Microbiology

[redacted]20[redacted] (RX DAY 252): OTHER SECRETA NPTST162-MICROORGANISM: Positive-STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 252): ACUPUNCTURE: COMMENT:[redacted]20[redacted]-[redacted]20[redacted] ACUPUNCTURE TREATMENT; CUPPING THERAPY: COMMENT:[redacted]20[redacted]-[redacted]20[redacted] CUPPING THERAPY TREATMENT; ECG: THE P-R INTERVAL IS SHORTENED,THE LEFT VENTRICLE WAS HYPERPOTENTIAL V1?V5?T WAVE HIGH V3?V4?V5; HE-NE LASER THERAPY: COMMENT:[redacted]20[redacted]-[redacted]20[redacted] HE-NE LASER THERAPY TREATMENT; [redacted]20[redacted] (RX DAY 253): COLOR DOPPLER ULTRASONOGRAPHY OF LIVER, BILE, PANCREAS AND SPLEEN: THE GALLBLADDER WALL IS NOT SMOOTH- CHOLECYSTITIS; PLAIN CT SCAN OF THE CHEST: CHEST CT PLAIN SCAN SHOWED NO CARDIOPULMONARY ABNORMALITY. TRIANGULAR-COSTAL HERNIA ON THE LEFT SIDE WAS CONSIDERED; UROLOGICAL SYSTEM COLOR ULTRASOUND: NO OBVIOUS STRUCTURAL ABNORMALITIES WERE OBSERVED IN BOTH KIDNEYS, BLADDER FILLING WAS POOR, AND PROSTATE GLAND WAS NOT ABNORMAL

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]20[redacted]:06:46

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。本被験者は中国の 3[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，帯状疱疹の事象を発現した。関連する病歴は，潰瘍性大腸炎，貧血，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与456日後＊，被験者は帯状疱疹を発現した。

投与456日後＊，被験者は腫脹を伴う右目の疼痛，及び頭痛を経験し始めた。病変の範囲は，1 つの皮膚分節までであった。投与458日後＊，皮膚科医により眼帯状疱疹と診断された。被験者には右目の腫脹及び頭痛も認められた。身体的診察では，右側の頭皮及び右目の周囲に散在

した紅斑及び集簇性の水疱が確認された。発疹は正中線を越えていなかった。

投与460日後＊ ，被験者は治療のために入院した。被験者は刺鍼法，ヘリウムネオンレーザー治療及びカッピング治療を受けた。投与472日後＊ ，被験者は発疹が消失し，すべての水疱が乾燥して痂皮化し，頭痛も寛解した。同日，被験者は退院した。

被験者には，水痘及び帯状疱疹の病歴並びに帯状疱疹ワクチン接種歴はなかった。

治験責任医師により，本事象のために治験薬の投与は完全に中止された。

投与された薬剤は，zhoongtongan capsule（漢方薬），リリカ，recombinant bovine basic fibroblast growth factor eye-gel，ノイロトロピン，クロラムフェニコール，シプロフロキサシン，クリンダマイシン塩酸塩及びメトロニダゾール，pranopulin，メコバラミン，paracetamol 及びジヒドロコデイン，ビタミン B1，bozhi glycopeptide，コバマミド，ブリブジン，recombinant human interferon α2b gel，recombinant human epidermal growth factor derivative eye drops，ガンシクロビル並びにファムシクロビルであった。

The patient's past medictions include:

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

SUBTILIS ENTERIC SOLUTION CAPSULE WITH TWO LIVE BACTERIA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

CEFOPERAZONE SODIUM; SULBACTAM SODIUM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

SODIUM CHLORIDE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

HYDROCORTISONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

INTERLEUKIN 6 for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PIPERACILLIN SODIUM TAZOBACTAM SODIUM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.23.1] [10019974]

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 HERPES ZOSTER

- Investigator: Not applicable

- AbbVie: Not applicable.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL US:** THE GALLBLADDER WALL IS NOT SMOOTH- CHOLECYSTITIS

[redacted] **CRP:** 22.12 MG/L (normal 0 to 10)

[redacted] **ESR:** 23 MM/HR (normal 0 to 15)

[redacted] **MICROORGANISM SECRETA:** POSITIVE - STAPHYLOCOCCUS AUREUS

[redacted] **PCR:** positive for herpes zoster

[redacted] **SERUM AMYLOID A:** 267.76 MG/L (normal 0 to 10)

[redacted] **STOOL ANALYSIS - PUS BULB:** 8 to 10 INDIVIDUAL/HP

[redacted] **STOOL ANALYSIS - RBC:** 1 TO 2 INDIVIDUAL/HP

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
イレウス	X			

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

Medical History	Onset Year
ANEMIA: SUBJECT HADD AN ANEMIA IN 20[redacted] RELATED TO ULCERATIVE COLITIS. NOWDAYS IS HEMOGLOBIN LEVEL IS NORMAL	20[redacted]
DEPRESSION: DEPRESION	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: AMOCLEN ALERGY	19[redacted]
OTHER: MUTATED HETEROZYGOTE - THIOPURINE METHYLTRANSFERASE - NOT ABLE TO BE TREATED WITH AZATHIOPRINE	20[redacted]
OTHER: PSORIASIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56

M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 365	309
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 367		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	0 mg	QD	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	50 mg	TID	Y-M: 20[redacted]-[redacted]
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted]-[redacted]
METRONIDAZOLE	250 mg	BID	Y: 20[redacted]
BROMAZEPAM	1,5 mg	PRN	Y: 20[redacted]
ESCITALOPRAM	20 mg	QD	Y: 20[redacted]
MESALAZINE	2 g	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
DIAZEPAM	5 mg	QD	Y-M: 20[redacted]-[redacted] / 157	Y-M: 20[redacted]-[redacted] / 432
SERTRALINE	200 mg	QD	Y-M: 20[redacted]-[redacted] / 157	Not reported
COLECALCIFEROL	10- 30 OTHER: DROPS	OTHER: ONCE A WEEK OR ONCE IN TWO WEEKS	Y-M: 20[redacted]-[redacted] / 230	Y-M: 20[redacted]-[redacted] / 432
METOPROLOL	25 mg	BID	Y-M: 20[redacted]-[redacted] / 230	Not reported
THIAMAZOLE	10 mg	BID	Y-M: 20[redacted]-[redacted] / 230	Not reported
SODIUM CHLORIDE	NOT SPECIFIED mL	QD	Y-M: 20[redacted]-[redacted] / 326	Y-M: 20[redacted]-[redacted] / 327
BROMAZEPAM	1,5 mg	PRN	Y: 20[redacted]	Not reported
MESALAZINE	2 g	BID	Y: 20[redacted]	Not reported

