

[redacted] **20[redacted] BLOOD CULTURE:** NEGATIVE,NO GROWTH IN 5 DAYS

[redacted] **20[redacted] BLOOD PRESSURE:** 104/68 mmHg

[redacted] **20[redacted] BMI:** 20.1 %

[redacted] **20[redacted] BNP:** 18 PG/ML (normal 100 to 400)

[redacted] **20[redacted] BODY TEMPERATURE:** 101 F

[redacted] **20[redacted] CHEST X-RAY:** MILD PATCHY BILATERAL PULMONARY OPACITIES, RAISING QUESTION OF COVID PUMONIA

[redacted] **20[redacted] CHEST X-RAY:** WORSENING BILATERAL DIFFUSE INTERSITUAL AIRSPACE OPACITIES

[redacted] **20[redacted] CHEST X-RAY:** PERSISTANT BILATERAL INFILTRATES

[redacted] **20[redacted] CHEST X-RAY:** HAZY DIFFUSE BILATERAL PULMONARY OPACITIES ARE STABLE

[redacted] **20[redacted] CO2:** 28 MEQ/L (normal 23 to 29)

[redacted] **20[redacted] CO2:** 31 MEQ/L (normal 23 to 29)

[redacted] **20[redacted] CO2:** 36 MEQ/L (normal 23 to 29)

[redacted] **20[redacted] COVID-19 TEST NAA:** POSITIVE

[redacted] **20[redacted] CRP:** 6.07 mg/dL (normal 0 to 0.5)

[redacted] **20[redacted] CRP:** 3.79 mg/dL (normal 0.00 to 0.5)

[redacted] **20[redacted] CT ANGIOGRAPHY:** MULTIPLE SMALL NEW FINDINGS OF PULMONARY EMBOLI BILATERALLY. PERSISTING DIFFUSE INTERSTITIAL AND AIRSPACE DENSITY CONSISTENT

OF ATYPICAL/VIRAL PNEUMONIA

[redacted] **20[redacted] CTA CHEST:** NO PULMONARY EMBOLISM

[redacted] **20[redacted] D-DIMER:** 1.32 UG/ML (normal 0.23 to 0.50)

[redacted] **20[redacted] D-DIMER:** 5.2 mg/dL (normal 0.10 to 0.50)

[redacted] **20[redacted] D-DIMER:** 5.2 mg/dL (normal 0.10 to 0.50)

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

[redacted] **20[redacted] FERRITIN:** 336 NG/ML (normal 22 to 275)

[redacted] **20[redacted] FERRITIN:** 649 NG/ML (normal 22 to 275)

[redacted] **20[redacted] HEART RATE:** 80 /min

[redacted] **20[redacted] NEUTROPHILS:** 86.3 % (normal 45 to 75)

[redacted] **20[redacted] OXYGEN SATURATION:** 80% on room air

[redacted] **20[redacted] OXYGEN SATURATION:** 92% on 6 liters oxygen via nasal cannula

[redacted] **20[redacted] RESPIRATORY RATE:** 29 /min

[redacted] **20[redacted] SARS-COV-2:** positive

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

[redacted] **20[redacted] VENOUS DOPPLER BILATERAL LOWER EXTREMITIES:** NO FINDINGS OF DEEP VENOUS THROMBOSIS

[redacted] **20[redacted] WBC:** 5.7 X10**3/MCL (normal 4.5 to 11)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 15 X10**9/L (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
虚血性心筋症				X
心筋梗塞	X			X

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

Medical History	Onset Year
ANXIETY RELATED TO STEROID USE	20[redacted]
ATRIAL FIBRILLATION	20[redacted]
CARDIAC ABLATION	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHOGEAL REFLUX	19[redacted]
HYPERTENSION	20[redacted]
INSOMNIA RELATED TO STEROIDS	20[redacted]
OSTEOARTHRITIS	20[redacted]
RECTAL BLEEDING	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: CARDIAC ABLATION (TIMES 3)	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	1 PACK	30	
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 63	63
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 64	[redacted]20[redacted] / 105	42
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 106		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
OMEPRAZOLE	20 mg	QD	Y: 20[redacted]
PARACETAMOL	500 mg	PRN	Y: 20[redacted]
METOPROLOL	50 mg	BID	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LISINOPRIL	5 mg	QD	Y-M: 20[redacted] / 213	Y-M: 20[redacted] / 730
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 416
BIVALIRUDIN	1.75 OTHER: MG/KG/HR	OTHER: CONTINUOUS	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
BIVALIRUDIN	15 mL	OTHER: ONCE	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
CARVEDILOL	3.125 mg	BID	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 325
FENTANYL	25 ug	OTHER: ONCE	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
GLYCERYL TRINITRATE	200 ug	OTHER: ONCE	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
HEPARIN	1000 OTHER: UNITS	OTHER: ONCE	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
LIDOCAINE	20 mL	OTHER: ONCE	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
MAGNESIUM SULFATE	1 g	QD	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 324
MIDAZOLAM	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
OXYGEN	3 OTHER: L/NC	OTHER: ONCE	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 326
TICAGRELOR	90 mg	BID	Y-M: 20[redacted] / 323	ONGOING
TIROFIBAN	12,500 ug	OTHER: CONTINUOUS	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 324
TIROFIBAN	50 mL	OTHER: ONCE	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 323

ATORVASTATIN	20 mg	QD	Y-M: 20[redacted] / 324	Y-M: 20[redacted] / 730
LOSARTAN	25 mg	QD	Y-M: 20[redacted] / 324	Not reported
SPIRONOLACTONE	12.5 mg	QD	Y-M: 20[redacted] / 324	Y-M: 20[redacted] / 336
APIXABAN	5 mg	BID	Y-M: 20[redacted] / 326	ONGOING
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	160 mL	BID	Y-M: 20[redacted] / 414	Y-M: 20[redacted] / 414
LIDOCAINE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 415	Y-M: 20[redacted] / 415
PROPOFOL	300 mg	OTHER: ONCE	Y-M: 20[redacted] / 415	Y-M: 20[redacted] / 415
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 501	Y-M: 20[redacted] / 507
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / 701	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted] / 701	ONGOING
FENOFIBRATE	145 mg	QD	Y-M: 20[redacted] / 701	ONGOING
OMEPRAZOLE	20 mg	QD	Y: 20[redacted]	Not reported
PARACETAMOL	500 mg	PRN	Y: 20[redacted]	Not reported
METOPROLOL	50 mg	BID	Y: 20[redacted]	Not reported

Event #1: Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated MACE *

Event Description	ISCHEMIC CARDIOMYOPATHY
Preferred term	虚血性心筋症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 428 / 323
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated MACE *

Event Description	MYOCARDIAL INFARCTION
Preferred term	心筋梗塞
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 428 / 323
Age at AE Onset	5[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 323): Cholesterol: 8.01753 [5.1726 - 7.7589] MMOL/L; NPTST115-D-DIMER: 2.44 [0.5 - 0.5] MG/DL; NPTST209-MAGNESIUM: 1.7 [1.8 - 2.4] MG/DL; NPTST258-PRO BNP: 279 [900 - 900] PG/ML; NPTST326-TROPONIN I QNT: > 200 [0 - 0.056] NG/ML; NPTST326-TROPONIN I QNT: 11.964 [0 - 0.056] NG/ML; Triglycerides: 2.486 [1.695 - 1.695] MMOL/L; [redacted]20[redacted] (RX DAY 324): NPTST326-TROPONIN I QNT: 93.552 [0 - 0.056] NG/ML

Microbiology	

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	431 / 326
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PT HAS A H/O HTN, A. FIB, EX SMOKER X 30 YEARS, HIGH CHOLESTEROL
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，心筋梗塞の事象を発現した。関連する病歴は，高血圧，心房細動，潰瘍性大腸炎，心臓アブレーション，心臓アブレーション（3 回），喫煙者（1 日 1 箱を 30 年間），現飲酒者（1 日 2 杯未満），コレステロール高値及び心臓病の家族歴（母親及び父親）であった。

Event 2 の臨床経過：

投与428日後＊ ，被験者は心筋梗塞を発現した。投与431日後＊，心筋梗塞は消失した。

投与428日後＊ ，被験者は 3 時間前から胸部痛及び頚部痛があり，救急治療室を受診した。息切れ，悪心，嘔吐又は発汗はなかった。被験者は，左腕の電撃痛及び胸部痛よりも強い後頚部痛を訴えたが，身体検査では胸部痛が確認され，その他は確認されなかった。被験者は，ステント留置を伴う心臓カテーテル治療を 3 回受け，ペナンブラシステムを用いた血栓除去後の左前下行枝のアテローム血栓性疾患を原因とする非 ST 上昇型心筋梗塞が明らかとなった。被験者は，aggrastat を 12 時間投与され，集中治療室で観察された。エコー検査が実施された。エリキュースの投与を開始した。aggrastat 投与後，左室駆出率は 35%–40%であった。高血圧は安定していた。リピトール及び toprol XR は継続された。主訴はなかった。胸部痛及び頚部痛は消失した。被験者の状態は改善した。投与431日後＊，被験者は退院した。

投与された薬剤は，coreg，リピトール，チカグレロル，アスピリン，cozaar，aggrastat，酸素，ヘパリン，スピロノラクトン，ニトログリセリン及び angiomax であった。

Causality for UPADACITINIB (Open Label)

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1) Myocardial infarction (10028596) (Myocardial infarction (10028596)) [v.23.1] [10028596]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of MYOCARDIAL INFARCTION

- Investigator: Pt has a h/o HTN, A. Fib, ex smoker x 30 years, high cholesterol

- AbbVie: risk factors include history of hypertension, atrial fibrillation and smoking status of 1 PPD for 30 years.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY WEIGHT:** 10[redacted].[redacted] KG

[redacted] **20[redacted] CHOLESTEROL:** 310 mg/dL (normal 200 to 300)

[redacted] **20[redacted] D-DIMER:** 2.44 mg/dL (normal 0.50 to 0.50)

[redacted] **20[redacted] ECHO:** small thrmbus in the left ventricle with a size of 0.8 cm x 0.6 cm. LVEF 35-40% S/P AGGRASTAT.

[redacted] **20[redacted] EKG:** ABNORMAL EKG WITH MINIMAL ST ELEVATION

[redacted] **20[redacted] TRIGLYCERIDES:** 220 mg/dL (normal 150 to 150)

[redacted] **20[redacted] TROPONIN I QNT:** >200 ng/mL (normal 0.00 to 0.056

[redacted] **20[redacted] TROPONIN I QNT:** 11.964 NG/ML (normal 0.000 to 0.056)

[redacted] **20[redacted] TROPONIN I QNT:** 93.552 NG/ML (normal 0.000 to 0.056)

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
疼痛	X			
肋骨骨折	X			
自殺企図	X			

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

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
ASTHMA	19[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO IODINE	19[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO NAPROSYN	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO REGLAN	20[redacted]
DRUG ALLERGIES/REACTIONS: ALLERGY TO SHELLFISH	19[redacted]
EMPHYSEMA/CHRONIC OBSTRUCTIVE PULMONARY DISEASE	19[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
LEFT SIDED UC	19[redacted]
OTHER: ABDOMINAL PAIN	20[redacted]
OTHER: ANXIETY DISORDER	19[redacted]
OTHER: BILATERAL PLANTAR FASCIOTOMY	20[redacted]
OTHER: CHRONIC BRONCHITIS	19[redacted]
OTHER: COLON POLYPS	20[redacted]
OTHER: DYSPEPSIA	20[redacted]
OTHER: GALL STONES	20[redacted]
OTHER: GASTROPARESIS	20[redacted]
OTHER: H-PYLORI	20[redacted]
OTHER: HEART CATH	20[redacted]
OTHER: HEART PALPATATIONS	20[redacted]
OTHER: HIATEL HERNIA	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: PLANTAR FASCITIS BILATERAL	20[redacted]

Prior Procedures	Procedure Year
SURGERY: CHOLECYSTECTOMY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	14	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 57		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	800 mg	TID	Y-M: 20[redacted]
SALBUTAMOL	108 OTHER: MCG	PRN	Y-M: 20[redacted]
ALPRAZOLAM	1 mg	QD	Y-M: 20[redacted]
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY OTHER WEEK	Y-M: 20[redacted]
VENLAFAXINE	50 mg	QD	Y-M: 20[redacted]
TEMAZEPAM	15 mg	PRN	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
GOLIMUMAB	100 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted] / -364
FISH OIL	1000 mg	QD	Y-M: 20[redacted] / -365
SULFASALAZINE	500 mg	TID	Y-M: 20[redacted] / -365
VITAMIN B12 NOS	250 OTHER: MCG	QD	Y-M: 20[redacted] / -365

VITAMIN D NOS	1000 OTHER: UNITS	QD	Y-M: 20[redacted] / -365
IRON	125 mg	OTHER: MONTHLY	Y-M: 20[redacted] / -312
DICYCLOVERINE	20 mg	TID	Y-M: 20[redacted] / -168
INFLIXIMAB	100 mg	OTHER: EVERY 8 WEEKS	Y: 20[redacted]
PREDNISONE	20 mg	QD	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SALBUTAMOL	108 OTHER: MCG	PRN	Y-M: 20[redacted]	ONGOING
ALPRAZOLAM	1 mg	QD	Y-M: 20[redacted]	ONGOING
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted]	ONGOING
VENLAFAXINE	50 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 429
TEMAZEPAM	15 mg	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 551
FISH OIL	1000 mg	QD	Y-M: 20[redacted] / -365	Y-M: 20[redacted] / 434
SULFASALAZINE	500 mg	TID	Y-M: 20[redacted] / -365	ONGOING
VITAMIN B12 NOS	250 OTHER: MCG	QD	Y-M: 20[redacted] / -365	Y-M: 20[redacted] / 434
VITAMIN D NOS	1000 OTHER: UNITS	QD	Y-M: 20[redacted] / -365	Y-M: 20[redacted] / 434
IRON	125 mg	OTHER: MONTHLY	Y-M: 20[redacted] / -312	Y-M: 20[redacted] / 422
DICYCLOVERINE	20 mg	TID	Y-M: 20[redacted] / -168	Y-M: 20[redacted] / 538
METOCLOPRAMIDE	10 mg	TID	Y-M: 20[redacted] / 189	ONGOING
CHLORDIAZEPOXIDE;CLIDINIUM	5 mg	BID	Y-M: 20[redacted] / 263	ONGOING
ONDANSETRON	4 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 263	ONGOING
BISACODYL	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 343
MACROGOL 3350	280 g	OTHER: ONCE	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 343
LIDOCAINE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 344
PROPOFOL	400 mg	OTHER: ONCE	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 344
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 423	ONGOING
ARIPIPRAZOLE	2 mg	QD	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 551
BUPROPION	75 mg	QD	Y-M: 20[redacted] / 429	Y-M: 20[redacted] / 551
DULOXETINE	30 mg	QD	Y-M: 20[redacted] / 430	ONGOING
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 552	ONGOING
TRAZODONE	150 mg	PRN	Y-M: 20[redacted] / 552	ONGOING
BISACODYL	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 709	Y-M: 20[redacted] / 709
MACROGOL 3350	238 g	OTHER: ONCE	Y-M: 20[redacted] / 709	Y-M: 20[redacted] / 709

LIDOCAINE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 710	Y-M: 20[redacted] / 710
PROPOFOL	400 mg	OTHER: ONCE	Y-M: 20[redacted] / 710	Y-M: 20[redacted] / 710
MACROGOL 3350	238 g	OTHER: ONCE	Y-M: 20[redacted] / 1102	Y-M: 20[redacted] / 1102
BISACODYL	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 1103	Y-M: 20[redacted] / 1103
LIDOCAINE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 1103	Y-M: 20[redacted] / 1103
PROPOFOL	270 mg	OTHER: ONCE	Y-M: 20[redacted] / 1103	Y-M: 20[redacted] / 1103
METHYLPHENIDATE	20 mg	QD	Y-M: 20[redacted] / 1107	ONGOING

Event #1: Serious Adverse Event

Event Description	CLOSED LEFT RIB FRACTURE
Preferred term	肋骨骨折
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 96 / 40
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PATIENT FELL OFF OF A LADDER
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	SUICIDAL ATTEMPT SECONDARY TO CHRONIC PAIN
Preferred term	疼痛，自殺企図
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 484 / 428
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	490 / 434
Duration of AE	7 DAYS
Severity	SEVERE

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUICIDAL ATTEMPT SECONDARY TO CHRONIC PAIN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，閉鎖性左肋骨骨折の事象を発現した。関連する病歴は，両側足底筋膜切開，両側足底筋膜炎，動悸，前喫煙者（1 日 1 箱を 14 年間），心臓カテーテル治療，潰瘍性大腸炎及び非飲酒者であった。

Event 1 の臨床経過：

投与96日後＊，被験者は閉鎖性左肋骨骨折を発現した。

被験者は，滑って転倒後，背部痛，左側腹部痛，肋骨痛及び頚部痛を訴えた。　投与96日後＊　，被験者は入院した。精密検査で左第 9 肋骨骨折が明らかとなった。投与97日後＊，被験者は，可能な範囲での活動を指示され，鎮痛薬を処方されて退院した。

投与された薬剤は，リドカインパッチ，bentyl，イフェクサー，ビタミン D，炭酸カルシウム，ロバキシン及び norco であった。

The patient's past medications include:

IODINE for UNKNOWN INDICATION

NAPROSYN for UNKNOWN INDICATION

REGLAN for UNKNOWN INDICATION

Causality for ABT-494 (Open Label)

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1) Closed fracture of one rib (10009570) (Rib fracture (10039117)) [v.21.1] [10009570]

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 (Open Label)

Event of CLOSED LEFT RIB FRACTURE

- Investigator: PATIENT FELL OFF OF A LADDER.

- AbbVie: EVENT IS MORE LIKELY RELATED TO ACCIDENTAL TRAUMA.

Relevant Laboratory & Other Diagnostic Tests

Unknown date CT SCAN OF CERVICAL SPINE, THORACIC SPINE AND LUMBAR SPINE: Not reported

Unknown date CT SCAN OF THE CHEST: Not reported

Unknown date CT SCAN OF THE HEAD: Not reported
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，慢性疼痛に続発する自殺企図の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），不安障害，元喫煙者（1 日 1 箱を 14 年間），ヘリコバクター・ピロリ感染，不眠症，消化不良，胃食道逆流性疾患，胃不全麻痺及び非飲酒者であった。

Event 2 の臨床経過：

投与484日後＊，被験者は慢性疼痛に続発する自殺企図を発現した。投与490日後＊　，慢性疼痛に続発する自殺企図は消失した。

投与484日後＊　　，被験者は入院した。入院時，腹部は柔らかく，圧痛があった。被験者は，抑うつ気分で自殺念慮を示し，目を合わせなかった。被験者からその妻への直近のメッセージを除き，本事象に至る徴候や症状はなかったと報告された。そのメッセージには「I am done」と記載されており，更なる評価の結果，被験者は自身の胃食道逆流性疾患の医学的問題に関して，痛みを受け入れることができなかったと報告した。被験者は，更なる評価のため，精神科病棟に移された。投与490日後＊，被験者は退院した。

投与された薬剤は，wellbutrin，サインバルタ及びエビリファイであった。

The patient's past medications include:

REMICADE for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

ASACOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISONE for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SIMPONI for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REGLAN for UNKNOWN INDICATION

NAPROSYN for UNKNOWN INDICATION

Causality for ABT-494 (Open Label)

---

1)　Suicide attempt (10042464)　(Suicide attempt (10042464))　[v.22.0]　[10042464]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2) Chronic pain (10049475) (Pain (10033371)) [v.22.0] [10049475]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Open Label)

Event of SUICIDAL ATTEMPT SECONDARY TO CHRONIC PAIN

- Investigator: Suicidal attempt secondary to chronic pain.

- AbbVie: Event's etiology not consistent with study drug's mechanism of action. Additional risk factor includes pre-existing history of anxiety.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Normal

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

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

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
急性腎障害				X
大球性貧血				X
感染性胆嚢炎	X			X
γ-グルタミルトランスフェラーゼ増加				X
ヘモグロビン減少				X
肝酵素上昇				X
帯状疱疹				X
リンパ球減少症				X

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

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: ALLERGY TO CODEINE	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO SULFA	NOT REPORTED
DRUG ALLERGIES/REACTIONS: ALLERGY TO TRAMADOL	NOT REPORTED
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERTENSION	20[redacted]
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
OTHER: ARTHRITIS IN SHOULDER	NOT REPORTED
OTHER: CHICKEN POX	NOT REPORTED
OTHER: CHRONIC PAIN, UNSPECIFIED REGION	20[redacted]
OTHER: GRADE II HEMORRHOIDS	20[redacted]
OTHER: LICHEN PLANUS	20[redacted]
OTHER: LOCALIZED HERPES SIMPLEX GENITAL OUTBREAK	20[redacted]
OTHER: PERIANAL SKIN TAGS	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	22	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 57		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ATENOLOL	50 mg	QD	Y-M: 20[redacted]
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted] / -162
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -115
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / -1
PROPOFOL	300 mL	OTHER: ONCE	Y-M: 20[redacted] / -2
RANITIDINE	150 mg	PRN	Y-M: 20[redacted] / -8
CALCIUM CARBONATE	2 OTHER: TABLET	PRN	Y: 20[redacted]
TRIAMCINOLONE	UNK OTHER: UNKNOWN	PRN	Y: 20[redacted]
ACETYLSALICYLIC ACID	1000 mg	PRN	Y: 20[redacted]
LISINOPRIL	12.5 mg	BID	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ATENOLOL	50 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 907

AMLODIPINE	10 mg	QD	Y-M: 20[redacted]	ONGOING
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted] / -162	ONGOING
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / -1	ONGOING
PROPOFOL	300 mL	OTHER: ONCE	Y-M: 20[redacted] / -2	Y-M: 20[redacted] / -2
RANITIDINE	150 mg	PRN	Y-M: 20[redacted] / -8	Not reported
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 1	ONGOING
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 22
CYANOCOBALAMIN	1000 OTHER: MCG	QD	Y-M: 20[redacted] / 18	Y-M: 20[redacted] / 53
IRON	325 mg	QD	Y-M: 20[redacted] / 18	Not reported
FENTANYL	100 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 7
MIDAZOLAM	7 mg	OTHER: ONCE	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 7
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 14
ASCORBIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 53	Not reported
CYANOCOBALAMIN	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 53	Not reported
FOLIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 53	Y-M: 20[redacted] / 449
VALACICLOVIR	1 g	OTHER: BID PRN	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 206
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 77	Not reported
GABAPENTIN	300 mg	BID	Y-M: 20[redacted] / 313	Y-M: 20[redacted] / 334
VALACICLOVIR	1 g	TID	Y-M: 20[redacted] / 313	Y-M: 20[redacted] / 320
PROPOFOL	150 mg	OTHER: ONCE	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 347
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	1 L	OTHER: PRN	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 788
HYDROMORPHONE	0.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 779
MORPHINE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 779
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 779
ONDANSETRON	4 mg	OTHER: Q6HOURS PRN	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 781
PARACETAMOL	650 mg	OTHER: Q4 HOURS PRN	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 788
PIPERACILLIN;TAZOBACTAM	3.375 g	OTHER: Q8HOURS	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 785
PIPERACILLIN;TAZOBACTAM	4.5 g	OTHER: ONCE	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 779
POTASSIUM	20 mEq	OTHER: ONCE	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 779
SODIUM CHLORIDE	1500 mL	OTHER: ONCE	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 779
FENTANYL	50 ug	OTHER: ONCE	Y-M: 20[redacted] / 780	Y-M: 20[redacted] / 780
FOLIC ACID	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 780	Y-M: 20[redacted] / 780

HYDROMORPHONE	0.1 mg	OTHER: Q 2 HOURS PRN	Y-M: 20[redacted] / 780	Y-M: 20[redacted] / 786
IOPAMIDOL	50 mL	OTHER: ONCE	Y-M: 20[redacted] / 780	Y-M: 20[redacted] / 780
MIDAZOLAM	1 mL	OTHER: ONCE	Y-M: 20[redacted] / 780	Y-M: 20[redacted] / 780
OXYCODONE	5 mg	OTHER: Q 4 HOURS PRN	Y-M: 20[redacted] / 780	Y-M: 20[redacted] / 783
SODIUM CHLORIDE	1000 mL	OTHER: PRN	Y-M: 20[redacted] / 780	Y-M: 20[redacted] / 788
THIAMINE	200 mg	OTHER: ONCE	Y-M: 20[redacted] / 780	Y-M: 20[redacted] / 780
HEPARIN	5000 IU	OTHER: Q 12 HOURS	Y-M: 20[redacted] / 781	Y-M: 20[redacted] / 788
CEFTRIAXONE	1 g	OTHER: ONCE	Y-M: 20[redacted] / 782	Y-M: 20[redacted] / 782
FENTANYL	150 ug	OTHER: ONCE	Y-M: 20[redacted] / 782	Y-M: 20[redacted] / 782
METRONIDAZOLE	500 mg	OTHER: Q8HOURS	Y-M: 20[redacted] / 782	Y-M: 20[redacted] / 815
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 782	Y-M: 20[redacted] / 782
CEFTRIAXONE	2000 mg	QD	Y-M: 20[redacted] / 783	Y-M: 20[redacted] / 787
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 783	Y-M: 20[redacted] / 815
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted] / 784	Y-M: 20[redacted] / 788
FENTANYL	100 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 786	Y-M: 20[redacted] / 786
LIDOCAINE	2 OTHER: CC	OTHER: ONCE	Y-M: 20[redacted] / 786	Y-M: 20[redacted] / 786
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 786	Y-M: 20[redacted] / 786
OXYCODONE	5 mg	OTHER: Q6 HRS PRN	Y-M: 20[redacted] / 786	Y-M: 20[redacted] / 788
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 787	Y-M: 20[redacted] / 788
VALACICLOVIR	1 g	PRN	Y-M: 20[redacted] / 816	Not reported
CEFTRIAXONE	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
FENTANYL	50 ug	OTHER: ONCE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
IOPAMIDOL	50 mL	OTHER: ONCE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
MIDAZOLAM	1 OTHER: MG/ML	OTHER: ONCE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
SODIUM CHLORIDE	30 OTHER: ML/HR	OTHER: ONCE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 840	Y-M: 20[redacted] / 869
BUPIVACAINE	20 mL	OTHER: ONCE	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 866
FENTANYL	100 ug	OTHER: ONCE	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 866
HEPARIN	5000 IU	OTHER: ONCE	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 866
HYDROCODONE;PARACETAMOL	1 OTHER: TABLET	QID	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 869
HYDROMORPHONE	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 866
LABETALOL	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 866
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 866
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 866

ATENOLOL	100 mg	QD	Y-M: 20[redacted] / 877	Y-M: 20[redacted] / 998
ATENOLOL	200 mg	QD	Y-M: 20[redacted] / 969	Not reported
LIDOCAINE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 1021	Y-M: 20[redacted] / 1021
PROPOFOL	200 mg	OTHER: ONCE	Y-M: 20[redacted] / 1021	Y-M: 20[redacted] / 1021
VARICELLA ZOSTER VACCINE	0.5 mL	OTHER: ONCE	Y-M: 20[redacted] / 1069	Y-M: 20[redacted] / 1069
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / 1084	Not reported
PLANTAGO OVATA	3.4 g	QD	Y-M: 20[redacted] / 1176	Not reported
GUAIFENESIN	600 mg	OTHER: Q 12HR PRN	Y-M: 20[redacted] / 1343	Y-M: 20[redacted] / 1348
CALCIUM CARBONATE	2 OTHER: TABLET	PRN	Y: 20[redacted]	ONGOING
TRIAMCINOLONE	UNK OTHER: UNKNOWN	PRN	Y: 20[redacted]	ONGOING
ACETYLSALICYLIC ACID	1000 mg	PRN	Y: 20[redacted]	Y-M: 20[redacted] / 56
LISINOPRIL	12.5 mg	BID	Y: 20[redacted]	ONGOING

Event #1: Event of Interest - Anemia

Event Description	LOW HEMOGLOBIN
Preferred term	ヘモグロビン減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 55 / -2 DAYS BEFORE TREATMENT
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	112 / 56
Duration of AE	58 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER ON TORSO
Preferred term	帯状疱疹

AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 372 / 316
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	410 / 354
Duration of AE	39 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Event of Interest - Renal Dysfunction

Event Description	ACUTE KIDNEY INJURY
Preferred term	急性腎障害
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 835 / 779
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	843 / 787
Duration of AE	9 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Event of Interest - Anemia

Event Description	MACROCYTIC ANEMIA
Preferred term	大球性貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 835 / 779
Age at AE Onset	7[redacted]

Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	843 / 787
Duration of AE	9 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	ACUTE GANGRENOUS CHOLECYSTITIS
Preferred term	感染性胆嚢炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 835 / 779
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 779): Alanine Aminotransferase: 79 [12 - 65] U/L; Alkaline Phosphatase: 241 [46 - 116] U/L; Aspartate Aminotransferase: 139 [15 - 37] U/L; Blood Urea Nitrogen: 45.33519 [2.49879 - 6.42546] MMOL/L; Creatinine: 454.392756 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 3.78 [4.6 - 6.2] 10^12/L; Hematocrit: 0.355 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 130 [135 - 180] G/L; Leukocytes: 15.91 [4 - 11] 10^9/L; NPTST123-EGFR NON AFRICAN/AMERICAN: 11 [15 - 60] ML/MIN; NPTST207-LIPASE: 506 [73 - 393] U/L; NPTST209-MAGNESIUM: 2.6 [1.8 - 2.4] MG/DL; Potassium: 2.8 [3.5 - 5.1] MMOL/L; Sodium: 127 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 780): Alanine Aminotransferase: 73 [0 - 41] U/L; Albumin: 29 [34 - 48] G/L; Alkaline Phosphatase: 280 [40 - 129] U/L; Blood Urea Nitrogen: 22.13214 [3.5697 - 7.1394] MMOL/L; Blood Urea Nitrogen: 33.55518 [3.5697 - 7.1394] MMOL/L; Chloride: 92 [95 - 107] MMOL/L; Creatinine: 265.20978 [53.041956 - 106.083912] UMOL/L; Erythrocytes: 3.4 [4.5 - 6.2] 10^12/L; Hematocrit: 0.33 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 116 [132 - 177] G/L; Leukocytes: 16 [3.7 - 10.5] 10^9/L; NPTST049-BILIRUBIN, DIRECT: 0.9 [0 - 0.2] MG/DL; NPTST050-BILIRUBIN, TOTAL: 1.4 [NOT REPORTED - 1.2] mg/dL; NPTST123-EGFR NON AFRICAN/AMERICAN: 20 [60 - NOT REPORTED] mL/min/1.73m2; NPTST207-LIPASE: 102 [13 - 60] U/L; Sodium: 131 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 781): Alanine Aminotransferase: 55 [0 - 41] U/L; Albumin: 28 [34 - 48] G/L; Alkaline Phosphatase: 232 [40 - 129] U/L; Aspartate Aminotransferase: 70 [0 - 40] U/L; Creatinine: 150.285542 [53.041956 - 106.083912] UMOL/L; Erythrocytes: 3.06 [4.5 - 6.2] 10^12/L; Hematocrit: 0.3 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 104 [132 - 177] G/L; Leukocytes: 25 [3.7 - 10.5] 10^9/L; NPTST050-BILIRUBIN, TOTAL: 1.2 [NOT REPORTED - 1.2] mg/dL; NPTST123-EGFR NON AFRICAN/AMERICAN: 40 [60 - NOT REPORTED] mL/min; Potassium: 3.1 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 782): Alanine Aminotransferase: 42 [0 - 41] U/L; Albumin: 28 [34 - 48] G/L; Alkaline Phosphatase: 214 [40 - 129] U/L; Aspartate Aminotransferase: 39 [0 - 40] U/L; Blood Urea Nitrogen: 13.20789 [3.5697 - 7.1394] MMOL/L; Creatinine: 97.243586 [53.041956 - 106.083912] UMOL/L; Erythrocytes: 3.04 [4.5 - 6.2] 10^12/L; Hematocrit: 0.3 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 103 [132 - 177] G/L; Leukocytes: 20.7 [3.7 - 10.5] 10^9/L; NPTST050-BILIRUBIN, TOTAL: 1.0 [NOT REPORTED - 1.2] mg/dL; NPTST123-EGFR NON AFRICAN/AMERICAN: 68 [60 - NOT REPORTED] mL/min; Potassium: 3.2 [3.5 - 5] MMOL/L; Sodium: 136 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 783): Alanine Aminotransferase: 31 [0 - 41] U/L; Albumin: 30 [34 - 48] G/L; Alkaline Phosphatase: 184 [40 - 129] U/L;

Blood Urea Nitrogen: 5.71152 [3.5697 - 7.1394] MMOL/L; Creatinine: 70.722608 [53.041956 - 106.083912] UMOL/L; Erythrocytes: 2.94 [4.5 - 6.2] 10^12/L; Hematocrit: 0.29 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 102 [132 - 177] G/L; Leukocytes: 23.4 [3.7 - 10.5] 10^9/L; NPTST050-BILIRUBIN, TOTAL: 1.0 [NOT REPORTED - 1.2] mg/dL; NPTST125-EGFR NON-AFRICAN/AMERICAN: 90 [60 - NOT REPORTED] mL/min; Potassium: 3.5 [3.5 - 5] MMOL/L; Sodium: 136 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 784): Albumin: 32 [34 - 48] G/L; Aspartate Aminotransferase: 259 [40 - 129] U/L; Bilirubin: 1.0 [NOT REPORTED - 1.2] mg/dL; Erythrocytes: 3.08 [4.5 - 6.2] 10^12/L; Hematocrit: 0.32 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 106 [132 - 177] G/L; Leukocytes: 29.8 [3.7 - 10.5] 10^9/L; NPTST031-ANION GAP: 17 [NOT REPORTED - 17] mEq/L; [redacted]20[redacted] (RX DAY 785): Albumin: 29 [34 - 48] G/L; Alkaline Phosphatase: 301 [40 - 129] U/L; Erythrocytes: 2.89 [4.5 - 6.2] 10^12/L; Hematocrit: 0.3 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 99 [132 - 177] G/L; Leukocytes: 28.5 [3.7 - 10.5] 10^9/L; NPTST031-ANION GAP: 15 [NOT REPORTED - 17] mEq/L; [redacted]20[redacted] (RX DAY 786): Albumin: 32 [34 - 48] G/L; Erythrocytes: 2.96 [4.5 - 6.2] 10^12/L; Hematocrit: 0.31 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 101 [132 - 177] G/L; Leukocytes: 28.1 [3.7 - 10.5] 10^9/L; NPTST031-ANION GAP: 16 [NOT REPORTED - 17] mEq/L; [redacted]20[redacted] (RX DAY 787): Albumin: 28 [34 - 48] G/L; Alkaline Phosphatase: 302 [40 - 129] U/L; Erythrocytes: 2.84 [4.5 - 6.2] 10^12/L; Hematocrit: 0.3 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 98 [132 - 177] G/L; Leukocytes: 20.6 [3.7 - 10.5] 10^9/L; [redacted]20[redacted] (RX DAY 788): Albumin: 29 [34 - 48] G/L; Alkaline Phosphatase: 304 [40 - 129] U/L; Erythrocytes: 2.89 [4.5 - 6.2] 10^12/L; Hematocrit: 0.3 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 97 [132 - 177] G/L; Leukocytes: 20 [3.7 - 10.5] 10^9/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	922 / 866
Duration of AE	88 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #6: Event of Interest - Hepatic Disorder

Event Description	ELEVATED LIVER ENZYMES
Preferred term	肝酵素上昇
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 835 / 779
Age at AE Onset	7[redacted]
Laboratory Testing	

NOT APPLICABLE

Microbiology

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	844 / 788
Duration of AE	10 DAYS
Severity	MODERATE

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #7: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER OUTBREAK ON TORSO
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 872 / 816
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	872 / 816
Duration of AE	1 DAY
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #8: Event of Interest - Hepatic Disorder

Event Description	ELEVATED GGT
Preferred term	γ-グルタミルトランスフェラーゼ増加
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 980 / 924
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1063 / 1007
Duration of AE	84 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE

Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #9: Event of Interest - Anemia

Event Description	MACROCYTIC ANEMIA
Preferred term	大球性貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1064 / 1008
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #10: Event of Interest - Hepatic Disorder

Event Description	ELEVATED GGT
Preferred term	γ-グルタミルトランスフェラーゼ増加
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1064 / 1008
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO

SAE Criteria	NONE

Event #11: Event of Interest - Hepatic Disorder

Event Description	ELEVATED LIVER ENZYMES
Preferred term	肝酵素上昇
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1064 / 1008
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #12: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER OUTBREAK ON TORSO
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1152 / 1096
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1159 / 1103
Duration of AE	8 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #13: Event of Interest - Lymphopenia

Event Description	LYMPHOPENIA
Preferred term	リンパ球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1243 / 1187
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，急性壊疽性胆嚢炎の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 22 年間），胃食道逆流性疾患，高血圧，潰瘍性大腸炎，汎大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 4 の臨床経過：

投与835日後＊　，被験者は急性壊疽性胆嚢炎を発現した。投与922日後＊　，急性壊疽性胆嚢炎は消失した。

投与835日後＊　，被験者は，息切れ，胸痛，脱力，発熱，体重減少，悪心，嘔吐，皮膚の黄染及び上腹部痛があり，救急科を受診した。また，鎖骨，手及び肩に軽度の筋肉疲労もあった。症状は 1 週間前に開始し，最初は 10 時間の酷い腹痛にみまわれた。その翌日，痛みは右上腹部

に移動した。被験者はその翌日から 6 日間にわたり持続的な痛みを感じ，華氏 100.5°F 前後の微熱が 1 週間続いていた。息切れ，胃炎を伴う脱力感があり，食欲が減退していた。鼻閉，咽頭痛又は咳嗽はなかった。間欠的な嘔吐を伴う吐き気が 1 週間続いていた。最後の排便は入院 3 日前であった。失神，血尿又は血便はなかった。投与835日後＊　，被験者は評価のために入院した。CT 検査では，穿孔を伴う胆嚢炎が懸念された。また，臨床検査値で急性腎障害（非重篤）が認められた。被験者は，急性壊疽性胆嚢炎のため，及び腎不全の更なる評価のために入院した。右上腹部超音波検査では，胆嚢結石は認められなかった。胆嚢造瘻術のチューブ留置に成功し，抗生物質を投与されていた。救急科の受診が遅れたことを考慮すると，胆嚢切除術のリスクがベネフィットを上回っていた。投与844日後＊　，被験者は，胆嚢切除術のフォローのためにインターベンショナルラジオロジー及び一般外科を紹介され，抗生物質を処方されて退院した。投与873日後＊，胆嚢造瘻術のチューブ置換に成功した。投与922日後＊　，腹腔鏡下の胆嚢切除術に成功した。

投与された薬剤は，フラジール，ロセフィン，オキシコドン，ラクトリンゲル，ヒドロモルフォン，アセトアミノフェン，塩化ナトリウム，塩化カリウム，ピペラシリン・タゾバクタム合剤，オンダンセトロン塩酸塩，モルヒネ及びセフトリアキソンであった。

The patient's past medications include:

CODEINE for UNKNOWN INDICATION

SULFA for UNKNOWN INDICATION

TRAMADOL for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1)　Gangrenous cholecystitis (10063158)　(Cholecystitis infective (10062631))　[v.23.1]　[10063158]

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 (Open Label)

Event of ACUTE GANGRENOUS CHOLECYSTITIS

- Investigator: Not applicable

- AbbVie: Gallbladder attacks or cholecystitis most frequently arises from gallstone disease. The prevalence of gallstones in non-Hispanic white men is 8.6 percent.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 73 U/L (normal 0 to 41)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 31 U/L (normal 0 to 41)

[redacted] **20[redacted] ALBUMIN:** 2.8 G/DL (normal 3.4 to 4.8)

[redacted] **20[redacted] ALBUMIN:** 3.0 G/DL (normal 3.4 to 4.8)

[redacted] **20[redacted] ALBUMIN:** 2.9 G/DL (normal 3.4 to 4.8)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 280 U/L (normal 40 to 129)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 184 U/L (normal 40 to 129)

[redacted] **20[redacted] ASPARATATE AMINO TRANSFERASE:** 139 U/L (normal 15 to 37)

[redacted] **20[redacted] ASPARATATE AMINO TRANSFERASE:** 39 U/L (normal 0 to 40)

[redacted] **20[redacted] BUN:** 127 mg/dL (normal 7 to 18)

[redacted] **20[redacted] BUN:** 16 mg/dL (normal 10 to 20)

[redacted] **20[redacted] CHLORIDE:** 92 MEQ/L (normal 95 to 107)

[redacted] **20[redacted] CHOLECYSTOGRAM:** Successful cholecystogram through existing drain shows good position of drain with patent cystic duct.