Event #1: Serious Adverse Event

Event Description	ILEUS OF SMALL INTESTINE
Preferred term	イレウス
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 691 / 325
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 326): Alanine Aminotransferase: 0.95 [NOT REPORTED - NOT REPORTED] ukat/L; Glucose: 5.9 [4.1 - 5.9] MMOL/L; Leukocytes: 13.6 [4.5 - 11] 10^9/L; NPTST085-CRP: 6.2 [NOT REPORTED - NOT REPORTED] mg/L; NPTST120-GGT: 1.27 [NOT REPORTED - NOT REPORTED] ukat/L; [redacted]20[redacted] (RX DAY 327): NPTST085-

CRP: 92.3 [NOT REPORTED - NOT REPORTED] mg/L; [redacted]20[redacted] (RX DAY 329): Hematocrit: 0.395 [0.39 - 0.49] FRACTION OF 1; Hemoglobin: 132 [132 - 173] G/L; Leukocytes: 5.8 [4.5 - 11] 10^9/L; NPTST085-CRP: 11.7 [NOT REPORTED - NOT REPORTED] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 326): ABDOMEN NATIV XRAY: SMALL INTESTINE ILEUS, NO SIGNS OF PNEUMOPERITONEUM; [redacted]20[redacted] (RX DAY 327): ABDOMEN NATIV XRAY: NO SIGNS OS SMALL INTESTINE ILEUS, NO SIGNS OF PNEUMO PERITONEUM

AE Stopped Initial Rx Day / Rx Day	695 / 329
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	CAUSE IS UNKNOWN AT THE MOMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

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。本被験者はチェコ共和国の 3[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，小腸イレウスの事象を発現した。関連する病歴は，潰瘍性大腸炎，乾癬，うつ病，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691日後＊，被験者は小腸イレウスを発現した。投与695日後＊，小腸イレウスは消失した。

投与692日後＊ ，被験者は発熱，悪心，嘔吐，並びに上腹部及び右中腹部の腹痛があり，入院した。診察の結果，被験者は腹部の触診時に広範囲にわたり過敏であり，軽い痛みを感じた。検体検査及び腹部 X 線検査が行われた。保存的治療として，経鼻胃管を用いた胃腸管の減圧及び静脈内投与での水分補給を開始した。本事象は自然に消失した。投与695日後＊ ，被験者は

退院した。

The patient's past medications include:

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

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

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

AMOCLAN for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1) Ileus of intestine (10021332) (Ileus (10021328)) [v.24.0] [10021332]

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 ILEUS OF SMALL INTESTINE

- Investigator: CAUSE IS UNKNOWN AT THE MOMENT

- AbbVie: Reported event more likely related to pre-existing Ulcerative Colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMEN X-RAY:** small intestine ileus, no sign of pneumoperitoneum

[redacted] **20[redacted] ABDOMEN X-RAY:** No signs of small intestine ileus, no signs of penumoperitoneum

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 0.95 ukal/L

[redacted] **20[redacted] CRP:** 6.2 MG/L

[redacted] **20[redacted] CRP:** 92.3 MG/L

[redacted] **20[redacted] CRP:** 11.7 MG/L

[redacted] **20[redacted] GGT:** 1.27 ukal/.L

[redacted] **20[redacted] HEMATOCRIT:** 0.395 L/L

[redacted] **20[redacted] HEMOGLOBIN:** 132 G/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 13.6 X10**9/L

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.8 X10**9/L

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血				X
子宮頚部障害	X			

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

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
OTHER: ALERGIC RHINITIS	19[redacted]
OTHER: AXIAL ARTHROPATHY	20[redacted]
OTHER: CUSHING-LIKE CHANGES	20[redacted]
OTHER: PERIPHERAL ARTHROPATHY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: UMBILICAL HERNIA	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	NEVER	

Study Drug Administration

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

M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 365	308
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 366		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	500 mg	BID	Y-M: 20[redacted]
MESALAZINE	1600 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	300 mg	OTHER: E6W	Y-M: 20[redacted]
ETROLIZUMAB	105 mg	OTHER: E4W	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
MESALAZINE	1600 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted]
FAMOTIDINE	40 mg	QD	Y-M: 20[redacted]
CALCIUM CARBONATE	1 OTHER: TBL	QD	Y-M: 20[redacted] / -320
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -17
DESOGESTREL;ETHINYLESTRADIOL	1 OTHER: TBL	QD	Y: 20[redacted]
METHYLPREDNISOLONE	2 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
MESALAZINE	1600 mg	BID	Y-M: 20[redacted]	ONGOING
FAMOTIDINE	40 mg	QD	Y-M: 20[redacted]	ONGOING
CALCIUM CARBONATE	1 OTHER: TBL	QD	Y-M: 20[redacted] / -320	ONGOING
FOLIC ACID;IRON	1 OTHER: TBL	QD	Y-M: 20[redacted] / 591	Y-M: 20[redacted] / 622
CLINDAMYCIN	0.5 g	QD	Y-M: 20[redacted] / 625	Y-M: 20[redacted] / 629
NIFURATEL	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 625	Y-M: 20[redacted] / 632
DESOGESTREL;ETHINYLESTRADIOL	1 OTHER: TBL	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	CERVIX CONISATION AFTER PREBIOPSIAN SUSPECT
Preferred term	子宮頚部障害
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 590 / 225
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 226): CERVIX CONISATION: SURGERY SUCCESFUL, LABORATORY RESULTS NOT KNOWN AT THIS TIME	
AE Stopped Initial Rx Day / Rx Day	592 / 227
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DUE TO SCREENING PROCEDURE, NO SYMPTOMS, PAITIENT INDICATED TO CONISATION OF CERVIX OF UTERUS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 954 / 589
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1002 / 637
Duration of AE	49 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