[redacted] **20[redacted] CREATININE:** 5.14 mg/dL (normal 0.7 to 1.3)

[redacted] **20[redacted] CREATININE:** 0.8 mg/dL (normal 0.6 to 1.2)

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** Interval resolution of the right paracolic fluid collection and posterior inferior right hepatic lobe fluid collection. Stable placement of the percutaneous cholecystectomy

tube without interval complication.

[redacted] 20[redacted] **CT ABDOMEN AND PELVIS W/O CONTRAST:** Marked inflammation of the gallbladder with some stones, suspicious for gangrenous cholecystitis with perforation. Fluid collection along the posterior right hemi liver and tracking along the right pelvic side wall is likely secondary to cholecystitis.

[redacted] 20[redacted] **CT ABDOMEN AND PELVIS WITH CONTRAST:** Paracolic abscess, biloma, and right pleural effusion

[redacted] 20[redacted] **DIRECT BILIRUBIN:** 0.9 mg/dL (normal <0.2)

[redacted] 20[redacted] **EGFR NON AFRICAN/AMERICAN:** 11 ML/Min (normal 15 to 60)

[redacted] 20[redacted] **EGFR NON AFRICAN/AMERICAN:** 90 ML/Min (normal <60)

[redacted] 20[redacted] **EKG 12 LEAD:** Sinus rhythm, atrial premature complex, left anterior fascicular block.

[redacted] 20[redacted] **HEMATOCRIT:** 35.5 % (normal 40.0 to 50.0)

[redacted] 20[redacted] **HEMATOCRIT:** 29 % (normal 40.0 to 52)

[redacted] 20[redacted] **HEMOGLOBIN:** 13.0 G/DL (normal 13.5 to 18.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 10.2 G/DL (normal 13.2 to 17.7)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.7 G/DL (normal 13.2 to 17.7)

[redacted] 20[redacted] **LIPASE:** 506 U/L (normal 73 to 393)

[redacted] 20[redacted] **LIPASE:** 102 U/L (normal 13 to 60)

[redacted] 20[redacted] **MAGNESIUM:** 2.6 mg/dL (normal 1.8 to 2.4)

[redacted] 20[redacted] **POTASSIUM:** 2.8 MMOL/L (normal 3.5 to 5.1)

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

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.78 X10**6/MCL (normal 4.60 to 6.20)

[redacted] 20[redacted] **RED BLOOD CELLS:** 2.94 M/MM3 (normal 4.50 to 6.20)

[redacted] 20[redacted] **SODIUM:** 127 MMOL/L (normal 136 to 145)

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

[redacted] 20[redacted] **TEMPERATURE:** 100.5 F

[redacted] 20[redacted] **TOTAL BILIRUBIN:** 1.4 mg/dL (normal <1.2)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 1.0 mg/dL (normal <1.2)

[redacted] **20[redacted] US RUQ:** Thickened hyperchoic gallbladder wall and small pericholecystic fluid collection consistent acute cholecystitis, likely associated rupture. No obstructing stone identified.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 15.91 X10**3/MCL (normal 4.00 to 11.00)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 16.0 K/MM3 (normal 3.7 to 10.5)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 25.0 K/MM3 (normal 3.7 to 10.5)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 29.8 K/MM3 (normal 3.7 to 10.5)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 20.0 K/MM3 (normal 3.7 to 10.5)

[redacted] **20[redacted] XR CHEST 1 VIEW:** No pneumothorax or pleural effusion, normal heart size.

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes zoster: ([redacted]20[redacted]) One dermatome. Study drug interrupted.
Acute kidney injury: Study drug interrupted. Symptoms of shortness of breath, chest pain, weakness, and fever. Vomiting preceding the event.
Hepatic enzyme increased ([redacted]20[redacted]): Intermittent. Asymptomatic. User of alcohol, 4-8 oz of wine most nights.
Anaemia macrocytic: Intermittent.
Herpes zoster: ([redacted]20[redacted]) One dermatome. Subject was on an IP interruption as this time due to SAE.
Gamma-glutamyltransferase increased ([redacted]20[redacted]): Intermittent. Asymptomatic. User of Alcohol, 12 oz of wine daily.
Hepatic enzyme increased ([redacted]20[redacted]): Intermittent. Asymptomatic. User of Alcohol, 12 oz of wine daily. Study drug interrupted.
Gamma-glutamyltransferase increased ([redacted]20[redacted]): Intermittent. Fatigue, dark urine, loss of appetite. User of Alcohol, 12 oz of wine daily.
Herpes zoster: ([redacted]20[redacted]) One dermatome.
Lymphopenia: Intermittent.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎	X			
帯状疱疹				X
尿管閉塞	X			
尿管結石症	X			

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

Medical History	Onset Year
ASTHMA	20[redacted]
DRUG ALLERGIES/REACTIONS: PENICILLIN - RASH	19[redacted]
LEFT SIDED UC	20[redacted]
OTHER: B-12 DEFICANCY	20[redacted]
OTHER: CHERRY ANGIOMAS	NOT REPORTED
OTHER: CHICKEN POX	19[redacted]
OTHER: CHRONIC DVT OF THE POSTERIOR TIBIAL AND GASTROCNEMIUS VEINS	20[redacted]
OTHER: EXTERNAL HEMORRHOIDS	20[redacted]
OTHER: HISTORY OF LEFT LOWER EXTREMITY DEEP VEIN THROMBOSIS IN [redacted] 20[redacted]	20[redacted]
OTHER: HISTORY OF LEFT LOWER EXTREMITY DEEP VEIN THROMBOSIS IN [redacted] 20[redacted]	20[redacted]
OTHER: HISTORY OF LEFT UPPER EXTREMITY DVT	20[redacted]
OTHER: HISTORY OF RECURRENT COLD SORES	20[redacted]
OTHER: HYPERLIPIDEMIA	20[redacted]
OTHER: INTERMITTENT ANEMIA - -SECONDARY TO UC	20[redacted]
OTHER: INTERMITTENT HEADACHES	20[redacted]
OTHER: INVITRO FERTILIZATION	19[redacted]
OTHER: MYOPIA	19[redacted]
OTHER: PERIANAL RASH	20[redacted]
OTHER: POST MENOPAUSAL	20[redacted]
OTHER: RECTAL POLYP - TUBULAR ADENOMA	20[redacted]
OTHER: RECURRENT C-DIFF	20[redacted]

OTHER: SEASONAL ALLERGIES	20[redacted]
OTHER: SINGLE EPISODE OF SHINGLES. NOT WIDE SPREAD OR RECURRENT	20[redacted]
OTHER: SINUS SURGERY	20[redacted]
OTHER: TONSILLECTOMY	19[redacted]
OTHER: VITAMIN D DEFICANCY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: REPAIR OF NASAL SEPTUM	20[redacted]
SURGERY: WISDOM TEETH REMOVAL	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 57		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	QD	Y-M: 20[redacted]
INFLIXIMAB	10 mg/kg	OTHER: Q 8 WEEKS	Y-M: 20[redacted]
WARFARIN	5 mg	QD	Y-M: 20[redacted]
VITAMINS NOS	2 OTHER: CHEWS	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: Q 8 WKS	Y-M: 20[redacted]
METHOTREXATE	15 mg	OTHER: WEEKLY	Y-M: 20[redacted] / -340

ADALIMUMAB	40 mg	OTHER: WEEKLY	Y-M: 20[redacted] / -284
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -152
ASCORBIC ACID	500 mg	BID	Y-M: 20[redacted] / -171
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -118
CALCIUM	2 OTHER: GUMMIES	QD	Y-M: 20[redacted] / -109
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -82
CYANOCOBALAMIN	1000 OTHER: MCG	QD	Y-M: 20[redacted] / -95
VITAMIN D NOS	2000 OTHER: UNITS	QD	Y-M: 20[redacted] / -95
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y-M: 20[redacted]	ONGOING
WARFARIN	5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 33
VITAMINS NOS	2 OTHER: CHEWS	QD	Y-M: 20[redacted]	ONGOING
ASCORBIC ACID	500 mg	BID	Y-M: 20[redacted] / -171	Y-M: 20[redacted] / 317
CALCIUM	2 OTHER: GUMMIES	QD	Y-M: 20[redacted] / -109	Y-M: 20[redacted] / 317
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -82	Y-M: 20[redacted] / 84
CYANOCOBALAMIN	1000 OTHER: MCG	QD	Y-M: 20[redacted] / -95	Y-M: 20[redacted] / 317
VITAMIN D NOS	2000 OTHER: UNITS	QD	Y-M: 20[redacted] / -95	Y-M: 20[redacted] / 317
PARACETAMOL	600 mg	OTHER: Q6HRS	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 36
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	UNKNOWN OTHER: ML	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
CEFAZOLIN	UNKNOWN mg	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
CEFTRIAXONE	1 g	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
DEXAMETHASONE	4 OTHER: MG/ML	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
FENTANYL	100 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
HYDROMORPHONE	1 mg	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
HYPROMELLOSE	2 OTHER: DROPS	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
KETOROLAC	30 OTHER: MG/ML	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
LIDOCAINE	2 %	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
ONDANSETRON	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
POTASSIUM	40 OTHER: MEQ	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34

PROPOFOL	UNKNOWN OTHER: UNKNOWN DOSE	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
SODIUM CHLORIDE	1000 mL	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
WARFARIN	7.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
ENOXAPARIN	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35
WARFARIN	5 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 483
CEFALEXIN	500 mg	BID	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 43
OXYCODONE;PARACETAMOL	50/325 mg	QID	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 56
WARFARIN	7.5 mg	OTHER: 2 TIMES PER WEEK	Y-M: 20[redacted] / 469	Y-M: 20[redacted] / 791
WARFARIN	10 mg	OTHER: 5 DAYS PER WEEK	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 791
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 560	Not reported
WARFARIN	10 mg	OTHER: 5X/WEEK	Y-M: 20[redacted] / 791	Not reported
WARFARIN	12.5 mg	OTHER: 2X/WEEK	Y-M: 20[redacted] / 791	Not reported
I.V. SOLUTIONS	UNKNOWN mL	PRN	Y-M: 20[redacted] / 803	Y-M: 20[redacted] / 805
INFLUENZA VACCINE	1 OTHER: DOSE	OTHER: ONCE	Y-M: 20[redacted] / 1396	Y-M: 20[redacted] / 1396
VALACICLOVIR	1 g	TID	Y-M: 20[redacted] / 1399	Y-M: 20[redacted] / 1410

Event #1: Serious Adverse Event

Event Description	OBSTRUCTIVE DISTAL LEFT URETER STONE, URETERIC OBSTRUCTION, URETEROLITHIASIS
Preferred term	尿管閉塞，尿管結石症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 81 / 25
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 34): Albumin: 35 [32 - 50] G/L; Alkaline Phosphatase: 75 [28 - 126] U/L; Bilirubin: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Calcium: 2.195688 [2.120835 - 2.619855] MMOL/L; Creatinine: 71.606641 [53.041956 - 106.083912] UMOL/L; Erythrocytes: 4.17 [4 - 5.5] 10^12/L; Glucose: 5.661714 [3.607955 - 6.66084] MMOL/L; Glucose: NEGATIVE [73.8646 - 106.2929] mg/dL; Ketones: NEGATIVE [NOT REPORTED - NOT REPORTED] MG/DL; Leukocytes: 12.21 [4 - 12] 10^9/L; NPTST007-A:G RATIO: 1.2 [NOT REPORTED - NOT REPORTED] N/A; NPTST008-ABS BASOS: 0.03 [0 - 0.2] K/UL; NPTST009-ABS EOS: 0.07 [0 - 0.4] K/UL; NPTST010-ABS IMMATURE GRANS: 0.06 [0 - 0.05] K/UL; NPTST011-ABS LYMPHS: 1.53 [0.8 - 3.3] K/UL; NPTST012-ABS MONOS: 1.09 [0.1 - 1] K/UL; NPTST013-ABS NEUTS: 9.43 [1.8 - 7.8] K/UL; NPTST014-ABS NRBCS: 0.00 [0 - 0] K/UL; NPTST032-ANION GAP W/O K: 15 [7 - 15] N/A; NPTST046-BASOS: 0.2 [NOT REPORTED - NOT REPORTED] %; NPTST048-BILIRUBIN TOTAL: 0.6 [0.2 - 1.4] MG/DL; NPTST059-BUN: 15 [8 - 24] MG/DL; NPTST090-CL: 106 [98 - 109] MMOL/L; NPTST096-CO2: 22 [21 - 28] MMOL/L; NPTST129-EOS: 0.6 [NOT REPORTED - NOT REPORTED] %; NPTST154-GFR NON AFRICAN AMERICAN: 74 [59 - NOT REPORTED] mL/min; NPTST161-GLOBULIN(CALC): 2.9 [2 - 4.5] G/DL; NPTST165-HCT: 36.2 [37 - 47] %; NPTST172-HGB: 11.8

[12 - 16] G/DL; NPTST182-IMMATURE GRANS: 0.5 [0 - 0.6] %; NPTST189-INR: 2.0 [0 - 3.5] N/A; NPTST195-K: 3.1 [3.6 - 5.3] MMOL/L; NPTST197-LACTATE: 1.4 [0.7 - 2] MMOL/L; NPTST197-LACTATE: 2.9 [0.7 - 2] MMOL/L; NPTST205-LEUKOCYTE ESTERASE: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; NPTST207-LIPASE: 21 [8 - 78] IU/L; NPTST208-LYMPHS: 12.5 [NOT REPORTED - NOT REPORTED] %; NPTST211-MCH: 28.3 [27 - 33] PG; NPTST212-MCHC: 32.6 [32 - 37] G/DL; NPTST213-MCV: 86.8 [80 - 98] FL; NPTST219-MONOS: 8.9 [NOT REPORTED - NOT REPORTED] %; NPTST229-NA: 143 [135 - 145] MMOL/L; NPTST231-NEUTS: 77.3 [NOT REPORTED - NOT REPORTED] %; NPTST232-NRBC: 0.0 [0 - 100] WBC; NPTST252-PLT: 276 [150 - 450] K/UL; NPTST264-PROTIME: 23.3 [11.3 - 15.2] SEC; NPTST272-RDW: 14.4 [11.5 - 15] %; NPTST301-SGOT/AST: 10 [5 - 40] IU/L; NPTST302-SGPT/ALT: 11 [6 - 60] IU/L; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; Occult Blood: 3+ (A) [NOT REPORTED - NOT REPORTED] N/A; Protein: 64 [62 - 80] G/L; Protein: 20 [NOT REPORTED - NOT REPORTED] MG/DL; Urobilinogen: <2.0 [NOT REPORTED - NOT REPORTED] mg/dL; pH: 5.5 [5 - 8] UNIT NOT REPORTED

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	92 / 36
Duration of AE	12 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNRELATED DISORDER
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Event #2: Serious Adverse Event

Event Description	ACUTE FLARE OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 859 / 803
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 803): Bilirubin: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Erythrocytes: 10-20 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: NEGATIVE [73.8646 - 106.2929] mg/dL; Ketones: 40 [NOT REPORTED - NOT REPORTED] mg/dL; Leukocytes: 10-20 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST205-LEUKOCYTE ESTERASE: 3+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST308-SQUAMOUS CELLS: 310 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Occult Blood: 1+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 20 [NOT REPORTED - NOT REPORTED] mg/dL; Specific Gravity: .1.030 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Urobilinogen: 2.0 [NOT REPORTED - NOT REPORTED] mg/L; pH: 7.5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 804): Erythrocytes: 3.85 [4 - 5.5] 10^12/L; Hematocrit: 0.359 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 112 [120 - 160] G/L; Leukocytes: 7.16 [4 - 12] 10^9/L; NPTST069-C-REACTIVE PROTEIN: 0.9 [0 - 1] MG/DL; NPTST071-CALPROTECTIN: >500 [0 - 50] UG/G; NPTST072-CAMPYLOBACTER DNA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST128-ENTEROINVASIVE ECOLI: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST212-MCHC: 31.2 [32 - 37] G/DL; NPTST264-PROTIME: 35.4 [11.3 - 15.2] SEC; NPTST291-SALMONELLA SP DNA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST303-SHIGA TOXIN GENE DNA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST304-SHIGELLA SP DNA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 61 [62 - 80] G/L; [redacted]20[redacted] (RX DAY 805): Albumin: 30 [32 - 50] G/L; Calcium: 2.021031 [2.120835 - 2.619855] MMOL/L; Chloride: 110 [98 - 109] MMOL/L; Erythrocytes: 3.67 [4 - 5.5] 10^12/L; Hematocrit: 0.34 [0.37 - 0.47] FRACTION OF 1; Hemoglobin: 107 [120 - 160] G/L; Leukocytes: 6.35 [4 - 12] 10^9/L; NPTST032-ANION GAP W/O K: 6 [7 - 15] UNIT NOT REPORTED; NPTST212-MCHC: 31.5 [32 - 37] G/DL; NPTST298-SED RATE (ESR): 22 [0 - 30] MM/H; Protein: 55 [62 - 80] G/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	889 / 833
Duration of AE	31 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COEXISTENT MEDICAL PROBLEM: KIDNEY STONES, BACK PAIN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER INFECTION
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1450 / 1394
Age at AE Onset	5[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	1466 / 1410
Duration of AE	17 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，閉塞性の左腎遠位尿細管結石，尿管閉塞及び尿管結石症の事象を発現した。関連する病歴は，高脂血症，ビタミン B12 欠乏，ビタミン D 欠乏，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与81日後＊　，被験者は，閉塞性の左腎遠位尿細管結石，尿管閉塞及び尿管結石症を発現した。投与92日後＊，閉塞性の左腎遠位尿細管結石，尿管閉塞及び尿管結石症は消失した。

投与90日後＊　，被験者は，突然の側腹部痛が発現したため，救急治療室を受診した。前の週には，時折，通常 1 回 2 時間程度持続する痛みがあった。同日，被験者は左腎の閉塞性尿管結石で入院した。投与90日後＊　，被験者は逆行性腎盂造影を伴う膀胱鏡検査を受け，蛍光透視下で左腎に尿管カテーテルを挿入，ステントを留置された。投与92日後＊　，被験者は退院した。

投与された薬剤は，アセトアミノフェン・オキシコドン合剤，塩化カリウム，塩化ナトリウム，ヒドロモルフォン，オンダンセトロン，ケフレックス及びタイレノールであった。

The patient's past medications include:

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

MESALAMINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

UCERIS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PENICILLIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1) Ureteric obstruction (10046406) (Ureteric obstruction (10046406)) [v.22.0] [10046406]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2) Ureterolithiasis (10077989) (Ureterolithiasis (10077989)) [v.22.0] [10077989]

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 (Open Label)

Event of OBSTRUCTIVE DISTAL LEFT URETER STONE, URETERIC OBSTRUCTION, URETEROLITHIASIS

- Investigator: UNRELATED DISORDER.

- AbbVie: WEAK TEMPORAL ASSOCIATION. KIDNEY STONE FORMATION IS UNLIKELY WITH LESS THAN 3 MONTHS OF STUDY DRUG EXPOSURE (INCLUDING PRIOR CLINICAL TRIAL). ADDITIONALLY, RENAL STONE DISEASE IS A RELATIVELY COMMON PROBLEM WITH AN ESTIMATED 19 PERCENT OF MEN AND 9 PERCENT OF WOMEN WILL BE DIAGNOSED WITH A KIDNEY STONE BY THE AGE OF 70 YEARS. (CURHAN G. RISK FACTORS FOR CALCIUM STONES IN ADULTS. IN: UPTODATE, POST TW(ED), UPTODATE, WALTHAM, MA. (ACCESSED ON [redacted] 20[redacted].))

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ABSOLUTE NEUTROPHILS:** 9.43 KU/L (normal 1.8 to 7.8)

[redacted] 20[redacted] **BUN:** 15 mg/dL (normal 8 to 24)

[redacted] 20[redacted] **CREATININE:** 0.81 mg/dL (normal 0.6 to 1.2)

[redacted] 20[redacted] **CT KUB STONE PROTOCOL W/O IV CONTRAST:** MILD LEFT HYDROURETER AND HYDRONEPHROSIS RELATED TO TINY 3MM LEFT UVJ STONE.

[redacted] 20[redacted] **GFR:** 74 mg/dL (normal >59)

[redacted] 20[redacted] **HGB:** 11.8 G/DL (normal 12 to 16)

[redacted] 20[redacted] **INR:** 2.0 no unit (normal 0 to 3.5)

[redacted] 20[redacted] **PROTIME:** 23.3 SEC (normal 11.3 to 15.2)

[redacted] 20[redacted] **RBC:** 4.17 MIL/UL (normal 4 to 5.5)

[redacted] 20[redacted] **URINE OCCULT BLOOD:** 3+ (A)

[redacted] 20[redacted] **URINE PH:** 5.5 no unit (normal 5.0 to 8.0)

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

[redacted] 20[redacted] **WBC:** 12.21 KU/L (normal 4 to 12)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，急性の潰瘍性大腸炎の再燃の事象を発現した。関連する病歴は，閉経期，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与859日後＊ ，被験者は急性の潰瘍性大腸炎の再燃を発現した。投与889日後＊ ，急性の潰瘍性大腸炎の再燃は消失した。

投与859日後＊ ，被験者は腰背部痛及び急性下痢で入院した。検査を受け，静脈内輸液（詳細不明）を投与された。投与861日後＊，被験者は退院した。

治験責任医師は，過去の腎臓結石が本事象の危険因子であると判断した。

The patient's past medications include:

PENICILLIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.24.1] [10009901]

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 (Open Label)

Event of ACUTE FLARE OF ULCERATIVE COLITIS

- Investigator: Coexistent medical problem: kidney stones, back pain

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 3.0 G/DL (normal 3.2 to 5.0)

[redacted] **20[redacted] ANION GAP W/O K:** 6 no units (normal 7 to 15)

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 0.9 mg/dL (normal 0 to 1.0)

[redacted] **20[redacted] CALCIUM:** 8.1 mg/dL (normal 8.5 to 10.5)

[redacted] **20[redacted] CALPROTECTIN:** >500 ug/g (normal 0 to 50)

[redacted] **20[redacted] CHLORIDE:** 110 MMOL/L (normal 98 to 109)

[redacted] **20[redacted] CT KUB STONE PROTOCOL W/O IV CONTRAST:** Nonobstructive punctate intrarenal calculus without evidence of ureteral calculi, mild increased densities along the renal pyramid in the appropriate contect, considerations include medullary nephrocalcinosis. Appendix is Upper limits of mildly enlarged 7mm without periappendiceal stranding or fluid.

[redacted] **20[redacted] ESR:** 22 MM/HR (normal 0 to 30)

[redacted] **20[redacted] HEMATOCRIT:** 35.9 % (normal 37 to 47)

[redacted] **20[redacted] HEMATOCRIT:** 34.0 % (normal 37 to 47)

[redacted] **20[redacted] HEMOGLOBIN:** 11.2 G/DL (normal 12.0 to 16.0)

[redacted] **20[redacted] HEMOGLOBIN:** 10.7 G/DL (normal 12.0 to 16.0)

[redacted] **20[redacted] MCHC:** 31.2 G/DL (normal 32 to 37)

[redacted] **20[redacted] MCHC:** 31.5 G/DL (normal 32 to 37)

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

[redacted] **20[redacted] OCCULT BLOOD:** Urine: 1+

[redacted] **20[redacted] PROTEIN:** 6.1 G/DL (normal 6.2 to 8.0)[redacted] 20[redacted] PROTEIN: 5.5 G/DL (normal 6.2 to 8.0)

[redacted] **20[redacted] PROTIME:** 35.4 SEC (normal 11.3 to 15.2)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.85 mil/uL (normal 4.0 to 5.5)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.67 mil/uL (normal 4.0 to 5.5)

[redacted] **20[redacted] STOOL CULTURE:** Negative for: Salmonella, Shigella, Campylobacter, Enteroinvasive E. coli, shiga toxin.

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

[redacted] **20[redacted] URINE CYTOLOGY:** Squamous cells: 310 (no units)

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

[redacted] **20[redacted] URINE KETONES:** 40 mg/dL

[redacted] **20[redacted] URINE LEUKOCYTE ESTERASE:** 2.0 MG/L

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

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

[redacted] **20[redacted] URINE RBC:** 10-20 (no units)

[redacted] **20[redacted] URINE SPECIFIC GRAVITY:** 1.030 (no units)

[redacted] **20[redacted] URINE WBC:** 10-20 (no units)

[redacted] **20[redacted] UROBILINOGEN:** 2.0 MG/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.16 K/uL (normal 4.0 to 12.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 6.35 K/uL (normal 4.0 to 12.0)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes zoster: One dermatome. Study drug interrupted.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血				X
深部静脈血栓症	X	X		X
リンパ球減少症				X
好中球減少症				X
肺塞栓症	X	X		X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	7[redacted]	FEMALE	WHITE

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: PENICILLIN ALLERGY	19[redacted]
DRUG ALLERGIES/REACTIONS: SULFA ALLERGY	19[redacted]
EXTENSIVE UC/PANCOLITIS	19[redacted]
OSTEOPOROSIS	20[redacted]
OTHER: BILATERAL LOWER EXTREMITIES EDEMA	20[redacted]
OTHER: KYPHOSIS	19[redacted]
OTHER: OSTEOPENIA	20[redacted]
OTHER: POST MENOPAUSAL	19[redacted]
OTHER: SEASONAL ALLERGIES	19[redacted]
OTHER: ULCERATIVE COLITIS	19[redacted]
OTHER: VARICOSE VEINS BILATERAL LEG	19[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	ORAL	QD	[redacted] / 1	[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted] / 57	[redacted] / 791	735

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	50 mg	TID	Y-M: [redacted]
ADALIMUMAB	40 mg	OTHER: Q2WEEKS	Y-M: [redacted]
PREDNISONE	20 mg	BID	Y-M: [redacted]
BALSALAZIDE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
VEDOLIZUMAB	300 mg	OTHER: Q8WEEKS	Y-M: [redacted]
MAGNESIUM CITRATE	10 OTHER: OUNCE	OTHER: ONCE	Y-M: [redacted] / -8
PROPOFOL	450 mg	OTHER: ONCE	Y-M: [redacted] / -8
ACETYLSALICYLIC ACID	81 mg	QD	Y: [redacted]
ASCORBIC ACID;BIOTIN;CALCIUM;CHLORINE;CHROMIUM;COLECALCIFEROL;COPPER;CYANOCOBALAMIN;FOLIC ACID;IODINE;IRON;MAGNESIUM;MANGANESE;MOLYBDENUM;NICKEL;NICOTINAMIDE;PANTOTHENIC ACID;PHOSPHORUS;PHYTOMENADION	1 OTHER: TABLET	QD	Y: [redacted]
AZELASTINE	30 mg	PRN	Y: [redacted]
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM LONGUM;LACTOBACILLUS GASSERI	1 OTHER: TABLET	QD	Y: [redacted]
CALCIUM CARBONATE;COLECALCIFEROL	1 OTHER: TABLET	QD	Y: [redacted]
COLECALCIFEROL	5000 IU	OTHER: QOD	Y: [redacted]
FEXOFENADINE;PSEUDOEPHEDRINE	60-120 OTHER: TABLET	PRN	Y: [redacted]
IRON	1/2 OTHER: TABLET	OTHER: QOD	Y: [redacted]
LINUM USITATISSIMUM	1000 mg	QD	Y: [redacted]

MAGNESIUM;MAGNESIUM CITRATE;MAGNESIUM OXIDE	400 mg	QD	Y: 20[redacted]
METHYLSULFONYLMETHANE	1000 mg	QD	Y: 20[redacted]
POTASSIUM	99 mg	QD	Y: 20[redacted]
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y: 20[redacted]
XANTOFYL;ZEAXANTHIN	1 OTHER: TABLET	QD	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LIDOCAINE	3 OTHER: CC	OTHER: Q4S	Y-M: 20[redacted] / 518	ONGOING
BISACODYL	4 OTHER: TABLET	OTHER: ONCE	Y-M: 20[redacted] / 670	Y-M: 20[redacted] / 671
MACROGOL 3350	298 g	OTHER: ONCE	Y-M: 20[redacted] / 670	Y-M: 20[redacted] / 671
MAGNESIUM CITRATE	10 OTHER: OUNCE	OTHER: ONCE	Y-M: 20[redacted] / 670	Y-M: 20[redacted] / 671
PROPOFOL	250 mg	OTHER: ONCE	Y-M: 20[redacted] / 671	Y-M: 20[redacted] / 671
GLUCOSE;HEPARIN	11.84 mL	OTHER: HOURLY	Y-M: 20[redacted] / 715	Y-M: 20[redacted] / 718
AZITHROMYCIN;GLUCOSE	500/250 OTHER: MG/ML	QD	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
CEFTRIAXONE	2/20 OTHER: G/ML	QD	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
DIPHENHYDRAMINE	50 mg	OTHER: QHS	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
DOCUSATE;SENNA ALEXANDRINA	50-8.6 mg	BID	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
HYDRALAZINE	10/0.5 OTHER: MG/ML	OTHER: Q4H	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
MAGNESIUM HYDROXIDE	30 mL	OTHER: Q6H	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
MELATONIN	5 mg	OTHER: QHS	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
ONDANSETRON	4/2 OTHER: MG/ML	OTHER: Q4H	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 720
PARACETAMOL	325 (2 TABS) mg	OTHER: Q4-Q6	Y-M: 20[redacted] / 716	Y-M: 20[redacted] / 730
APIXABAN	5 (2 TABS) mg	BID	Y-M: 20[redacted] / 718	Y-M: 20[redacted] / 724
FOLIC ACID	1 mg	QD	Y-M: 20[redacted] / 721	ONGOING
APIXABAN	5 mg	BID	Y-M: 20[redacted] / 725	ONGOING
FEXOFENADINE	60 mg	PRN	Y-M: 20[redacted] / 730	ONGOING
DENOSUMAB	60 mg	OTHER: Q 6 MONTHS	Y-M: 20[redacted] / 737	ONGOING
MESALAZINE	0.375 (4 TABS) g	QD	Y-M: 20[redacted] / 749	Y-M: 20[redacted] / 831
FLUTICASONE;VILANTEROL	1 OTHER: INH	QD	Y-M: 20[redacted] / 827	ONGOING
SALBUTAMOL	2 OTHER: INH	OTHER: Q4-6H	Y-M: 20[redacted] / 827	ONGOING

ACETYLSALICYLIC ACID	81 mg	QD	Y: 20[redacted]	ONGOING
ASCORBIC ACID;BIOTIN;CALCIUM;CHLORINE;CHROMIUM;COLECALCIFEROL;COPPER;CYANOCOBALAMIN;FOLIC ACID;IODINE;IRON;MAGNESIUM;MANGANESE;MOLYBDENUM;NICKEL;NICOTINAMIDE;PANTOTHENIC ACID;PHOSPHORUS;PHYTOMENADION	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING
AZELASTINE	30 mg	PRN	Y: 20[redacted]	ONGOING
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM LONGUM;LACTOBACILLUS GASSERI	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING
CALCIUM CARBONATE;COLECALCIFEROL	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING
COLECALCIFEROL	5000 IU	OTHER: QOD	Y: 20[redacted]	ONGOING
FEXOFENADINE;PSEUDOEPHEDRINE	60-120 OTHER: TABLET	PRN	Y: 20[redacted]	Y-M: 20[redacted] / 729
IRON	1/2 OTHER: TABLET	OTHER: QOD	Y: 20[redacted]	ONGOING
LINUM USITATISSIMUM	1000 mg	QD	Y: 20[redacted]	ONGOING
MAGNESIUM;MAGNESIUM CITRATE;MAGNESIUM OXIDE	400 mg	QD	Y: 20[redacted]	ONGOING
METHYLSULFONYLMETHANE	1000 mg	QD	Y: 20[redacted]	ONGOING
POTASSIUM	99 mg	QD	Y: 20[redacted]	ONGOING
VITAMIN B COMPLEX	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING
XANTOFYL;ZEAXANTHIN	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING

Event #1: Event of Interest - Lymphopenia

Event Description	LYMPHOPENIA
Preferred term	リンパ球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 734 / 678
Age at AE Onset	7[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	773 / 717
Duration of AE	40 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 734 / 678
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	771 / 715
Duration of AE	38 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #3: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 771 / 715
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	

Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	869 / 813 (78 DAYS AFTER LAST TREATMENT)
Duration of AE	99 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	DEEP VEIN THROMBOSIS - RIGHT LEG, PULMONARY EMBOLISM
Preferred term	深部静脈血栓症，肺塞栓症
AE Onset Date / Initial Rx Day / Rx Day	[redacted] / 771 / 715
Age at AE Onset	7[redacted]
Laboratory Testing	

[redacted] (RX DAY 715): NPTST189-INR: 1.1 [0.9 - 1.1] RATIO; NPTST266-PT: 11.1 [9.5 - 12] SEC; NPTST323-TROPONIN: 0.075 [0 - 0.039] NG/ML; [redacted] (RX DAY 716): NPTST270-PTT: 58 [22 - 32] SEC

Microbiology

[redacted] (RX DAY 715): OTHER NASAL SWAB NPTST296-SARS-COV-2, NAA LC: Negative; [redacted] (RX DAY 716): URINE NPTST202-LEGIONELLA AG: Negative; URINE NPTST311-STREPNEUMO AG: Negative

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]:16:51

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，右下肢の深部静脈血栓症及び肺塞栓症の事象を発現した。関連する病歴は，両下肢の静脈瘤，潰瘍性大腸炎，両下肢の浮腫，非喫煙者及び非飲酒者であった。

Event 4 の臨床経過：

投与771日後＊，被験者は，右下肢の深部静脈血栓症及び肺塞栓症を発現した。

投与771日後＊　，被験者は大腸内視鏡検査の前処置（詳細不明）後の疲労感のため入院した。咳嗽の増加，胸膜炎による胸痛及び間欠的な熱感があった。CTA 検査及び下肢ドップラー検査が実施され，右側及び左側の肺塞栓及び右下肢に 2 つの血栓が認められた。投与776日後＊　，被験者は退院した。

本事象により本被験者の治験は中止された。

投与された薬剤は，ヘパリン，エリキュース，albuterol sulfate，オンダンセトロン，メラトニン，水酸化マグネシウム，ヒドララジン，docusate senna，葉酸，アセトアミノフェン，セフトリアキソン・注射用水合剤，アジスロマイシン・5%ブドウ糖注射液合剤，ファモチジン及びジフェンヒドラミンであった。

The patient's past medications include:

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

PREDNISONE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BALSALAZIDE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PENICILLIN for UNKNOWN INDICATION

SULFA for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1)　Pulmonary embolism (10037377)　(Pulmonary embolism (10037377))　[v.23.1]　[10037377]

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

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

Dechallenge: No

2) Deep vein thrombosis leg (10065052) (Deep vein thrombosis (10051055)) [v.23.1] [10065052]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Open Label)

Event of DEEP VEIN THROMBOSIS RIGHT LEG, PULMONARY EMBOLISM

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing varicose veins (odds ratio of 7.33) and pre-existing ulcerative colitis which confers a 3-fold increase risk of developing venous thromboembolism and advanced age which shows an exponential increase in first-time venous thromboembolism incidence particularly after the age of 60.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] 2D ECHO:** Normal left ventricular size and left ventricular systolic function, estimated EF 65-70 %

[redacted] **20[redacted] CHEST X RAY:** Mild diffuse prominence of interstitial lung markings

[redacted] **20[redacted] CTA CHEST:** PE in left and right.