Generated: [redacted]20[redacted]:06:46
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。本被験者はチェコ共和国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，生検のための子宮頚部の円錐切除の事象を発現した。関連する病歴は，臍ヘルニア，潰瘍性大腸炎（左側），非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与590日後＊ ，被験者は生検のための子宮頚部の円錐切除を発現した。投与592日後＊，生検のための子宮頚部の円錐切除は消失した。

投与590日後＊ ，年 1 回の婦人科受診時に「生検の必要性」を指摘され，子宮頚部の円錐切除術を受けるために入院した。投与591日後＊ に手術を受けた。手術は成功し，投与592日後＊に被験者は退院した。

The patient's past medications include:

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

MEDROL for ULCERATIVE COLITIS and AE DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - 20[redacted], 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

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

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

Causality for UPADACITINIB (Open Label)

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1) Cervix lesion (10008353) (Cervix disorder (10008351)) [v.23.0] [10008353]

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

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

Dechallenge: Not ApplicableAlternative Etiology for UPADACITINIB (Open Label)

Event of CERVIX CONISATION AFTER PREBIOPSIAN SUSPECT

- Investigator: due to screening procedure, no symptoms, patient indicated to conisation of cervix of uterus.

- AbbVie: Event more likely related to suspected cervical neoplasia. Human papillomavirus (HPV) is central to the development of cervical neoplasia and can be detected in 99.7 percent of cervical cancers.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
子宮頚部の炎症	X			
潰瘍性大腸炎		X		

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANAEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	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	0.3 PACK	2	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 88	33
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 89	[redacted]20[redacted] / 280	192

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4 g	BID	Y-M: 20[redacted]
MESALAZINE	3.2 g	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 mg	OTHER: 1/4 TABL. PER DAY	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	TID	Y-M: 20[redacted]
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	75 mg	QD	Y-M: 20[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	75 mg	QD	Y-M: 20[redacted]
BUDESONIDE	6 mg	BID	Y-M: 20[redacted]
IRON	500 mg	NOT REPORTED	Y-M: 20[redacted]
RED BLOOD CELLS	900 mL	NOT REPORTED	Y-M: 20[redacted]
IRON	500 mg	NOT REPORTED	Y-M: 20[redacted]
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / -286
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -286
AZATHIOPRINE	150 mg	OTHER: 1 TABL.X 3 TIMES PER DAY	Y-M: 20[redacted] / -299
INTRAUTERINE CONTRACEPTIVE DEVICE	N/A OTHER: NON APLICABLE	OTHER: N/A	Y-M: 20[redacted] / -252
IRON	500 mg	NOT REPORTED	Y-M: 20[redacted] / -104
BUDESONIDE	9 mg	TID	Y-M: 20[redacted] / -33

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
INTRAUTERINE CONTRACEPTIVE DEVICE	N/A OTHER: NON APLICABLE	OTHER: N/A	Y-M: 20[redacted] / -252	Y-M: 20[redacted] / 143
BUDESONIDE	9 mg	TID	Y-M: 20[redacted] / -33	Y-M: 20[redacted] / 118
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 113
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 144
CEFUROXIME	500 mg	BID	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 138
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 138
AMOXICILLIN	1000 mg	TID	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 144
CLAVULANIC ACID	200 mg	TID	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 144

DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 145 Y-M: 20[redacted] / 154
ERTAPENEM	1 g	QD	Y-M: 20[redacted] / 145 Y-M: 20[redacted] / 151
PREDNISOLONE	75 mg	QD	Y-M: 20[redacted] / 145 Y-M: 20[redacted] / 151
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / 152 Y-M: 20[redacted] / 158
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 159 Y-M: 20[redacted] / 165
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 166 Y-M: 20[redacted] / 172
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 173 Y-M: 20[redacted] / 179
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 180 Y-M: 20[redacted] / 186
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / 187 Y-M: 20[redacted] / 193
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted] / 194 Y-M: 20[redacted] / 260
ADALIMUMAB	160 mg	QD	Y-M: 20[redacted] / 246 Y-M: 20[redacted] / 246
ADALIMUMAB	80 mg	OTHER: Q2WK	Y-M: 20[redacted] / 260 Y-M: 20[redacted] / 260
METHYLPREDNISOLONE	28 mg	QD	Y-M: 20[redacted] / 261 Y-M: 20[redacted] / 267
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / 268 Y-M: 20[redacted] / 274
ADALIMUMAB	40 mg	OTHER: Q2W	Y-M: 20[redacted] / 274 Y-M: 20[redacted] / 274
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 275 Y-M: 20[redacted] / 281
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 282 Y-M: 20[redacted] / 288
ADALIMUMAB	40 mg	OTHER: Q2WK	Y-M: 20[redacted] / 288 Y-M: 20[redacted] / 288
METHYLPREDNISOLONE	12 mg	QD	Y-M: 20[redacted] / 289 Y-M: 20[redacted] / 298
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 299 Y-M: 20[redacted] / 315
ADALIMUMAB	40 mg	OTHER: Q2WK	Y-M: 20[redacted] / 302 Y-M: 20[redacted] / 302
ADALIMUMAB	40 mg	OTHER: QW	Y-M: 20[redacted] / 309 Y-M: 20[redacted] / 309
ADALIMUMAB	40 mg	OTHER: QW	Y-M: 20[redacted] / 316 Y-M: 20[redacted] / 316
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted] / 316 Y-M: 20[redacted] / 350
ADALIMUMAB	40 mg	OTHER: QW	Y-M: 20[redacted] / 323 Y-M: 20[redacted] / 323
VEDOLIZUMAB	300 mg	QD	Y-M: 20[redacted] / 326 Y-M: 20[redacted] / 326
VEDOLIZUMAB	300 mg	QD	Y-M: 20[redacted] / 340 Y-M: 20[redacted] / 340
METHYLPREDNISOLONE	28 mg	QD	Y-M: 20[redacted] / 351 Y-M: 20[redacted] / 360
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / 361 Y-M: 20[redacted] / 370
VEDOLIZUMAB	300 mg	QD	Y-M: 20[redacted] / 368 Y-M: 20[redacted] / 368
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 371 Y-M: 20[redacted] / 380
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 381 Y-M: 20[redacted] / 390
METHYLPREDNISOLONE	12 mg	QD	Y-M: 20[redacted] / 391 Y-M: 20[redacted] / 400
VEDOLIZUMAB	300 mg	QD	Y-M: 20[redacted] / 396 Y-M: 20[redacted] / 396
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 401 Y-M: 20[redacted] / 411
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted] / 412 Y-M: 20[redacted] / 427
VEDOLIZUMAB	300 mg	QD	Y-M: 20[redacted] / 421 Y-M: 20[redacted] / 421