[redacted] **20[redacted] LE VENOUS DOPPLER:** Non occlusive thrombus in right popliteal vein and right peroneal vein

[redacted] **20[redacted] NASAL SWAB SARS-COV-2:** Negative

[redacted] **20[redacted] PT:** 11.1 SEC

[redacted] **20[redacted] PTT:** 58 SEC (normal 22 to 32)

[redacted] **20[redacted] TROPONIN:** 0.075 NG/ML (normal 0.000 to 0.039)

[redacted] **20[redacted] URINE LEGIONELLA AG:** negative

[redacted] **20[redacted] URINE STREP PNEUMO AG:** Negative

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19 肺炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	3[redacted]	FEMALE	BLACK OR AFRICAN AMERICAN

Medical History	Onset Year
ARTHRALGIAS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GERD	20[redacted]
INTERMITTENT LOWER ABDOMINAL CRAMPING	20[redacted]
IRON DEFICIENCY ANEMIA	20[redacted]
PSORIASIS	20[redacted]
SCAR TISSUE REMOVED	NOT REPORTED
SEASONAL ALLERGIES	20[redacted]
SINUS CONGESTION	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: C-SECTION	20[redacted]
PRIOR PROCEDURES: C-SECTION	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 57	[redacted] / 421	365
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted] / 422	[redacted] / 756	335

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	40 mg	OTHER: Q2WEEKS	Y-M: [redacted]
PREDNISONE	10 mg	QD	Y-M: [redacted]
CETIRIZINE	10 mg	QD	Y-M: [redacted]
DEXTROMETHORPHAN;DOXYLAMINE;GUAIFENESIN;PARACETAMOL;PHENYLEPHRINE	2 OTHER: CAPSULE	PRN	Y-M: [redacted]
DEXLANSOPRAZOLE	60 mg	QD	Y-M: [redacted]
IRON;VITAMINS NOS	1 OTHER: TAB	QD	Y-M: [redacted]
HYDROCODONE	10 mg	PRN	Y-M: [redacted] / -323
PARACETAMOL	325 mg	PRN	Y-M: [redacted] / -57
TRAMADOL	50 mg	PRN	Y-M: [redacted] / -57
MESALAZINE	2.4 g	QD	Y: [redacted]
PREDNISONE	15 mg	QD	Y: [redacted]
LORATADINE	10 mg	QD	Y: [redacted]
ETHINYLESTRADIOL;NORETHISTERONE	1 OTHER: TABLET	QD	Y: [redacted]
AZATHIOPRINE	50 mg	QD	Y: [redacted]
CLOBETASOL	1 OTHER: APPLICATION	PRN	Y: [redacted]
IRON	325 mg	QD	Y: [redacted]
OXYMETAZOLINE	1 OTHER: SPRAY	PRN	Y: [redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	ONGOING
DEXTROMETHORPHAN;DOXYLAMINE;GUAIFENESIN;PARACETAMOL;PHENYLEPHRINE	2 OTHER: CAPSULE	PRN	Y-M: 20[redacted]	ONGOING
DEXLANSOPRAZOLE	60 mg	QD	Y-M: 20[redacted]	ONGOING
IRON;VITAMINS NOS	1 OTHER: TAB	QD	Y-M: 20[redacted]	ONGOING
HYDROCODONE	10 mg	PRN	Y-M: 20[redacted] / -323	ONGOING
PARACETAMOL	325 mg	PRN	Y-M: 20[redacted] / -57	ONGOING
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / -57	ONGOING
AZITHROMYCIN	NOT REPORTED	QD	Y-M: 20[redacted] / 10	Y-M: 20[redacted] / 15
LORATADINE	10 mg	QD	Y: 20[redacted]	ONGOING
ETHINYLESTRADIOL;NORETHISTERONE	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING
CLOBETASOL	1 OTHER: APPLICATION	PRN	Y: 20[redacted]	ONGOING
IRON	325 mg	QD	Y: 20[redacted]	ONGOING
OXYMETAZOLINE	1 OTHER: SPRAY	PRN	Y: 20[redacted]	ONGOING

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

Event Description	COVID-19 PNEUMONIA INFECTION
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 431 / 10
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 15): Basophils: 0.02 [0 - 0.2] 10^9/L; Basophils/Leukocytes: 0.2 [0 - 2] %; Eosinophils: 0 [0 - 0.45] 10^9/L; Eosinophils/Leukocytes: 0 [0 - 6.04] %; Erythrocytes: 4.32 [3.41 - 5.25] 10^12/L; Hematocrit: 0.395 [0.296 - 0.468] FRACTION OF 1; Hemoglobin: 121 [99 - 159] G/L; Leukocytes: 10.35 [4.8 - 11.7] 10^9/L; Lymphocytes: 0.88 [0.55 - 3.16] 10^9/L; Lymphocytes/Leukocytes: 8.5 [8.6 - 45.3] %; Monocytes: 0.22 [0.16 - 0.9] 10^9/L; Monocytes/Leukocytes: 2.1 [3.38 - 11.8] %; NPTST173-HGBA1C: 6.2 [4.5 - 5.7] %; NPTST180-IG%: 0.40 [0 - 1.99] %; NPTST189-INR: 1.2 [0.8 - 1.2] RATIO; NPTST192-IPF: 0.0 [1.2 - 8.6] %; NPTST210-MBGLU: 131 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST211-MCH: 28.0 [26.1 - 33.6] PG; NPTST212-MCHC: 30.6 [32.4 - 35.2] G/DL; NPTST213-MCV: 91.4 [79.1 - 97.9] FL; NPTST220-MPV: 10.0 [6.64 - 11.5] FL; NPTST266-PT: 12.2 [9.2 - 12.2] SEC; NPTST272-RDW: 15.4 [11.1 - 17.3] %; Neutrophils: 9.19 [1.07 - 7.96] 10^9/L; Neutrophils/Leukocytes: 88.8 [42.2 - 82] %; Platelets: 331 [138.2 - 386.2] 10^9/L; [redacted]20[redacted] (RX DAY 16): Alanine Aminotransferase: 84 [12 - 78] U/L; Alkaline Phosphatase: 47 [50 - 136] U/L; Aspartate Aminotransferase: 27 [15 - 37] U/L; Blood Urea Nitrogen: 3.92667 [2.49879 - 6.42546] MMOL/L; Calcium: 2.220639 [2.120835 - 2.4951] MMOL/L; Chloride: 103 [100 - 108] MMOL/L; Cholesterol: 5.767449 [2.5863 - 5.1726] MMOL/L; Creatine Kinase: 34 [26 - 192] U/L; Creatinine: 53.041956 [53.041956 - 114.924238] UMOL/L; Glucose: 6.438812 [3.88549 - 6.10577] MMOL/L; HDL Cholesterol: 55 [NOT REPORTED - 65] mg/dL; LDL Cholesterol:

3.750135 [0 - 3.36219] MMOL/L; NPTST005-A/G: 0.5 [1 - 3] G/DL; NPTST034-ANIONGAP: 14 [3 - 19] UNIT NOT REPORTED; NPTST051-BILT: 0.50 [0 - 1] MG/DL; NPTST096-CO2: 25 [21 - 32] MMOL/L; NPTST159-GLOBULIN: 5.3 [2.2 - 4.2] G/DL; NPTST215-MG: 2.4 [1.8 - 2.4] MG/DL; NPTST234-OSMOC: 276 [250 - 300] MOSM/KG; NPTST331-TSH: 0.204 [0.36 - 3.74] IU/ML; Potassium: 3.8 [3.6 - 5.5] MMOL/L; Sodium: 138 [135 - 145] MMOL/L; Triglycerides: 1.2995 [0.339 - 2.26] MMOL/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	455 / 34
Duration of AE	25 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID 19 RELATED SYMPTOMS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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，COVID-19 肺炎の感染症の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与431日後＊ ，被験者はCOVID-19肺炎の感染症を発現した。投与455日後＊ ，COVID-19肺炎の感染症は消失した。

投与436日後＊ ，被験者は COVID-19 肺炎で救急治療室を受診した。被験者は，続発性の低酸素症及び呼吸状態の悪化のため入院した。徴候及び症状には，息切れ，咳嗽，悪心，嘔吐，発熱及び悪寒が含まれた。投与437日後＊ ，呼吸窮迫，発熱，鼻閉及び両側性肺炎の COVID-19 の症状の訴えはなかった。酸素飽和度は室内気で 90%半ばであり，発熱はなかった。投与438日後＊，被験者は退院した。

投与された薬剤は，アジスロマイシンであった。

The patient's past medications include:

MESALAMINE for ULCERATIVE COLITIS (20[redacted] - 20[redacted], 20[redacted] - 20[redacted])

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

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 PNEUMONIA INFECTION

- Investigator: COVID 19 RELATED SYMPTOMS

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 84 U/L (normal 12 to 78)

[redacted] **20[redacted] BMI:** 28.7 kg/m2

[redacted] **20[redacted] BODY WEIGHT:** 14[redacted] Pounds

[redacted] **20[redacted] CHOLESTEROL:** 223 mg/dL (normal 100 to 200)

[redacted] **20[redacted] CT SCAN:** Increased minimal bilateral upper lobe and right middle lobe peripheral rounded triangular shaped ground-glass opacities. Increased moderate right and left lower lobe wedge-shaped areas of ground-glass opacity and patchy consolidation. Findings could be consistent with worsening COVID 19.

[redacted] **20[redacted] EOSINOPHILS ABS:** 0.00 10^3/uL (normal 0 to 0.45)

[redacted] **20[redacted] GLOBULIN:** 5.3 G/DL (normal 2.2 to 4.2)

[redacted] **20[redacted] GLUCOSE:** 116 mg/dL (normal 70 to 110)

[redacted] **20[redacted] HGBA1C:** 6.2 % (normal 4.5 to 5.7)

[redacted] **20[redacted] INR:** 1.2 no units (normal 0.8 to 1.2)

[redacted] **20[redacted] LDL CHOLESTEROL:** 145 mg/dL (normal 0 to 130)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.88 10^3/uL (normal 0.55 to 3.16)

[redacted] **20[redacted] MONOCYTES %:** 2.1 % (normal 3.38 to 11.8)

[redacted] **20[redacted] MONOCYTES ABS:** 0.22 X10**3/MCL (normal 0.16 to 0.9)

[redacted] **20[redacted] NEUTROPHILS %:** 88.8 % (normal 42.2 to 82)

[redacted] **20[redacted] NEUTROPHILS ABS:** 9.19 X10**3/MCL (normal 1.07 to 7.96)

Unknown date OXYGEN SATURATION: 97 %

[redacted] **20[redacted] RED BLOOD CELLS:** 4.32 10^6/uL (normal 3.41 to 5.25)

[redacted] **20[redacted] SAR-COV-2 TEST:** POSITIVE

[redacted] **20[redacted] WHITE BLOOD CELLS:** 10.35 10^3/uL (normal 4.8 to 11.7)

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

Reason for Narrative

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

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
HIGH CHOLESTEROL	20[redacted]
NECK FUSION C6-C7	20[redacted]
PARTIAL THYROID REMOVAL	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 65	65
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 66	[redacted]20[redacted] / 441	376

M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 442

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PRAVASTATIN	10 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	200 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
DESOGESTREL;ETHINYLESTRADIOL	0.15 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
PRAVASTATIN	10 mg	QD	Y-M: 20[redacted]	Not reported
DESOGESTREL;ETHINYLESTRADIOL	0.15 mg	QD	Y-M: 20[redacted]	Not reported
BUPIVACAINE;EPINEPHRINE	0.5 %	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	900 mL	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	UNK mg	OTHER: CONTINUOUS	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 181
DEXAMETHASONE	10 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
DEXMEDETOMIDINE	8 OTHER: MCG	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
DIPHENHYDRAMINE	25 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
ERTAPENEM	1 g	OTHER: ONE TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
GLYCOPYRRONIUM	0.4 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
HYDROMORPHONE	0.5 mg	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 185
HYDROMORPHONE	1 mg	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 181
HYDROMORPHONE	2 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
IOHEXOL	150 mL	OTHER: ONCE	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
KETAMINE	40 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
LIDOCAINE	50 mg	OTHER: ONE TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180

MIDAZOLAM	2 mg	OTHER: ONE TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
MORPHINE	4 mg	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
NALOXONE	0.04 mg	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 181
NALOXONE	0.4 mg	OTHER: ONE TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
NEOSTIGMINE	3 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
ONDANSETRON	4 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
ONDANSETRON	4 mg	OTHER: EVERY 6 HOURS AS NEEDED	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 185
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 181
OXYCODONE	10 mg	OTHER: EVERY 4 HOURS AS NEEDED	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 185
OXYCODONE	5 mg	OTHER: EVERY 4 HOURS AS NEEDED	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 185
PARACETAMOL	1000 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
PARACETAMOL	1000 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 185
PHENYLEPHRINE	1000 OTHER: MCG	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
PHENYLEPHRINE	4500 OTHER: MCG	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
PROPOFOL	150 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
ROCURONIUM	90 mg	OTHER: ONE TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
SODIUM CHLORIDE	0.9 %	PRN	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 185
SUGAMMADEX	200 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
SUXAMETHONIUM	140 mg	OTHER: 1 TIME	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 180
ATORVASTATIN	5 mg	OTHER: EVERY 48 HOURS	Y-M: 20[redacted] / 181	Y-M: 20[redacted] / 185
BENZOCAINE;MENTHA X PIPERITA;MENTHOL	15-3.6 mg	PRN	Y-M: 20[redacted] / 181	Y-M: 20[redacted] / 185
CYCLOBENZAPRINE	5 mg	TID	Y-M: 20[redacted] / 181	Y-M: 20[redacted] / 185
ENOXAPARIN	40 mg	OTHER: EVERY 24 HOURS	Y-M: 20[redacted] / 181	Y-M: 20[redacted] / 185
GLUCOSE	5 %	OTHER: CONTINUOUS	Y-M: 20[redacted] / 181	Y-M: 20[redacted] / 184
POTASSIUM	20 mEq	OTHER: CONTINUOUS	Y-M: 20[redacted] / 181	Y-M: 20[redacted] / 184
SODIUM CHLORIDE	1000 mL	OTHER: CONTINUOUS	Y-M: 20[redacted] / 181	Y-M: 20[redacted] / 184
PHOSPHORUS	500 mg	BID	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 183
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 185	Not reported

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

Event Description	ACUTE APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 621 / 180
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 181): Albumin: 3.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood Urea Nitrogen: 4.28364 [1.78485 - 8.56728] MMOL/L; Calcium: 2.120835 [2.095884 - 2.619855] MMOL/L; Chloride: 105 [99 - 110] MMOL/L; Creatinine: 82.215032 [35.361304 - 88.40326] UMOL/L; Erythrocytes: 3.63 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: 9.602711 [3.88549 - 5.495193] MMOL/L; Hematocrit: 34.1 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 116 [112 - 155] G/L; Leukocytes: 15 [3.2 - 11] 10^9/L; NPTST031-ANION GAP: 11.0 [3 - 15] MEQ/L; NPTST073-CANCER AG 12 5: 16 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST074-CARBOHYD AG 19-9: 42 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST076-CEA: 32.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST096-CO2: 18 [19 - 29] MEQ/L; NPTST151-GFR CALCULATED: 60 [1.73 - 2] ML/MIN; NPTST209-MAGNESIUM: 1.8 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST211-MCH: 32.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST212-MCHC: 34.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST213-MCV: 93.9 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST250-PHOSPHORUS: 2.9 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST252-PLT: 304 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST272-RDW: 12.3 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 4.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Sodium: 134 [134 - 143] MMOL/L; [redacted]20[redacted] (RX DAY 182): Albumin: 2.7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood Urea Nitrogen: 4.64061 [1.78485 - 8.56728] MMOL/L; Calcium: 2.021031 [2.095884 - 2.619855] MMOL/L; Chloride: 109 [99 - 110] MMOL/L; Creatinine: 86.635195 [35.361304 - 88.40326] UMOL/L; Erythrocytes: 3.19 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: 7.659966 [3.88549 - 5.495193] MMOL/L; Hematocrit: 30.7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 101 [112 - 155] G/L; Leukocytes: 10.9 [3.2 - 11] 10^9/L; NPTST031-ANION GAP: 9.0 [3 - 15] MEQ/L; NPTST096-CO2: 19 [19 - 29] MEQ/L; NPTST209-MAGNESIUM: 2.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST211-MCH: 31.7 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST212-MCHC: 32.9 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST213-MCV: 96.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST250-PHOSPHORUS: 2.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST272-RDW: 12.6 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 280 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 3.8 [3.4 - 5.1] MMOL/L; Sodium: 137 [134 - 143] MMOL/L; [redacted]20[redacted] (RX DAY 183): Albumin: 2.8 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood Urea Nitrogen: 2.85576 [1.78485 - 8.56728] MMOL/L; Calcium: 2.095884 [2.095884 - 2.619855] MMOL/L; Chloride: 110 [99 - 110] MMOL/L; Creatinine: 74.258738 [35.361304 - 88.40326] UMOL/L; Erythrocytes: 3.46 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Glucose: 6.327798 [3.88549 - 5.495193] MMOL/L; Hematocrit: 32.5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 108 [112 - 155] G/L; Leukocytes: 8.5 [3.2 - 11] 10^9/L; NPTST031-ANION GAP: 9.0 [3 - 15] MEQ/L; NPTST096-CO2: 19 [19 - 29] MEQ/L; NPTST209-MAGNESIUM: 2.0 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST211-MCH: 31.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST212-MCHC: 33.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST213-MCV: 93.9 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST250-PHOSPHORUS: 2.3 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST272-RDW: 12.5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 309 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 3.8 [3.4 - 5.1] MMOL/L; Sodium: 138 [134 - 143] MMOL/L; [redacted]20[redacted] (RX DAY 184): Albumin: 2.9 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Blood Urea Nitrogen: 2.85576 [1.78485 - 8.56728] MMOL/L; Calcium: 2.170737

[2.095884 - 2.619855] MMOL/L; Chloride: 109 [99 - 110] MMOL/L; Creatinine: 73.374706 [35.361304 - 88.40326] UMOL/L; Glucose: 6.438812 [3.88549 - 5.495193] MMOL/L; NPTST031-ANION GAP: 7.0 [3 - 15] MEQ/L; NPTST096-CO2: 21 [19 - 29] MEQ/L; NPTST209-MAGNESIUM: 2.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST250-PHOSPHORUS: 3.2 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Potassium: 3.8 [3.4 - 5.1] MMOL/L; Sodium: 137 [134 - 143] MMOL/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	626 / 185
Duration of AE	6 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	LIKELY A RANDOM EVENT OR POSSIBLY RELATED TO THE IBD PROCESS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，急性虫垂炎の事象を発現した。関連する病歴は，コレステロール高値，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与621日後＊　，被験者は急性虫垂炎を発現した。投与626日後＊　，急性虫垂炎は消失した。

投与621日後＊　，被験者は右下腹部痛を訴えて救急科を受診した。精密検査により虫垂炎の可能性が明らかとなり，その後，被験者は入院した。被験者は，ムチン漏出を伴う穿孔が懸念されたことによる CT スキャン検査，及び臨床検査を含む診断法を受けた。試験開腹で上行結腸右半切除術（この時点では病理がまだ得られていなかったため結果は保留），結腸部分切除術，回腸結腸吻合術，回腸末端の切除及び虫垂切除術が施行された。投与626日後＊　，被験者は常食に耐容性があると診断され，便通が認められ，また，痛みは適切にコントロールされていた。