METHYLPREDNISOLONE	28 mg	QD	Y-M: 20[redacted] / 428	Y-M: 20[redacted] / 437
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / 438	Y-M: 20[redacted] / 447
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 448	Y-M: 20[redacted] / 457
VEDOLIZUMAB	300 mg	QD	Y-M: 20[redacted] / 450	Y-M: 20[redacted] / 450
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 458	ONGOING

Event #1: Serious Adverse Event

Event Description	INFLAMMATION OF THE CERVIX DUE TO AN IUD
Preferred term	子宮頚部の炎症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 212 / 124
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	239 / 151
Duration of AE	28 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INFLAMMATION OF INTRAUTERINE DEVICE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #2: 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] / 273 / 185
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	

SAE Supplemental Procedure	
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	YES
SAE Criteria	NONE

Generated: [redacted]20[redacted]:06:46
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。本被験者はエストニアの 2[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，子宮内避妊器具による子宮頚部の炎症の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.3 箱を 2 年間）及び非飲酒者であった。

Event 1 の臨床経過：

投与212日後＊ ，被験者は子宮内避妊器具による子宮頚部の炎症を発現した。投与239日後＊，子宮内避妊器具による子宮頚部の炎症は消失した。

本事象発現前の 投与の163日前＊ ，被験者は避妊のために子宮内避妊器具装着の処置を受けた。

投与の230日後＊ ，被験者は下腹部痛及び高熱があり，入院した。被験者は抗生物質での治療を受けた。投与の239日後＊，炎症は消失し，被験者は退院した。

投与された薬剤は，セフロキシム，アモキシシリン，クラブラン酸，ertapenem 及びドキシサイクリンであった。

The patient's past medications include:

MESALASINE for ULCERATIVE COLITIS ([redacted])

METHYLPREDNISOLONE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

CIPROFLOXACINE for ULCERATIVE COLITIS ([redacted])

METRONIDAZOLE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Cervix inflammation (10068402) (Cervix inflammation (10068402)) [v.23.1] [10068402]

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 INFLAMMATION OF THE CERVIX DUE TO AN IUD

- Investigator: inflammation of intrauterine device.

- AbbVie: Event is not consistent with study drug's mechanism of action. Additionally, inflammation can occur anytime following IUD insertion.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **TEMPERATURE:** High.

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
気管支炎	X			X
構語障害	X			
腸閉塞	X			
口腔咽頭痛	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: ALLERGIC REACTION TO REMICADE	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HYPERTENSION: HIGH BLOOD PRESSURE MEASUREMENTS IN 20[redacted] AND 20[redacted]. MEASUREMENTS NORMALIZED 20[redacted] AND NO MEDICATIONS FOR HYPERTENSION ARE IN USE.	20[redacted]
OTHER: ARTHROSIS OF THE KNEES	20[redacted]
OTHER: LEFT GLENOHUMERAL JOINT LUXATION	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	25	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 54		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PARACETAMOL	665 mg	PRN	Y-M: 20[redacted]-[redacted]
MESALAZINE	2400 mg	TID	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]-[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]-[redacted]
MESALAZINE	4000 mg	TID	Y-M: 20[redacted]-[redacted]
MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	400 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted]-[redacted] / -292
VITAMIN D NOS	15 ug	QD	Y-M: 20[redacted]-[redacted] / -117

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	665 mg	PRN	Y-M: 20[redacted]-[redacted]	ONGOING
MESALAZINE	4000 mg	TID	Y-M: 20[redacted]-[redacted]	ONGOING
VITAMIN D NOS	15 ug	QD	Y-M: 20[redacted]-[redacted] / -117	ONGOING
CLOPIDOGREL	75 mg	QD	Y-M: 20[redacted]-[redacted] / 447	Y-M: 20[redacted]-[redacted] / 449
SIMVASTATIN	10 mg	QD	Y-M: 20[redacted]-[redacted] / 447	Y-M: 20[redacted]-[redacted] / 449
LOSARTAN	50MG mg	QD	Y-M: 20[redacted]-[redacted] / 647	Not reported

Event #1: Serious Adverse Event

Event Description	BRONCHITIS, SORE THROAT
Preferred term	気管支炎，口腔咽頭痛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 317 / 264
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 268): Hemoglobin: 142 [134 - 167] G/L; Leukocytes: 9 [3.4 - 8.2] 10^9/L; NPTST085-CRP: 133 [0 - 10] MG/L; [redacted]20[redacted] (RX DAY 269): Hemoglobin: 137 [134 - 167] G/L; Leukocytes: 9.7 [3.4 - 8.2] 10^9/L; NPTST085-CRP: 87 [0 - 10] MG/L; [redacted]20[redacted] (RX DAY 273): Hemoglobin: 141 [134 - 167] G/L; Leukocytes: 7.5 [3.4 - 8.2] 10^9/L; NPTST085-CRP: 44 [0 - 10] MG/L; [redacted]20[redacted] (RX DAY 275): Hemoglobin: 143 [134 - 167] G/L; NPTST085-CRP: 22 [0 - 10] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 268): BLOOD NPTST046-BLOOD CULTURE: Negative; URINE NPTST260-URINE CULTURE: Negative; [redacted]20[redacted] (RX DAY 269): OTHER PHARYNX NPTST183-PHARYNGEAL STREPTOCOCCAL CULTUR: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 268): THORAX RTG: NO SIGNS OF INFECTION