同日，被験者は退院した。

投与された薬剤は，cyclobenzaprine，リン，lovenox，ブドウ糖水和物，塩化ナトリウム，塩化カリウム，benzocaine-menthol lozenge，zofran，dilaudid，タイレノール，invanz，モルヒネ，ラクトリンゲル，オキシコドン，リピトール，ケタミン，デキサメタゾン及びジフェンヒドラミンであった。

The patient's past medications include:

SULFASALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MESALAMINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PFIZER BIONTECH COVID-19 VACCINE for PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.24.1] [10000677]

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 (Open Label)

Event of ACUTE APPENDICITIS

- Investigator: Likely a random event or possibly related to the IBD process

- AbbVie: Event of appendicitis is common in the general population; lifetime incidence is 6.7 percent in females. Additional risk factor includes pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 3.0 no unit

[redacted] **20[redacted] ALBUMIN:** 2.9 no unit

[redacted] **20[redacted] ANION GAP:** 11 MEQ/L (normal 3 to 15)

[redacted] **20[redacted] ANION GAP:** 7 MEQ/L (normal 3 to 15)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 13 mg/dL (normal 5 to 24)

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 8 mg/dL (normal 5 to 24)

[redacted] **20[redacted] CA19-9:** 42 no unit

[redacted] **20[redacted] CALCIUM:** 8.5 mg/dL (normal 8.4 to 10.5)

[redacted] **20[redacted] CALCIUM:** 8.7 mg/dL (normal 8.4 to 10.5)

[redacted] **20[redacted] CANCER ANTIGEN 125:** 16 no unit

[redacted] **20[redacted] CEA:** 32.2 no unit

[redacted] **20[redacted] CHLORIDE:** 105 MEQ/L (normal 99 to 110)

[redacted] **20[redacted] CHLORIDE:** 109 MEQ/L (normal 99 to 110)

[redacted] **20[redacted] CO2:** 18 MEQ/L (normal 19 to 29)

[redacted] **20[redacted] CO2:** 21 MEQ/L (normal 19 to 29)

[redacted] **20[redacted] CREATININE:** 0.93 mg/dL (normal 0.40 to 1.00)

[redacted] **20[redacted] CREATININE:** 0.83 mg/dL (normal 0.4 to 1.0)

[redacted] **20[redacted] CT:** CT Abdomen/Pelvis - findings suggested a large mucocele with surrounding extraluminal mucin/fluid, fibroid uterus including a large, likely degenerating fibroid fundus, and hepatomegaly and hepatic steatosis

[redacted] **20[redacted] GFR CALCULATED:** 60 ML/Min (normal 1.73 to 2)

[redacted] **20[redacted] GLUCOSE:** 173 mg/dL (normal 70 to 99)

[redacted] **20[redacted] GLUCOSE:** 116 mg/dL (normal 70 to 99)

[redacted] **20[redacted] HEMATOCRIT:** 34.1 no unit

[redacted] **20[redacted] HEMATOCRIT:** 32.5 no unit

[redacted] **20[redacted] HEMOGLOBIN:** 11.6 G/DL (normal 11.2 to 15.5)

[redacted] **20[redacted] HEMOGLOBIN:** 10.8 G/DL (normal 11.2 to 15.5)

[redacted] **20[redacted] MAGNESIUM:** 1.8 no units

[redacted] **20[redacted] MAGNESIUM:** 2.2 no unit

[redacted] **20[redacted] PHOSPHORUS:** 2.9 no units

[redacted] **20[redacted] PHOSPHORUS:** 2.0 no unit

[redacted] **20[redacted] PHOSPHORUS:** 3.2 no unit

[redacted] **20[redacted] PLATELET COUNT:** 309 no unit

[redacted] **20[redacted] PLT:** 304 no unit

[redacted] **20[redacted] POTASSIUM:** 4 no unit

[redacted] **20[redacted] POTASSIUM:** 3.8 MEQ/L (normal 3.4 to 5.1)

[redacted] **20[redacted] POTASSIUM:** 3.8 MEQ/L (normal 3.4 to 5.1)

[redacted] **20[redacted] RED BLOOD CELLS:** 3.19 no unit

[redacted] **20[redacted] RED BLOOD CELLS:** 3.46 no unit

[redacted] **20[redacted] SODIUM:** 134 MEQ/L (normal 134 to 143)

[redacted] **20[redacted] SODIUM:** 137 MEQ/L (normal 134 to 143)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 15.0 X10**9/L (normal 3.2 to 11.0)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.5 X10**9/L (normal 3.2 to 11.0)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
血中クレアチンホスホキナーゼ増加				X
薬物依存	X			
肺塞栓症	X			

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

Medical History	Onset Year
DEPRESSION	20[redacted]
DVT	20[redacted]
ELEVATED C- REACTIVE PROTEIN	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HISTORY OF DRUG ABUSE (COCAINE)	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
REVISE MEDIAN N/CARPAL TUNNEL	20[redacted]
RIGHT HIP PAIN	20[redacted]
SUICIDE ATTEMPT	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	20[redacted]
PRIOR PROCEDURES: BUNIONECTOMY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: INCISION OF WRIST CAPSULE	20[redacted]
PRIOR PROCEDURES: TONSILLECTOMY	19[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			

CIGARETTES	FORMER	1 PACK	20	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 61	61
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 62	[redacted]20[redacted] / 430	369
M14-533 ABT-494 (LTE)	30 mg	ORAL	QD	[redacted]20[redacted] / 431	[redacted]20[redacted] / 613	183

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]
MESALAZINE	1.2 g	QD	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]
HYDROCHLOROTHIAZIDE;LISINOPRIL	20-12.5 mg	QD	Y-M: 20[redacted] / -308
LACTOBACILLUS ACIDOPHILUS	2 OTHER: CAPSULES	QD	Y-M: 20[redacted] / -99
APIXABAN	5 mg	BID	Y-M: 20[redacted] / -4
VITAMINS NOS	1 OTHER: TAB	QD	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]	ONGOING
HYDROCHLOROTHIAZIDE;LISINOPRIL	20-12.5 mg	QD	Y-M: 20[redacted] / -308	ONGOING
LACTOBACILLUS ACIDOPHILUS	2 OTHER: CAPSULES	QD	Y-M: 20[redacted] / -99	ONGOING

APIXABAN	5 mg	BID	Y-M: 20[redacted] / -4	ONGOING
BISACODYL	10 mg	OTHER: QD -PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
DOCUSATE	1 OTHER: ENEMA	OTHER: QD- PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
DOCUSATE;SENNA ALEXANDRINA	2 OTHER: TABS	OTHER: BID- PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
METOCLOPRAMIDE	5 mg	OTHER: EVERY 8 HOURS PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
ONDANSETRON	4 mg	OTHER: 4 TIMES A DAY - PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
OXYCODONE;PARACETAMOL	10-325 mg	OTHER: EVERY 8 HOURS - PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
OXYCODONE;PARACETAMOL	5-325 mg	OTHER: EVERY 6 HOURS - PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
SODIUM CHLORIDE	10 mL	BID	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
AMOXICILLIN;CLAVULANIC ACID	875-125 mg	BID	Y-M: 20[redacted] / 8	Y-M: 20[redacted] / 16
APIXABAN	10 mg	BID	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 16
SODIUM PHOSPHATE	250 mL	OTHER: 1 TIME	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 9
UBIDECARENONE	1 OTHER: CAP	QD	Y-M: 20[redacted] / 9	ONGOING
ACETYLCYSTEINE	1200 mg	BID	Y-M: 20[redacted] / 32	ONGOING
DIAZEPAM	5 mg	PRN	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 58
DOCUSATE	100 mg	PRN	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 58
ESCITALOPRAM	5 mg	QD	Y-M: 20[redacted] / 32	ONGOING
HYDROXYZINE	25 mg	PRN	Y-M: 20[redacted] / 32	ONGOING
MAGNESIUM HYDROXIDE	30 mL	PRN	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 58
MELATONIN	5 mg	PRN	Y-M: 20[redacted] / 32	ONGOING
NICOTINE	14 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 58
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 58
PLANTAGO OVATA	1 OTHER: PACKET	BID	Y-M: 20[redacted] / 32	ONGOING
SALBUTAMOL	180 OTHER: MCG	PRN	Y-M: 20[redacted] / 32	ONGOING
VITAMINS NOS	1 OTHER: TAB	QD	Y: 20[redacted]	ONGOING

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

Event Description	ELEVATED CREATININE PHOSPHOKINASE
Preferred term	血中クレアチンホスホキナーゼ増加
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 19 / -412 DAYS BEFORE TREATMENT

Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	RIGHT PULMONARY UPPER LOBE SEGMENTAL PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 437 / 7
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 7): NPTST108-CRP: 30.7 [0 - 8] MG/L; NPTST259-PROCALCITONIN: 0.04 [NOT REPORTED - 0.07] ng/mL; [redacted]20[redacted] (RX DAY 8): Blood Urea Nitrogen: 3.92667 [2.14182 - 7.85334] MMOL/L; Calcium: 2.145786 [2.120835 - 2.619855] MMOL/L; Chloride: 102 [99 - 110] MEQ/L; Creatinine: 83.099064 [70.722608 - 114.924238] UMOL/L; Erythrocytes: 3.94 [4.4 - 5.8] 10^12/L; Glucose: 5.5507 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.295 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 89 [135 - 175] G/L; Hemoglobin: 92 [135 - 175] G/L; Hemoglobin: 82 [135 - 175] G/L; Hemoglobin: 91 [135 - 175] G/L; Hemoglobin: 91 [135 - 175] G/L; Hemoglobin: 87 [135 - 175] G/L; Leukocytes: 9.2 [4 - 11] 10^9/L; NPTST018-ADENOVIRUS: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST033-ANION GAP WITH K: 13 [6 - 20] MEQ/L; NPTST037-APTT: 85 [24 - 35] SEC; NPTST037-APTT: 101 [24 - 35] SEC; NPTST037-APTT: 60 [24 - 35] SEC; NPTST037-APTT: 98 [24 - 35] SEC; NPTST056-BORDETELLA PARAPERTUSSIS: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST057-BORDETELLA PERTUSSIS: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST061-BUN/CREATININE RATIO: 11.7 [10 - 25] MG/DL; NPTST088-CHLAMYDOPHILLA PNEUMONIAE: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST096-CO2: 27 [20 - 29] MEQ/L; NPTST098-CORONAVIRUS 229E: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST099-CORONAVIRUS HKU1: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST100-CORONAVIRUS NL63: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST101-CORONAVIRUS OC43: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST121-EGFR AFRICAN AMERICAN: 90 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST124-EGFR NON-AFRICAN AMERICAN: 84 [60 - NOT REPORTED] ML/MIN/1.73M2; NPTST178-HUMAN METAPNEUMOVIRUS HUMAN: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST185-INFLUENZA A H3: NOT DETECTED [NOT REPORTED - NOT REPORTED]

UNIT NOT REPORTED; NPTST186-INFLUENZA A/H1: NOT DETETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST187-INFLUENZA A/H1-2009: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST188-INFLUENZA B: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST211-MCH: 23.1 [25.5 - 34] PG; NPTST212-MCHC: 30.8 [31.5 - 36.5] G/DL; NPTST213-MCV: 74.9 [80 - 98] FL; NPTST220-MPV: 10.3 [8.5 - 12] FL; NPTST225-MYCOPLASMA PNEUMONIAE: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST238-PARAINFLUENZA 1: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST239-PARAINFLUENZA 2: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST240-PARAINFLUENZA 3: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST241-PARAINFLUENZA 4: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST275-RDW-CV: 21.2 [11.5 - 15.5] %; NPTST276-RDW-SD: 54.9 [35.5 - 50] FL; NPTST285-RHINOVIRUS/ENTEROVIRUS INFLUENZ: NOT DETECETED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST287-RSV: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST294-SARS-COV-2: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST323-TROPONIN: 0.012 [0 - 0.028] NG/ML; Platelets: 326 [140 - 400] 10^9/L; Potassium: 3.4 [3.5 - 5.3] MMOL/L; Sodium: 139 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 9): Blood Urea Nitrogen: 3.21273 [2.14182 - 7.85334] MMOL/L; Calcium: 2.145786 [2.120835 - 2.619855] MMOL/L; Chloride: 106 [99 - 110] MEQ/L; Creatinine: 86.635195 [70.722608 - 114.924238] UMOL/L; Erythrocytes: 3.72 [4.4 - 5.8] 10^12/L; Glucose: 8.659092 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.277 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 85 [135 - 175] G/L; Hemoglobin: 85 [135 - 175] G/L; Leukocytes: 7.4 [4 - 11] 10^9/L; NPTST033-ANION GAP WITH K: 12 [6 - 20] MEQ/L; NPTST037-APTT: 112 [24 - 35] SEC; NPTST037-APTT: 96 [24 - 35] SEC; NPTST061-BUN/CREATININE RATIO: 9.2 [10 - 25] UNIT NOT REPORTED; NPTST096-CO2: 25 [20 - 29] MEQ/L; NPTST121-EGFR AFRICAN AMERICAN: 90 [60 - NOT REPORTED] ML/MIN1.73M2; NPTST124-EGFR NON-AFRICAN AMERICAN: 80 [60 - NOT REPORTED] ML/MIN1.73M2; NPTST209-MAGNESIUM: 1.9 [1.8 - 2.4] MG/DL; NPTST211-MCH: 22.8 [25.5 - 34] PG; NPTST212-MCHC: 30.7 [31.5 - 36.5] G/DL; NPTST213-MCV: 74.5 [80 - 98] FL; NPTST220-MPV: 10.6 [8.5 - 12] FL; NPTST250-PHOSPHORUS: 1.6 [2.5 - 4.5] MG/DL; NPTST275-RDW-CV: 20.8 [11.5 - 15.5] %; NPTST276-RDW-SD: 54.4 [35.5 - 50] FL; Platelets: 317 [140 - 400] 10^9/L; Potassium: 3.7 [3.5 - 5.3] MMOL/L; Sodium: 139 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	439 / 9
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THROMBOPHELIA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	CHEMICAL USE DISORDER - DEPENDENCE
Preferred term	薬物依存
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 462 / 32
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 33): Albumin: 40 [36 - 51] G/L; Bilirubin: 5.131167 [3.420778 - 20.524668] UMOL/L; Calcium: 2.170737 [2.145786 - 2.569953] MMOL/L; Chloride: 110 [98 - 110] MMOL/L; Creatinine: 87.519227 [61.882282 - 117.576336] UMOL/L; Erythrocytes: 4.85 [4.8 - 5.8] 10^12/L; Glucose: 6.050263 [3.607955 - 5.495193] MMOL/L; Hematocrit: 0.362 [0.385 - 0.5] FRACTION OF 1; Hemoglobin: 112 [132 - 171] G/L; Leukocytes: 5.2 [3.8 - 10.8] 10^9/L; NPTST022-ALBULIN/GLOBULIN RATIO: 1.8 [1 - 2.5] CALC; NPTST024-ALKALINE PHOPASTASE: 70 [35 - 144] U/L; NPTST026-ALT: 28 [9 - 46] U/L; NPTST040-AST: 25 [10 - 35] U/L; NPTST075-CARBON DIOXIDE: 26 [20 - 32] MMOL/L; NPTST121-EGFR AFRICAN AMERICAN: 103 [NOT REPORTED - NOT REPORTED] > OR = TO 60 ML/MIN/1.73M2; NPTST126-EGRF NON-AFR. AMERICAN: 87 [NOT REPORTED - NOT REPORTED] > OR = 60 ML/MIN/1.73M2; NPTST157-GGT: 133 [3 - 95] U/L; NPTST159-GLOBULIN: 2.2 [1.9 - 3.7] G/DL; NPTST168-HEP A IGM TEST: NON-REACTIVE [NOT REPORTED - NOT REPORTED] NO UNITS; NPTST169-HEPATITIS B CORE ANTIBODY (IGM): NON-REACTIVE [NOT REPORTED - NOT REPORTED] NO UNITS; NPTST170-HEPATITIS B SURFACE ANTIGEN: NON-REACTIVE [NOT REPORTED - NOT REPORTED] NO UNITS; NPTST171-HEPATITIS C ANTIBODY: NON-REACTIVE [NOT REPORTED - NOT REPORTED] NO UNITS; NPTST211-MCH: 23.1 [27 - 33] PG; NPTST212-MCHC: 31.0 [32 - 36] G/DL; NPTST213-MCV: 74.4 [80 - 100] FL; NPTST220-MPV: 11.1 [7.5 - 12.5] FL; NPTST333-URAN NITROGEN: 13 [7 - 25] MG/DL; Platelets: 263 [140 - 400] 10^9/L; Potassium: 3.4 [3.5 - 5.3] MMOL/L; Protein: 62 [61 - 82] G/L; Sodium: 143 [135 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 42): Erythrocytes: 5.24 [4.2 - 5.8] 10^12/L; Hematocrit: 0.409 [0.385 - 0.5] FRACTION OF 1; Hemoglobin: 120 [132 - 171] G/L; Leukocytes: 6.3 [3.8 - 10.8] 10^9/L; NPTST211-MCH: 22.9 [27 - 32] PG; NPTST212-MCHC: 29.3 [32 - 36] G/DL; NPTST220-MPV: 11.6 [7.5 - 12.5] FL; NPTST272-RDW: 19.3 [11 - 15] %; Platelets: 315 [140 - 400] 10^9/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	488 / 58
Duration of AE	27 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ALCOHOL AND COCAINE ADDICTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:51

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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，化学物質使用障害–依存の事象を発現した。関連する病歴は，コカイン乱用，潰瘍性大腸炎（左側 UC）及び元飲酒者（1 日 4 杯超）であった。

Event 3 の臨床経過：

投与462日後＊，被験者は化学物質使用障害–依存を発現した。投与488日後＊，化学物質使用障害 - 依存は消失した。

投与462日後＊　，被験者はコカインの使用を開始したため治療を求めて受診した。被験者は同日に入院し，アルコール及びコカインを中止するために観察された。被験者は連日，薬物を使用したいという衝動と願望を訴えた。投与488日後＊，被験者は退院し，治療施設へ移った。

治験責任医師によると，被験者には薬物及びアルコール乱用の病歴があるが，数年間はクリーンであった。被験者には，依存症の家族歴もあった。

投与された薬剤は，ヒドロキシジン，メラトニン，レクサプロ，タイレノール，水酸化マグネシウム，colace，metamucil，経皮吸収ニコチン製剤，N-acetyl cysteine 及びジアゼパムであった。

The patient's past medications include:

MESALAMINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for UPADACITINIB (Blinded)

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1)　Drug dependence (10013663)　(Drug dependence (10013663))　[v.24.0]　[10013663]

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 CHEMICAL USE DISORDER DEPENDENCE

- Investigator: ALCOHOL AND COCAINE ADDICTION

- AbbVie: Risk factors include medical history of cocaine abuse, alcohol abuse, depression, and family history of addiction reported per PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ALBUMIN:** 4.0 G/DL (normal 3.6 to 5.1)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 70 U/L (normal 35 to 144)