AE Stopped Initial Rx Day / Rx Day	330 / 277
Duration of AE	14 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 #2: Serious Adverse Event

Event Description	DYSARTRIA
Preferred term	構語障害
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 492 / 439
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 447): Cholesterol: 5 [0 - 5] MMOL/L; Creatinine: 97 [60 - 100] UMOL/L; HDL Cholesterol: 2.1 [0.8 - 2.1] MMOL/L; Hemoglobin: 132 [134 - 167] G/L; LDL Cholesterol: 2.7 [0 - 3] MMOL/L; NPTST085-CRP: <1 [0 - 10] MG/L; NPTST253-TROPONINE T: 12 [0 - 15] NG/L; Potassium: 3.9 [3.3 - 4.9] MMOL/L; Sodium: 136 [137 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 447): HEAD COMPUTED TOMOGRAPHY: NO SIGNS OF INFARCTION OR HEMORRHAGIA. NORMAL.; THORAX RTG: NORMAL; [redacted]20[redacted] (RX DAY 448): CAROTID ARTERY COMPUTED TOMOGRAPHY-ANGIO: NO STENOSIS IN ICA, NO THROMBOTIC CHANGES.; [redacted]20[redacted] (RX DAY 449): HEAD MRI: NO INFARCTION. NO SIGNS OF ISCHEMIA.

AE Stopped Initial Rx Day / Rx Day	502 / 449
Duration of AE	11 DAYS

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

Event #3: Event of Interest - Creatine Phosphokinase (CPK) Elevation

Event Description	CK ELEVATION, CK ELEVATION
Preferred term	血中クレアチンホスホキナーゼ増加，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] / 565 / 512
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	651 / 598
Duration of AE	87 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

Event Description	OCCLUSIO INTESTINI
Preferred term	腸閉塞
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 724 / 671
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 671): Creatinine: 63 [60 - 100] UMOL/L; Hemoglobin: 144 [134 - 167] G/L; Leukocytes: 10.4 [3.4 - 8.2] 10^9/L; NPTST085-CRP: <1 [0 - 10] MG/L; Platelets: 346 [150 - 360] 10^9/L; Potassium: 3.9 [3.3 - 4.9] MMOL/L; Sodium: 134 [137 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 672): Creatinine: 65 [60 - 100] UMOL/L; Hemoglobin: 139 [134 - 167] G/L; Leukocytes: 7.4 [3.4 - 8.2] 10^9/L; NPTST085-CRP: 3 [0 - 10] MG/L; Platelets: 327 [150 - 360] 10^9/L;

Potassium: 3.5 [3.3 - 4.9] MMOL/L; Sodium: 135 [137 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 671): NASO-GASTRIC TUBE PLACEMENT: 2 LITERS OF LIQUID CAME OUT IMMEDIATELY AND PATIENTS SYMPTOMS RELIEVED; [redacted]20[redacted] (RX DAY 672): ABDOMINAL COMPUTED TOMOGRAPHY: NO SIGNS OF OCCLUSION WAS FOUND.

AE Stopped Initial Rx Day / Rx Day	725 / 672
Duration of AE	2 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 #5: Event of Interest - Creatine Phosphokinase (CPK) Elevation

Event Description	CK ELEVATION
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] / 825 / 772
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	901 / 848
Duration of AE	77 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

Generated: [redacted]20[redacted]:06:46

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。本被験者はフィンランドの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，気管支炎及び咽頭痛の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 25 年間），潰瘍性大腸炎，高血圧及び現飲酒者（1 日 2–4 杯）であった。

Event 1 の臨床経過：

投与317日後＊ ，被験者は気管支炎及び咽頭痛を発現した。投与330日後＊ ，気管支炎及び咽頭痛は消失した。

投与317日後＊ ，被験者は咽頭痛及びインフルエンザ様症状を訴えた。被験者は摂氏 39°C の発熱があった。投与321日後＊ ，被験者は入院した。インフルエンザの検査は陰性で，CRP 検査の結果は 133 mg/dL であった。身体検査では異常は認められなかった。投与322日後＊，被験者の熱は下がり，感染症のパラメータは低下していた。被験者は問題なく回復し，投与322日後＊，被験者は退院した。

The patient's past medications include:

AZAMUN for ULCERATIVE COLITIS ([redacted])

SALAZOPYRIN EN for ULCERATIVE COLITIS ([redacted])

MERKAPTOPURIN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1) Sore throat (10041367) (Oropharyngeal pain (10068319)) [v.21.1] [10041367]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

2) Bronchitis (10006451) (Bronchitis (10006451)) [v.21.1] [10006451]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Open Label)

Event of BRONCHITIS, SORE THROAT

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] BODY TEMPERATURE:** 39 Degrees C

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

[redacted] **20[redacted] CRP:** 133 mg/dL (normal 0 to 10)

[redacted] **20[redacted] CRP:** 22 mg/dL

[redacted] **20[redacted] HEMOGLOBIN:** 142 G/L (normal 134 to 167)

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

[redacted] 20[redacted] PHARYNGEAL STREPTOCOCCAL CULTURE: negative

[redacted] 20[redacted] URINE CULTURE: negative

[redacted] 20[redacted] WBC: 9.0 X10**9/L (normal 3.4 to 8.2)

[redacted] 20[redacted] WBC: 9.7 X10**9/L

[redacted] 20[redacted] WBC: 7.5 X10**9/L (normal 3.4 to 8.2)

[redacted] 20[redacted] X-RAY THORAX: No signs of infection
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はフィンランドの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，構語障害の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 25 年間），潰瘍性大腸炎，高血圧，現飲酒者（1 日 2–4 杯），並びに心疾患及び高血圧の家族歴であり，父親が 5[redacted] 歳の時に心筋梗塞を発現していた。