[redacted] 20[redacted] **ALT:** 28 U/L (normal 9 to 46)

[redacted] 20[redacted] **AST:** 25 U/L (normal 10 to 35)

[redacted] 20[redacted] **BILIRUBIN:** 0.3 mg/dL (normal 0.2 to 1.2)

[redacted] 20[redacted] **CREATININE:** 0.99 mg/dL (normal 0.70 to 1.33)

[redacted] 20[redacted] **GGT:** 133 U/L (normal 3 to 95)

[redacted] 20[redacted] **HEMOGLOBIN:** 12 G/DL (normal 13.2 to 17.1)

[redacted] 20[redacted] **HEPATITIS B CORE ANTIBODY (IGM):** Non reactive

[redacted] 20[redacted] **HEPATITIS B SURFACE ANTIGEN**: Non reactive

[redacted] 20[redacted] **HEPATITIS C ANTIBODY:** Non reactive

[redacted] 20[redacted] **HGB:** 11.2 G/DL (normal 13.2 to 17.1)

[redacted] 20[redacted] **MCH:** 23.1 PG (normal 27 to 33)

[redacted] 20[redacted] **MCH:** 22.9 PG (normal 27 to 32)

[redacted] 20[redacted] **MCV:** 74.4 FL (normal 80 to 100)

[redacted] 20[redacted] **HEP A IGM TEST:** Non-reactive

[redacted] 20[redacted] **PLATELET COUNT:** 263 thousand/uL (normal 140 to 400)

[redacted] 20[redacted] **POTASSIUM:** 3.4 MMOL/L (normal 3.5 to 5.3)

[redacted] 20[redacted] **RDW:** 19.3 % (normal 11 to 15)

[redacted] 20[redacted] **SODIUM:** 143 MMOL/L (normal 135 to 146)

[redacted] 20[redacted] **WBC:** 5.2 thousand/uL (normal 3.8 to 10.8)

Subject Number: [redacted]

Protocol Number: M14-533

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，右上葉区域肺塞栓症の事象を発現した。関連する病歴は，深部静脈血栓症，高血圧，潰瘍性大腸炎，元喫煙者（1 日 1 箱を 20 年間）及び元飲酒者（1 日 4 杯超）であった。

Event 2 の臨床経過：

投与437日後＊　，被験者は右上葉区域肺塞栓症を発現した。投与439日後＊　，右上葉区域肺塞栓症は消失した。

投与437日後＊　，被験者は息切れがあり，入院した。身体検査では，被験者は正常律動の正常心拍数であり，呼吸努力は正常で，腫脹及び局所神経障害は認められなかった。被験者は過去に急性失血性貧血の病歴も有していた。被験者の c-スコープ（結腸内視鏡検査）では，活動性の出血点は認められなかったが，炎症性疾患に伴う複数の潰瘍が認められた。入院時の CT スキャン検査では，右上葉区域肺塞栓が顕著で，右心負荷の徴候は伴わなかった。また，両肺上葉に淡いすりガラス状陰影が認められ，肺炎が示唆された。ヘパリンの点滴投与が開始され，ヘパリン投与中はヘモグロビン値がモニタリングされた。肺炎に対してオーグメンチンの投与が開始された。経胸壁心エコー図では，駆出率は65%であり，局所壁運動異常は認められなかった。右上肢ドップラー検査では，右橈側皮静脈の急性血栓が顕著であった。被験者は，退院前に，ヘパリン点滴からエリキュースへ切り替えられた。投与439日後＊　，被験者は血行動態が安定しており，退院した。

本事象に関連する危険因子：深部静脈血栓症（DVT）及び肺塞栓症（PE）の既往歴。

投与された薬剤は，ヘパリン，オーグメンチン及びエリキュースであった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1)　Pulmonary embolism (10037377)　(Pulmonary embolism (10037377))　[v.24.0]　[10037377]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of RIGHT PULMONARY UPPER LOBE SEGMENTAL PULMONARY EMBOLISM

- Investigator: Thrombophilia

- AbbVie: Risk factor includes pre-existing thrombophilia, as noted by the PI and pre-existing DVT in 20[redacted].

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] 20[redacted] **COLONOSCOPY:** showed no active source of bleed but multiple ulcers in the setting of his inflammatory disease

[redacted] 20[redacted] **CT SCAN:** right upper lobe segmental pulmonary emboli without evidence of right heart strain. There was faint ground glass opacification in both upper lobes suggestive of pneumonia.

[redacted] 20[redacted] **HEMATOCRIT:** 29.5 % (normal 40.0 to 50.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.1 G/DL (normal 13.5 to 17.5)

[redacted] 20[redacted] **HEMOGLOBIN:** 9.1 G/DL (normal 13.5 to 17.5)

[redacted] 20[redacted] **HEMOGLOBIN:** 8.7 G/DL (normal 13.5 to 17.5)

[redacted] 20[redacted] **HEMOGLOBIN:** 8.2 G/DL (normal 13.5 to 17.5)

[redacted] 20[redacted] **MCH:** 23.1 PG (normal 25.5 to 34.0)

[redacted] 20[redacted] **MCHC:** 30.8 G/DL (normal 31.5 to 36.5)

[redacted] 20[redacted] **MCV:** 74.9 FL (normal 80.0 to 98.0)

[redacted] 20[redacted] **MPV:** 10.3 FL (normal 8.5 to 12.0)

[redacted] 20[redacted] **PLATELET COUNT:** 326 K/UL (normal 140 to 400)

[redacted] 20[redacted] **RBC:** 3.94 M/UL (normal 4.40 to 5.80)

[redacted] 20[redacted] **RDW-CV:** 21.2 % (normal 11.5 to 15.5)

[redacted] 20[redacted] **RDW-SD:** 54.9 FL (normal 35.0 to 50.0)

[redacted] 20[redacted] **RIGHT UPPER EXTREMITY DOPPLER:** acute thrombus in the right cephalic vein

[redacted] 20[redacted] **TRANSTHORACIC ECHOCARDIOGRAM:** Left ventricle: normal size, wall thickness, systolic function and no wall motion abnormalities. Ejection fraction is visual estimated to be 65% with Grade 1 left ventricular dysfunction. Left Atrium: normal size. Aortic Valve: normal tricuspid aortic valve function, no significant regurgitation and no aortic stenosis. Aorta: sinus of Valsalva normal size of 37.0mm, ascending aorta normal size measuring 32.0mm. Mitral Valve: normal structure, trivial regurgitation, no mitral stenosis. IAS: no evidence of atrial shunt, Right ventricle: normal size, dystolic function, normal wall thickness

[redacted] 20[redacted] **WBC:** 9.2 K/UL (normal 4.0 to 11.0)

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

Reason for Narrative

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

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

Medical History	Onset Year
ANXIETY	20[redacted]
BACK PAIN	20[redacted]
COMPRESSION FRACTURE L1 AND L2	20[redacted]
DEPRESSION	20[redacted]
DEVIATED NASAL SEPTUM	20[redacted]
HIGH CHOLESTEROL	20[redacted]
INTERMITTENT CONSTIPATION	20[redacted]
INTERMITTENT DIARRHEA	20[redacted]
INTERMITTENT HEADACHES	20[redacted]
INTERMITTENT SCIATICA PAIN	20[redacted]
INTERMITTENT TREMORS	20[redacted]
LEFT SIDED UC	20[redacted]
LEFT TORN ROTATOR CUFF	20[redacted]
MUSCLE SPASMS	20[redacted]
PERFORATED NASAL SEPTUM	20[redacted]
POOR CIRCULATION IN LEGS	20[redacted]
REM SLEEP BEHAVIOR DISORDER	20[redacted]
RIGHT WRIST FRACTURE	20[redacted]
SEASONAL ALLERGIES	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: KYPHOPLASTY	20[redacted]
PRIOR PROCEDURES: LEFT ROTATOR CUFF SURGERY	20[redacted]
PRIOR PROCEDURES: RIGHT WRIST SURGERY	20[redacted]

PRIOR PROCEDURES: SEPTOPLASTY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 142	86
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted]20[redacted] / 165		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	500 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	500 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
CERTOLIZUMAB PEGOL	0 mg	NOT REPORTED	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY TWO WEEKS	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted]
PREDNISONE	10 mg	OTHER: EVERY TWO DAYS	Y-M: 20[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]
GABAPENTIN	600 mg	QD	Y-M: 20[redacted] / -228
MESALAZINE	1.2 g	BID	Y-M: 20[redacted] / -88
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -14
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y: 20[redacted]

ACETYLSALICYLIC ACID	81 mg	QD	Y: 20[redacted]
ESCITALOPRAM	10 mg	QD	Y: 20[redacted]
MELATONIN	6 mg	PRN	Y: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]	Not reported
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted]	Not reported
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	Not reported
GABAPENTIN	600 mg	QD	Y-M: 20[redacted] / -228	Not reported
MESALAZINE	1.2 g	BID	Y-M: 20[redacted] / -88	Not reported
PREDNISONE	5 mg	OTHER: EVERY OTHER DAY TAPER	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 50
FENTANYL	100 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 81
MIDAZOLAM	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 81
DILTIAZEM	180 mg	QD	Y-M: 20[redacted] / 84	Not reported
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	4 L	OTHER: DRINK 8OZ EVERY 10 TO 15 MINTUES UNTIL ENTIRE PREP IS CONSUSMED	Y-M: 20[redacted] / 349	Y-M: 20[redacted] / 349
EPHEDRINE	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
LIDOCAINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
PROPOFOL	750 mg	OTHER: ONCE OVER 24 MINUTES	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 350
HYDROCODONE	10-325 mg	PRN	Y-M: 20[redacted] / 449	Not reported
MELOXICAM	7.5 mg	QD	Y-M: 20[redacted] / 449	Y-M: 20[redacted] / 494
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y: 20[redacted]	Not reported
ACETYLSALICYLIC ACID	81 mg	QD	Y: 20[redacted]	Not reported
ESCITALOPRAM	10 mg	QD	Y: 20[redacted]	Not reported
MELATONIN	6 mg	PRN	Y: 20[redacted]	Not reported

Event #1: Serious Adverse Event

Event Description	ATRIAL FIBRILLATION
Preferred term	心房細動
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 243 / 79

Age at AE Onset	6[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 80): NPTST323-TROPONIN: 0.130 [0 - 0.045] NG/ML	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	STRESS AND EXERTION WAS MOVING INTO A NEW HOME
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，心房細動の事象を発現した。関連する病歴は，不安，うつ病，潰瘍性大腸炎（左側），コレステロール高値，下肢血行循環不良，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与243日後＊，被験者は心房細動を発現した。

本事象発現の 2 時間前，被験者は息切れを伴う労作時の胸部絞扼感，動悸，酷い浮動性めまい感を経験した。心拍数は 160 回/分超を持続した。投与244日後＊　，被験者は，不安定狭心症，失神寸前の状態及び心拍数の上昇があり，救急治療室を受診し，更なる管理及び治療評価のために入院した。心エコー検査，心電図検査，血液検査，胸部 X 線検査及び心臓カテーテル検査が実施された。入院中，被験者は合併症を発現しなかった。投与245日後＊　，被験者は退院した。

The patient's past medications include:

SULFASALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REMICADE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CIMZIA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTIVYO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for UPADACITINIB (Open Label)

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1) Atrial fibrillation (10003658) (Atrial fibrillation (10003658)) [v.23.1] [10003658]

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 (Open Label)

Event of ATRIAL FIBRILLATION

- Investigator: stress and exertion of moving into a new home

- AbbVie: The life time risk of developing Atrial fibrillation is 26% in men with incidence increasing with age.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] ECHOCARDIOGRAM:** Ejection Fraction=60; mild mitral regurgitation

[redacted] **20[redacted] EKG:** NORMAL SINUS RHYTHM, PR interval 140ms, QRS duration 86ms, QT/QTc334/375 ms, no STEMI, undetermined rhythm; nonspecific T-wave abnormality. Abnormal EKG

[redacted] **20[redacted] HEART RATE:** 160 BPM

[redacted] **20[redacted] LEFT HEART CATHERTERIZATION, SELECTIVE RIGHT AND LEFT CORONARY ANGIOGRAPHY, LEFT VENTRICULOGRAM:** slow TIMI 2 flow in the coronary arteries, mild atherosclerosis native coronary arteries, right dominant system, mild coronary ectasia of the right coronary artery; preserved left ventricular systolic function Ejection fraction 65%

[redacted] **20[redacted] TROPONIN:** 0.130 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
肺塞栓症	X	X		X

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

Medical History	Onset Year
ABDOMINAL PAIN	20[redacted]
BPH	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
PULMONARY EMBOLISM	20[redacted]
VENTRICULAR TACHYCARDIA	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APPENDECTOMY	19[redacted]
PRIOR PROCEDURES: CHOLECYSTECTOMY	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: RIGHT HERNIORRHAPHY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	3.75	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 58	58
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted] / 59	[redacted] / 506	448
M14-533 ABT-494 (LTE)	30 mg	ORAL	QD	[redacted] / 507	[redacted] / 535	29

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ATORVASTATIN	20 mg	QD	Y-M: [redacted]
VERAPAMIL	80 mg	TID	Y-M: [redacted]
FINASTERIDE	0.75 mg	QD	Y-M: [redacted]
ESOMEPRAZOLE	40 mg	QD	Y-M: [redacted] / -199
ENOXAPARIN	90 mg	OTHER: Q12H	Y-M: [redacted] / -131
PARACETAMOL	650 mg	PRN	Y-M: [redacted] / -132
METFORMIN	500 mg	QD	Y-M: [redacted] / -98
TAMSULOSIN	0.4 mg	OTHER: EVERY OTHER DAY	Y: [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
ATORVASTATIN	20 mg	QD	Y-M: [redacted]	ONGOING
VERAPAMIL	80 mg	TID	Y-M: [redacted]	ONGOING
FINASTERIDE	0.75 mg	QD	Y-M: [redacted]	ONGOING
ESOMEPRAZOLE	40 mg	QD	Y-M: [redacted] / -199	ONGOING
ENOXAPARIN	90 mg	OTHER: Q12H	Y-M: [redacted] / -131	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: [redacted] / -132	ONGOING
METFORMIN	500 mg	QD	Y-M: [redacted] / -98	ONGOING
ACETYLSALICYLIC ACID	325 mg	OTHER: ONCE	Y-M: [redacted] / 11	Y-M: [redacted] / 11
CEFTRIAXONE	1 g	OTHER: ONCE	Y-M: [redacted] / 11	Y-M: [redacted] / 11
GLYCERYL TRINITRATE	1 OTHER: TAB	OTHER: ONCE	Y-M: [redacted] / 11	Y-M: [redacted] / 11
MORPHINE	4 mg	PRN	Y-M: [redacted] / 11	Y-M: [redacted] / 11

ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 11
TAMSULOSIN	0.4 mg	OTHER: EVERY OTHER DAY	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	PULMONARY EMBOLISM
Preferred term	肺塞栓症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 516 / 10
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	519 / 13
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION, LIFE THREATENING

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺塞栓症の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 3.75 年間），肺塞栓症，潰瘍性大腸炎，心室性頻脈及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与516日後＊ ，被験者は肺塞栓症を発現した。投与519日後＊，肺塞栓症は消失した。

投与516日後＊ ，被験者は低血圧，息切れ，疲労及び咳嗽の徴候及び症状があり，救急治療室を受診した。同日，被験者は血中酸素濃度低下のために入院した。事前情報から，被験者が肺塞栓症を発現していることが示唆された。CT スキャン検査による診断結果から，左肺の肺塞栓症が確認された。投与519日後＊，被験者は退院した。

治験責任医師によると，投与535日後＊ に，被験者は治験責任医師へ本事象について報告した。同日，本事象により治験薬の投与は中止された。

治験責任医師によると，本事象に関連する被験者の危険因子は，肥満，高血圧，高脂血症，心房細動及び肺塞栓症であった。

投与された薬剤は，オンダンセトロン塩酸塩，セフトリアキソンナトリウム，ニトログリセリン，アスピリン及びモルヒネ硫酸塩であった。

Causality for UPADACITINIB (Blinded)

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1) Pulmonary embolism (10037377) (Pulmonary embolism (10037377)) [v.24.0] [10037377]

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 PULMONARY EMBOLISM

- Investigator: Not applicable

- AbbVie: Risk factors include pre-existing history of pulmonary embolism, advanced age and obesity.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 30.01 kg/m2

[redacted] **20[redacted] CHEST CT:** EVIDENCE OF INTRALUMINAL PULMONARY ARTERIAL FILLING DEFETS IN THE LEFT LUNG CONSISTENT WITH PULMONARY EMBOLI. NOTE IS MADE OF PATCHY GROUNDGLASS INFILTRATE EXTENDING THROUGHOUT BOTH LUNGS GREATER ON THE RIGHT THAN THE LEFT.