Event 2 の臨床経過：

投与492日後＊，被験者は構語障害を発現した。投与502日後＊，構語障害は消失した。

投与500日後＊ ，被験者は 1–2 週間続く構語障害があり，入院した。他の神経学的症状は認められなかった。入院時には，舌の側面にいくつかのアフタ性潰瘍が認められた。脳血管発作が疑われたため，画像診断及び検体検査が行われた。プラビックス及びシンバスタチンの投与も開始された。被験者の症状は，入院中に消失した。投与502日後＊ ，被験者は障害もなく，退院した。

投与された薬剤は，シンバスタチン及びプラビックスであった。

The patient's past medications include:

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

SALAZOPYRIN EN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

ENTYVIO for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for COLITIS ULCEROSA ([redacted])

Causality for ABT-494 (Open Label)

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1) Dysarthria (10013887) (Dysarthria (10013887)) [v.22.0] [10013887]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Open Label)

Event of DYSARTHRIA

- Investigator: Not applicable.

- AbbVie: More likely related to history of hypertension, smoking, alcohol use, family history of cardiovascular disease, and obesity.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **CAROTID ARTERY COMPUTED TOMOGRAPHY-ANGIO:** NO STENOSIS IN ICA, NO THROMBOTIC CHANGES.

[redacted] **CHOLESTEROL:** 5.0 MMOL/L (normal 0 to 5)

[redacted] **CREATININE:** 97 MMOL/L (normal 60 to 100)

[redacted] **CRP:** <1 mg/L

[redacted] **HDL:** 2.1 MMOL/L (normal 0.8 to 2.1)

[redacted] **20[redacted]HEAD COMPUTED TOMOGRAPHY:** NO SIGNS OF INFARCTION OR HEMORRHAGIA. NORMAL.

[redacted] **20[redacted] HEAD MRI:** NO INFARCTION. NO SIGNS OF ISCHEMIA.

[redacted] **20[redacted] HEMOGLOBIN:** 132 G/L (normal 134 to 167)

[redacted] **20[redacted] LDL:** 2.7 MMOL/L (normal 0 to 3)

[redacted] **20[redacted] POTASSIUM:** 3.9 MMOL/L (normal 3.3 to 4.9)

[redacted] **20[redacted] SODIUM:** 136 MMOL/L (normal 137 to 145)

[redacted] **20[redacted] THORAX RTG:** Normal

[redacted] **20[redacted] TROPONINE T:** 12 NG/L (normal 0 to 15)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はフィンランドの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，腸閉塞の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 25 年間），広範囲な潰瘍性大腸炎（全大腸炎型）及び現飲酒者（1 日 2–4 杯）であった。

Event 4 の臨床経過：

投与724日後＊，被験者は腸閉塞を発現した。投与725日後＊，腸閉塞は消失した。

投与724日後＊　，被験者は結腸内視鏡検査の準備のために入院した。被験者は準備の一環として，3 L の colonsteril を飲んだ。colonsteril を飲んだ後，被験者の胃が膨張し，痛み出した。被験者は colonsteril を飲んだ後，腸からの排出がなかった。経鼻胃管を留置し，2 L の液体を採取したところ，被験者の症状が緩和され，腸が正常化した。投与725日後＊，被験者は退院した。

The patient's past medications include:

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

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

SALAZOPYRIN EN for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for COLITIS ULCEROSA ([redacted])

REMICADE for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1) Intestinal obstruction (10022687) (Intestinal obstruction (10022687)) [v.22.1] [10022687]

Causality per reporter (Drug/Vaccine): Reasonable possibility

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of OCCLUSIO INTESTINI

- Investigator: Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **ABDOMINAL COMPUTED TOMOGRAPHY:** No signs of occlusion was found.

[redacted] **CREATININE:** 63 umol/L (normal 60 to 100)

[redacted] **CREATININE:** 65 umol/L (normal 60 to 100)

[redacted] **CRP:** <1 MG/L (normal 0 to 10)

[redacted] **CRP:** 3 MG/L (normal 0 to 10)

[redacted] **20[redacted] HEMOGLOBIN:** 144 G/L (normal 134 to 167)

[redacted] **20[redacted] HEMOGLOBIN:** 139 G/L (normal 134 to 167)

[redacted] **20[redacted] PLATELET COUNT:** 346 X10**9/L (normal 150 to 360)

[redacted] **20[redacted] PLATELET COUNT:** 327 X10**9/L (normal 150 to 360)

[redacted] **20[redacted] POTASSIUM:** 3.9 MMOL/L (normal 3.3 to 4.9)

[redacted] **20[redacted] POTASSIUM:** 3.5 MMOL/L (normal 3.3 to 4.9)

[redacted] **20[redacted] SODIUM:** 134 MMOL/L (normal 137 to 145)

[redacted] **20[redacted] SODIUM:** 135 MMOL/L (normal 137 to 145)

[redacted] **20[redacted] WEIGHT:** 9[redacted].[redacted] KG

[redacted] **20[redacted] WHITE BLOOD CELLS:** 10.4 X10**9/L (normal 3.4 to 8.2)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.4 X10**9/L (normal 3.4 to 8.2)

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
低リン酸血症	X	X		

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: ANEMIA	20[redacted]
OTHER: DERMATITIS IGA LINEAR	20[redacted]
OTHER: GILBERT SYNDROM	20[redacted]
OTHER: HEMMORHOIDS	20[redacted]
OTHER: SLEEP DISORDER	20[redacted]
OTHER: SPONDYLITIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 111	55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	160 mg	NOT REPORTED	Y-M: 20[redacted]
MERCAPTOPURINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METHOTREXATE	NOT REPORTED	1 time per week	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
CERTOLIZUMAB	400 mg	OTHER: OTHER EVERY WEEKS	Y-M: 20[redacted]
PREDNISONE	NOT REPORTED	QD	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 6 WEEKS	Y-M: 20[redacted]
PREDNISOLONE	NOT REPORTED	QD	Y-M: 20[redacted]
GOLIMUMAB	100 mg	OTHER: EVERY WEEK	Y-M: 20[redacted]
AMINOSALICYLIC ACID	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -210
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -233
PREDNISOLONE	25 mg	QD	Y-M: 20[redacted] / -90
AZATHIOPRINE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
INFLIXIMAB	5 mg/kg	NOT REPORTED	Y: 20[redacted]
AMINOSALICYLIC ACID	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
METHOTREXATE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
PREDNISONE	NOT REPORTED	QD	Y: 20[redacted]
ESOMEPRAZOLE	20 mg	QD	Y: 20[redacted]
POTASSIUM	600 mg	QD	Y: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y: 20[redacted] / -141

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
AMINOSALICYLIC ACID	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / -210	Y: 20[redacted] / 224
PREDNISOLONE	25 mg	QD	Y-M: 20[redacted] / -90	Y-M: 20[redacted] / 52
FOLIC ACID	5 mg	BID	Y-M: 20[redacted] / 18	ONGOING
IRON	1000 mg	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 29

GLUCOSE 1-PHOSPHATE DISODIUM	ND mg	NOT REPORTED	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 47
CALCIUM PHOSPHATE;MAGNESIUM;PHOSPHORIC ACID;SODIUM PHOSPHATE	65 OTHER: DROPS	TID	Y-M: 20[redacted] / 47	Y-M: 20[redacted] / 50
GLUCOSE 1-PHOSPHATE DISODIUM	ND mg	NOT REPORTED	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51
CALCIUM PHOSPHATE;MAGNESIUM;PHOSPHORIC ACID;SODIUM PHOSPHATE	150 OTHER: DROPS	TID	Y-M: 20[redacted] / 52	ONGOING
COLECALCIFEROL	100 000 IU	OTHER: EVERY OTHER WEEKS	Y-M: 20[redacted] / 53	ONGOING
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 53	ONGOING
ESOMEPRAZOLE	20 mg	QD	Y: 20[redacted]	ONGOING
POTASSIUM	600 mg	QD	Y: 20[redacted]	ONGOING
MESALAZINE	NOT REPORTED	NOT REPORTED	Y: 20[redacted] / -141	Y: 20[redacted] / 224

Event #1: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 57 / 1
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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

Event #2: Serious Adverse Event

Event Description	HYPOPHOSPHOREMIA
Preferred term	低リン酸血症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 99 / 43
Age at AE Onset	3[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 45): NPTST184-PHOSPHORUS: 8 [25 - 45] MG/L; [redacted]20[redacted] (RX DAY 47): NPTST184-PHOSPHORUS: 13 [25 - 45] MG/L; [redacted]20[redacted] (RX DAY 53): NPTST184-PHOSPHORUS: 21 [25 - 45] MG/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	106 / 50
Duration of AE	8 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

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

Event Description	RECIDIVISM HYPOPHOSPHOREMIA
Preferred term	低リン酸血症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 107 / 51
Age at AE Onset	3[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 52): Glucose: 4.496067 [3.607955 - 5.5507] MMOL/L; NPTST184-PHOSPHORUS: 27 [25 - 45] MG/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
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]20[redacted]:06:46
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。本被験者はフランスの 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，低リン酸血症及び習慣性の低リン酸血症の事象を発現した。関連する病歴は，潰瘍性大腸炎及び貧血であった。

Event 2 及び 3 の臨床経過：

投与99日後＊ ，被験者は低リン酸血症を発現した。投与103日後＊ ，低リン酸血症は消失した。投与107日後＊，被験者は習慣性の低リン酸血症を発現した。

投与101日後＊ ，被験者は低リン値及び尿検査で糖尿があり，入院した。投与103日後＊，被験者は退院した。投与107日後＊，被験者は低リン酸血症の再発により再入院した。投与109日後＊，被験者は退院した。

投与された薬剤は，静注用リン，phocytan 及び phosphoneuros であった。

The patient's past medications include:

FERINJECT for ANEMIA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Hypophosphataemia (10021058) (Hypophosphataemia (10021058)) [v.21.0] [10021058]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, outcome unknown

2) Hypophosphataemia (10021058) (Hypophosphataemia (10021058)) [v.21.0] [10021058]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of HYPOPHOSPHOREMIA

- Investigator: NOT APPLICABLE

- AbbVie: RISK FACTORS INCLUDE PRE-EXISTING ULCERATIVE COLITIS AND RECENT TREATMENT WITH FERINJECT.

Event of RECIDIVISM HYPOPHOSPHOREMIA

- Investigator: NOT APPLICABLE

- AbbVie: RISK FACTORS INCLUDE PRE-EXISTING ULCERATIVE COLITIS AND RECENT TREATMENT WITH FERINJECT.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] PHOSPHORUS:** 8 MG/L (normal 25 to 45)

[redacted] **20[redacted] PHOSPHORUS:** 13 MG/L (normal 25 to 45)

[redacted] **20[redacted] PHOSPHORUS:** 21 MG/L (normal 25 to 45)

[redacted] **20[redacted] URINE TEST:** glycosuria

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
肝酵素上昇				X
精巣癌	X	X		X

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

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): STEATOSIS HEPATIS	20[redacted]
OTHER: ABDOMINAL PAIN	NOT REPORTED
OTHER: ARTHRITIS RIGHT HAND	NOT REPORTED

Prior Procedures	Procedure Year
SURGERY: HIPS, MULTIPLE CORRECTIONS OF LEFT AND RIGHT HIP	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56

M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 375	319
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 376	[redacted]20[redacted] / 1035	660

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	5 mg/kg	OTHER: 8 WEEKS	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
AZATHIOPRINE	250 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	OTHER: UNK	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	2 %	QD	Y-M: 20[redacted] / 368	Y-M: 20[redacted] / 368
PROPOFOL	150 mg	QD	Y-M: 20[redacted] / 368	Y-M: 20[redacted] / 368
SODIUM PHOSPHATE	120 mL	QD	Y-M: 20[redacted] / 368	Y-M: 20[redacted] / 368
PROBIOTICS NOS	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 528	Y-M: 20[redacted] / 532

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

Event Description	ELEVATED CK LEVEL
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] / 456 / 81
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1058 / 683 (23 DAYS AFTER LAST TREATMENT)