[redacted] **20[redacted] OXYGEN SATURATION:** 91 %

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
胃腸炎	X			X
好中球減少症				X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	3[redacted]	MALE	WHITE

Medical History	Onset Year
DUODENAL BULB EROSIONS	20[redacted]
ESOPHAGEAL EROSIONS	20[redacted]
ESOPHAGITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
INTERNAL HEMORRHOIDS	20[redacted]
LEFT SIDED UC	20[redacted]
NAUSEA	20[redacted]
SEASONAL ALLERGIES	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		ORAL	QD	[redacted] / 1	[redacted] / 53	53
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 54	[redacted] / 433	380
M14-533 Placebo (LTE)		ORAL	QD	[redacted] / 434		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	800 mg	TID	Y-M: [redacted]
MULTIVITAMINS, COMBINATIONS	1 OTHER: TABLET	QD	Y-M: [redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: [redacted]
LORATADINE	10 mg	PRN	Y-M: [redacted] / -226
SALBUTAMOL	90 ug	PRN	Y-M: [redacted] / -234
ASCORBIC ACID	500 mg	QD	Y-M: [redacted] / -7
ZINC	15 mg	QD	Y-M: [redacted] / -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MULTIVITAMINS, COMBINATIONS	1 OTHER: TABLET	QD	Y-M: [redacted]	Not reported
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: [redacted]	Not reported
LORATADINE	10 mg	PRN	Y-M: [redacted] / -226	Not reported
SALBUTAMOL	90 ug	PRN	Y-M: [redacted] / -234	Not reported
ASCORBIC ACID	500 mg	QD	Y-M: [redacted] / -7	Not reported
ZINC	15 mg	QD	Y-M: [redacted] / -7	Not reported
DICYCLOVERINE	10 mg	OTHER: ONCE	Y-M: [redacted] / 142	Y-M: [redacted] / 142
HYDROMORPHONE	0.5 mg	OTHER: EVERY 4 HOURS PRN	Y-M: [redacted] / 142	Y-M: [redacted] / 143
METHYLPREDNISOLONE	20 mg	OTHER: EVERY 6 HOURS	Y-M: [redacted] / 142	Y-M: [redacted] / 143
MORPHINE	4 mg	OTHER: EVERY 4 HRS PRN	Y-M: [redacted] / 142	Y-M: [redacted] / 142
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: [redacted] / 142	Y-M: [redacted] / 142
PARACETAMOL	650 mg	OTHER: EVERY 6 HOURS	Y-M: [redacted] / 142	Y-M: [redacted] / 143

PIPERACILLIN;TAZOBACTAM	3.375 g	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 143
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 142
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 143
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143
CYCLOBENZAPRINE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 167
BISACODYL	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
MACROGOL 3350	30 mL	OTHER: ONCE	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
LIDOCAINE	60 mg	OTHER: ONCE	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 337
PROPOFOL	300 mg	OTHER: ONCE	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 337

Event #1: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 434 / 1
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	469 / 36
Duration of AE	36 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	ACUTE GASTROENTERITIS
Preferred term	胃腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 571 / 138
Age at AE Onset	3[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 142): Alanine Aminotransferase: 21 [16 - 61] U/L; Albumin: 36 [32 - 48] G/L; Alkaline Phosphatase: 53 [26 - 162] U/L; Aspartate Aminotransferase: 13 [15 - 37] U/L; Basophils/Leukocytes: 0 [0 - 2] %; Bilirubin: 8.551945 [3.420778 - 22.235057] UMOL/L; Calcium: 2.220639 [2.070933 - 2.470149] MMOL/L; Chloride: 105 [98 - 110] MMOL/L; Creatinine: 80.446967 [61.882282 - 114.924238] UMOL/L; Eosinophils/Leukocytes: 1 [0 - 5] %;

Erythrocytes: 4.9 [4.5 - 5.9] 10^12/L; Glucose: 4.662588 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.442 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 147 [140 - 175] G/L; Leukocytes: 7.4 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 10 [15 - 49] %; Monocytes/Leukocytes: 14 [2 - 14] %; NPTST021-ALB/GLOB RATIO: 0.9 [1 - 2.2] UNIT NOT REPORTED; NPTST059-BUN: 8 [6 - 20] MG/DL; NPTST096-CO2: 27 [21 - 32] MMOL/L; NPTST119-DIRECT BILIRUBIN: 0.1 [0 - 0.3] MG/DL; NPTST155-GFR, AFR. AMER: >60 [60 - NOT REPORTED] ML/MN; NPTST156-GFR, CAUCASIAN: >60 [60 - NOT REPORTED] ML/MN; NPTST159-GLOBULIN: 4.2 [2 - 4.2] G/DL; NPTST199-LACTIC ACID: 0.7 [0.4 - 2] MMOL/L; NPTST207-LIPASE: 98 [73 - 393] U/L; NPTST209-MAGNESIUM: 1.7 [1.6 - 2.5] MG/DL; NPTST211-MCH: 30.0 [25 - 32] PG; NPTST212-MCHC: 33.3 [31 - 37] G/DL; NPTST214-META, MYELO, PRO: 0 [0 - 5] %; NPTST220-MPV: 10.0 [8.2 - 12.2] FL; NPTST223-MVC: 90.2 [80 - 100] FL; NPTST233-NUCLEATED RBC'S: 0 [0 - 1] 100WBC; NPTST273-RDW CV: 13.2 [11 - 16] %; NPTST274-RDW SD: 43.2 [37 - 54] FL; NPTST293-SARS COV 2-RNA: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST299-SEGS: 75 [29 - 66] %; Neutrophils: 5.53 [1.5 - 7] 10^9/L; Platelets: 198 [150 - 400] 10^9/L; Potassium: 3.6 [3.5 - 5.1] MMOL/L; Protein: 78 [64 - 83] G/L; Sodium: 138 [132 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 143): Calcium: 2.095884 [2.070933 - 2.470149] MMOL/L; Chloride: 107 [98 - 110] MMOL/L; Creatinine: 73.374706 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 4.46 [4.5 - 5.9] 10^12/L; Glucose: 4.884616 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.403 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 137 [140 - 175] G/L; Leukocytes: 6.6 [4.5 - 11] 10^9/L; NPTST059-BUN: 8 [6 - 20] MG/DL; NPTST075-CARBON DIOXIDE: 24 [21 - 32] MMOL/L; NPTST137-ESTIMATED GFR: >60 [60 - NOT REPORTED] UNIT NOT REPORTED; NPTST138-ESTIMATED GFR FOR AF/AM: >60 [60 - NOT REPORTED] ML/MN; NPTST207-LIPASE: 101 [73 - 393] U/L; NPTST209-MAGNESIUM: 1.5 [1.6 - 2.5] MG/DL; NPTST211-MCH: 30.7 [25 - 32] PG; NPTST212-MCHC: 34.0 [31 - 37] G/L; NPTST213-MCV: 90.4 [80 - 100] FL; NPTST220-MPV: 9.9 [8.2 - 12.2] FL; NPTST232-NRBC: 0 [0 - 1] 100WBC; NPTST275-RDW-CV: 12.9 [11 - 16] %; NPTST276-RDW-SD: 42.3 [37 - 54] FL; NPTST310-STOOL CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST319-TOXIGENIC C DIFF: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST346-WESTERGREN SED RATE: 20 [0 - 15] MM/H; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Sodium: 138 [132 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 152): Platelets: 181 [150 - 400] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 143): STOOL NPTST310-STOOL CULTURE: Negative; STOOL NPTST319-TOXIGENIC C DIFF: Negative

AE Stopped Initial Rx Day / Rx Day	577 / 144
Duration of AE	7 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 609 / 176
Age at AE Onset	3[redacted]
Laboratory Testing	

NOT APPLICABLE

Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は米国の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性胃腸炎の事象を発現した。関連する病歴は，十二指腸球部びらん，食道びらん，食道炎，胃食道逆流性疾患，悪心，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与571日後＊　，被験者は急性胃腸炎を発現した。投与577日後＊　，急性胃腸炎は消失した。

投与575日後＊　，被験者は 5 日前からの悪心，嘔吐，頻繁な非血性の少量便，腹痛及び無力感のため，入院した。これらの症状は，カウンターの上に 12 時間置いてあったブリトーを食べてから 1 日以内に開始した。被験者は，CT 検査で認められた小腸閉塞の可能性を懸念され，入院した。入院翌日までに，被験者は痛みが軽減したことを報告し，清澄流動食を摂取できた。投与576日後＊，被験者は退院した。

投与された薬剤は，メチルプレドニゾロン，モルヒネ，オンダンセトロン，ピペラシリン・タゾバクタム合剤，タイレノール，ヒドロモルフォン，ジサイクロミン，ソル・メドロール，ゾシン及び塩化ナトリウムであった。

The patient's past medications include:

DELZICOL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute gastroenteritis (10066762) (Gastroenteritis (10017888)) [v.24.0] [10066762]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE GASTROENTERITIS

- Investigator: Not Applicable

- AbbVie: Event is more likely secondary to consumption of contaminated food as reported by PI. Additional risk factor includes pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ALANINE AMINO TRANSFERASE:** 21 U/L (normal 16 to 61)

[redacted] 20[redacted] **ALB/GLOB RATIO:** 0.9 NO UNITS (normal 1.0 to 2.2)

[redacted] 20[redacted] **ALBUMIN:** 3.6 G/DL (normal 3.2 to 4.8)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 53 U/L (normal 26 to 162)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 13 U/L (normal 15 to 37)

[redacted] 20[redacted] **BASOPHILS %:** 0 % (normal 0 to 2)

[redacted] **20[redacted] BILIRUBIN:** 0.5 mg/dL (normal 0.2 to 1.3)

[redacted] **20[redacted] BODY WEIGHT:** 9[redacted] KG

[redacted] **20[redacted] BUN:** 8 mg/dL (normal 6 to 20)

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 2.9 mg/dL (normal >0.3)

[redacted] **20[redacted] CALCIUM:** 8.9 mg/dL (normal 8.3 to 9.9)

[redacted] **20[redacted] CALCIUM:** 8.4 mg/dL (normal 8.3 to 9.9)

[redacted] **20[redacted] CHLORIDE:** 105 MMOL/L (normal 98 to 110)

[redacted] **20[redacted] CHLORIDE:** 107 MMOL/L (normal 98 to 110)

[redacted] **20[redacted] CO2:** 27 MMOL/L (normal 21 to 32)

[redacted] **20[redacted] CO2:** 24 MMOL/L (normal 21 to 32)

[redacted] **20[redacted] CREATININE:** 0.91 mg/dL (normal 0.70 to 1.30)

[redacted] **20[redacted] CREATININE:** 0.83 mg/dL (normal 0.70 to 1.30)

[redacted] **20[redacted] CT SCAN ABDOMEN/PELVIS:** MID TO DISTAL SMALL BOWEL WITH ABNORMAL FLUID DISTENTION, MUCOSAL HYPER ENHANCEMENT AND DIFFUSE WALL THICKENING. IMPRESSION EXTENSIVE ENTERITIS, INFECTIOUS VERSUS INFLAMMATORY.

[redacted] **20[redacted] DIRECT BILIRUBIN:** 0.1 mg/dL (normal 0.0 to 0.3)

[redacted] **20[redacted] EOSINOPHILS %:** 1 % (normal 0 to 5)

[redacted] **20[redacted] GFR, CAUCASIAN:** >60 ML/MN

[redacted] **20[redacted] GLOBULIN:** 4.2 G/DL (normal 2.0 to 4.2)

[redacted] **20[redacted] GLUCOSE:** 84 mg/dL (normal 70 to 100)

[redacted] **20[redacted] GLUCOSE:** 88 mg/dL (normal 70 to 100)

[redacted] **20[redacted] HEMATOCRIT:** 44.2 % (normal 40.0 to 52.0)

[redacted] **20[redacted] HEMATOCRIT:** 40.3 % (normal 40.0 to 52.0)

[redacted] **20[redacted] HEMOGLOBIN:** 14.7 G/DL (normal 14.0 to 17.5)

[redacted] **20[redacted] HEMOGLOBIN:** 13.7 G/DL (normal 14.0 to 17.5)

[redacted] 20[redacted] **LACTIC ACID:** 0.7 MMOL/L (normal 0.4 to 2.0)

[redacted] 20[redacted] **LIPASE:** 98 U/L (normal 73 to 393)

[redacted] 20[redacted] **LIPASE:** 101 U/L (normal 73 to 393)

[redacted] 20[redacted] **LYMPHOCYTES %:** 10 % (normal 15 to 49)

[redacted] 20[redacted] **MAGNESIUM:** 1.7 mg/dL (normal 1.6 to 2.5)

[redacted] 20[redacted] **MAGNESIUM:** 1.5 mg/dL (normal 1.6 to 2.5)

[redacted] 20[redacted] **MCH:** 30.0 PG (normal 25.0 to 32.0)

[redacted] 20[redacted] **MCH:** 30.7 PG (normal 25.0 to 32.0)

[redacted] 20[redacted] **MCHC:** 33.3 G/DL (normal 31.0 to 37.0)

[redacted] 20[redacted] **MCHC:** 34.0 G/DL (normal 31.0 to 37.0)

[redacted] 20[redacted] **META, MYELO, PRO:** 0 % (normal 0 to 5)

[redacted] 20[redacted] **MONOCYTES %:** 14 % (normal 2 to 14)

[redacted] 20[redacted] **MPV:** 10.0 FL (normal 8.2 to 12.2)

[redacted] 20[redacted] **MPV:** 9.9 FL (normal 8.2 to 12.2)

[redacted] 20[redacted] **MVC:** 90.2 FL (normal 80.0 to 100.0)

[redacted] 20[redacted] **MVC:** 90.4 FL (normal 80.0 to 100.0)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 5.53 X10**3/MCL (normal 1.50 to 7.00)

[redacted] 20[redacted] **NUCLEATED RBC'S:** 0 (normal 0 to 1)

[redacted] 20[redacted] **NUCLEATED RBC'S:** 0 (normal 0 to 1)

[redacted] 20[redacted] **PLATELET COUNT:** 198 X10**3/MCL (normal 150 to 400)

[redacted] 20[redacted] **PLATELET COUNT:** 181 X10**3/MCL (normal 150 to 400)

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

[redacted] 20[redacted] **POTASSIUM:** 3.8 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **PROTEIN:** 7.8 G/DL (normal 6.4 to 8.3)

[redacted] 20[redacted] **RDW CV:** 13.2 % (normal 11.0 to 16.0)

[redacted] 20[redacted] **RDW CV:** 12.9 % (normal 11.0 to 16.0)

[redacted] 20[redacted] **RDW SD:** 43.2 FL (normal 37.0 to 54.0)

[redacted] 20[redacted] **RDW SD:** 42.3 FL (normal 37.0 to 54.0)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.90 X10**6/MCL (normal 4.50 to 5.90)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.46 X10**6/MCL (normal 4.50 to 5.90)

[redacted] 20[redacted] **SARS COV 2-RNA:NASOPHARYNGEAL:** Not Detected

[redacted] 20[redacted] **SEGS:** 75 % (normal 29 to 66)

[redacted] 20[redacted] **SODIUM:** 138 MMOL/L (normal 132 to 144)

[redacted] 20[redacted] **SODIUM:** 138 MMOL/L (normal 132 to 144)

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

[redacted] 20[redacted] **STOOL TOXIGENIC C DIFF:** Negative

[redacted] 20[redacted] **WESTERGREN SED RATE:** 20 MM/HR (normal 0 to 15)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 7.4 X10**3/MCL (normal 4.5 to 11.0)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 6.6 X10**3/MCL (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
貧血				X
横紋筋融解症	X	X		

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

Medical History	Onset Year
ABDOMINAL PAIN	20[redacted]
ACID REFLUX (GERD)	20[redacted]
ASTHMA	20[redacted]
CROHN'S DISEASE	20[redacted]
FIBROMYALGIA	20[redacted]
H. PYLORI INFECTION	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
LORDOSIS	20[redacted]
PERIPHERAL ARTHROPATHY	20[redacted]

Prior Procedures	Procedure Year
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 PACK	8	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[redacted] / 1	[redacted] / 57	57
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	[redacted] / 58	[redacted] / 109	52
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted] / 110	[redacted] / 380	271
M14-533 ABT-494 (LTE)	15 mg	ORAL	QD	[redacted] / 381	[redacted] / 483	103

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DIPHENHYDRAMINE	25 mg	BID	Y-M: [redacted]
PREDNISONE	20 mg	BID	Y-M: [redacted]
TRAMADOL	50 mg	BID	Y-M: [redacted]
ADALIMUMAB	40 mg	OTHER: Q2W	Y: [redacted]
MESALAZINE	1.5 g	BID	Y: [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
DIPHENHYDRAMINE	25 mg	BID	Y-M: [redacted]	ONGOING
TRAMADOL	50 mg	BID	Y-M: [redacted]	ONGOING
LOPERAMIDE;SIMETICONE	125/2 mg	PRN	Y-M: [redacted] / 100	ONGOING
DIPHENHYDRAMINE	25 mg	PRN	Y-M: [redacted] / 105	Y-M: [redacted] / 107
MAGNESIUM SULFATE	2 OTHER: GM	OTHER: Q 1 HOUR 50 ML/HR PRN	Y-M: [redacted] / 105	Y-M: [redacted] / 107
ONDANSETRON	4 mg	OTHER: Q 6 HRS PRN	Y-M: [redacted] / 105	Y-M: [redacted] / 105
PARACETAMOL	500 mg	PRN	Y-M: [redacted] / 105	Y-M: [redacted] / 107
POTASSIUM	10 mEq	OTHER: Q 1 HOUR	Y-M: [redacted] / 105	Y-M: [redacted] / 107
POTASSIUM	20 mEq	OTHER: Q 2 HOURS	Y-M: [redacted] / 105	Y-M: [redacted] / 105

ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	491 mg	OTHER: ONCE	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 112
LIDOCAINE	70 mg	OTHER: ONCE	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
PROPOFOL	250 mg	OTHER: ONCE	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
DIPHENHYDRAMINE	25 mg	OTHER: ONCE	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143
MORPHINE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143

Event #1: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 480 / 100
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	RHABDOMYOLYSIS
Preferred term	横紋筋融解症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 480 / 100
Age at AE Onset	3[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 105): Creatine Kinase: 3698 [29 - 169] U/L; NPTST137-ESTIMATED GFR: 91 [60 - 90] ML/MIN; Occult Blood: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 106): Creatine Kinase: 2035 [29 - 169] U/L; Creatine Kinase: 2661 [29 - 169] U/L; [redacted]20[redacted] (RX DAY 107): Creatine Kinase: 948 [29 - 169] U/L; Creatine Kinase: 709 [29 - 169] U/L; NPTST137-ESTIMATED GFR: 95 [60 - 90] ML/MIN

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	493 / 113 (10 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	ACUTE RHABDOMYOLYSIS NONTRAUMATIC
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:16:51
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

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）の治験でウパダシチニブが投与され，横紋筋融解症の事象を発現した。関連する病歴は，喘息，元喫煙者（1 日 20 箱を 8 年間），腹痛，胃酸逆流，クローン病，線維筋痛，高血圧，末梢性関節障害，潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与480日後＊ ，被験者は横紋筋融解症を発現した。投与493日後＊ ，横紋筋融解症は消失した。

治験責任医師によると，被験者は 投与の約6ヵ月後＊に CK 上昇（非重篤）を発現し，その際に治験薬の投与は中断されなかった。

投与485日後＊ ，被験者はCK 上昇のため医療機関を受診するよう医師に指示された。同日，腹痛，下痢，背部痛及び直腸出血で入院した。身体検査では，覚醒，意識清明及び見当識ありで，心音（S1 及び S2）は正常洞調律で，聴診では心雑音はなかった。被験者は，胸部 X 線検査を受け，心肺の急性病理学的所見は認められなかった。投与486日後＊ ，被験者は CPK 上昇のため受診した。気分は良好であり，閉塞性の排尿症状はなく，血尿，排尿障害又は排尿困難もなかった。また，胸部痛，息切れ，悪心又は嘔吐もなかった。被験者は，下痢と便秘を断続的に発現していた。直近に転倒はなく，直近の外傷の報告はなかった。投与487日後＊ ，被験者は，硫酸マグネシウム及び塩化カリウムを処方され，退院した。

本事象により治験薬の投与は完全に中止された。

投与された薬剤は，硫酸マグネシウム，アセトアミノフェン及び塩化カリウムであった。

The patient's past medications include:

APRISO for ULCERATIVE COLITIS (20[redacted] - 20[redacted], 20[redacted] - [redacted] 20[redacted])

HUMIRA for ULCERATIVE COLITIS (20[redacted] - 20[redacted])

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

Causality for UPADACITINIB (Open Label)

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1) Rhabdomyolysis (10039020) (Rhabdomyolysis (10039020)) [v.23.1] [10039020]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of RHABDOMYOLYSIS

- Investigator: Acute rhabdomyolysis nontraumatic

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** NO RADIOGRAPHIC EVIDENCE OF ACUTE CARDIOPULMONARY PATHOLOGY.

[redacted] **20[redacted] CK:** 93 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 142 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 1733 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 73 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 69 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 75 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 1515 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 3698 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 2661 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 116 U/L (normal 26 to 192)

[redacted] **20[redacted] HCT:** 33.9 %

[redacted] **20[redacted] HCT:** 32.3 %

[redacted] **20[redacted] HGB:** 11.1 G/DL

[redacted] **20[redacted] HGB:** 10.3 G/DL

[redacted] **20[redacted] HGB:** 10.1 G/DL

[redacted] **20[redacted] PLATELETS:** 422 No units

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Anaemia: Intermittent. Rectal bleed reported on [redacted]20[redacted].