Duration of AE	603 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 #2: 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] / 792 / 417
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1058 / 683 (23 DAYS AFTER LAST TREATMENT)
Duration of AE	267 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 #3: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC

Event Description	MALIGNANT TESTICULAR TUMOR (LEFT SIDED)
Preferred term	精巣癌
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1033 / 658
Age at AE Onset	4[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 658): NPTST002-?HCG: 112.1 [0.1 - 7] 099,MLU/ML; NPTST017-AFP: 2443 [0 - 16] NG/ML; NPTST147-LDH: 399 [NOT REPORTED - 250] U/L; [redacted]20[redacted] (RX DAY 667): Creatinine: 106.083912 [61.882282 - 106.083912] UMOL/L; Erythrocytes: 4.51 [4.57 - 5.98] 10^12/L; Hematocrit: 0.424 [0.396 - 0.518] FRACTION OF 1;

Hemoglobin: 138 [139 - 177] G/L; Leukocytes: 7.12 [3.79 - 10.33] 10^9/L; NPTST002-?HCG: 91.1 [0.1 - 7] 099,MLU/ML; NPTST017-AFP: 2125 [0 - 16] NG/ML; NPTST115-GFR CKD-EPI: 73 [60 - NOT REPORTED] ML/MIN; NPTST116-GFR MDRD: >60 [60 - NOT REPORTED] ML/MIN; NPTST147-LDH: 217 [NOT REPORTED - 250] U/L; Platelets: 286 [166 - 389] 10^9/L; Potassium: 4.6 [3.4 - 5.4] MMOL/L; Sodium: 143 [130 - 152] MMOL/L; [redacted] (RX DAY 680): NPTST002-?HCG: 51 [0.1 - 7] 099,MLU/ML; NPTST021-ALPHA-FETOPROTEIN: 3251 [0 - 16] NG/ML; NPTST147-LDH: 238 [NOT REPORTED - 250] U/L; [redacted] (RX DAY 685): NPTST002-?HCG: 53.7 [0.1 - 7] 099,MLU/ML; NPTST021-ALPHA-FETOPROTEIN: 2805 [0 - 16] NG/ML; NPTST147-LDH: 195 [NOT REPORTED - 250] U/L; [redacted] (RX DAY 706): NPTST002-?HCG: 0.1 [0.1 - 7] 099,MLU/ML; NPTST021-ALPHA-FETOPROTEIN: 107.6 [0 - 16] NG/ML; NPTST147-LDH: 694 [NOT REPORTED - 250] U/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted] (RX DAY 658): SONOGRAPHY TESTIS AND ABDOMINAL: TESTICAL TUMOR LEFT TESTICLE, MALIGNANCY SUSPECTED KIDNEYS AND URINARY BLADDER: NORMAL FINDINGS RIGHT TESTICLE: TESTICULAR MICROLITHIASIS,DOPPLER SIGNALS NORMAL; [redacted] (RX DAY 662): HISTOLOGY: 70% EMBRYONIC CARCINOMA, 20% SEMINOMA,10% YOLK SAC TUMOR. PT2 L0 V1 R0; MRI OF NEUROCRANIUM: NO PRESENCE OF CEREBRAL METASTASES; [redacted] (RX DAY 685): PEB CHEMOTHERAPY CYCLE 1, DAY 1-5 ([redacted] - [redacted]): NO COMPLICATIONS; [redacted] (RX DAY 692): CYCLE 1, DAY 8 BLEOMYCIN CHEMOTHERAPY: NO COMPLICATIONS; [redacted] (RX DAY 699): CYCLE 1,DAY 15 BLEOMYCIN CHEMOTHERAPY: NEUTROPENIE AND INFLAMMATION IN LEFT MOUTH AND JAW SINCE [redacted] MOUTH RINSE AND ANTIBIOTICS GIVEN AS THERAPY; [redacted] (RX DAY 706): START PEB CHEMOTHERAPY CYCLE 2: NO COMPLICATIONS; [redacted] (RX DAY 713): CYCLE 2, DAY 8 BLEOMYCIN CHEMOTHERAPY: NO COMPLICATIONS; [redacted] (RX DAY 720): CYCLE 2, DAY 15 BLEOMYCIN CHEMOTHERAPY: NO COMPLICATIONS

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]:06:46

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。本被験者はドイツの 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，悪性の精巣腫瘍（左側）の事象を発現した。関連する病歴は，潰瘍性大腸炎，腹痛，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 3 の臨床経過：

投与1033日後＊，被験者は悪性の精巣腫瘍（左側）を発現した。

投与1034日後＊，被験者は左精巣及び腹部の超音波検査を受け，精巣腫瘍が確認され，悪性腫瘍が疑われた。

投与1037日後＊ ，被験者は左精巣の切除のために入院した。徴候及び症状には，陰嚢の左半分の肥大，食欲不振及び体重減少が含まれた。停留精巣，クラインフェルター症候群，精巣癌及びヒト免疫不全ウイルス感染の病歴はなかった。職業上の危険性や発がん性物質への暴露は確認されなかった。臨床経過では，非セミノーマの精巣腫瘍，後腹膜リンパ節腫脹，及び両側の肺腫瘤が認められ，脳転移の徴候は認められなかった。病期分類では，pT2 V1 R0 cN2 cM1a S2CS であり，中程度の予後を示していた。投与1042日後＊，被験者は退院した。

被験者は PEB 療法及びブレオマイシンの化学療法を受けた。

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，ブレオマイシンであった。

The patient's past medications include:

5-ASA for ULCERATIVE COLITIS (20[redacted] - [redacted] 20[redacted])

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

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

PENTASA XTEND for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

Causality for UPADACITINIB (Open Label)

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1) Testis neoplasm malignant (10043362) (Testis cancer (10057644)) [v.23.1] [10043362]

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 MALIGNANT TESTICULAR TUMOR (LEFT SIDED)

- Investigator: UNKNOWN

- AbbVie: Currently published literature in both clinical trial and post-marketing setting indicates that Janus kinase inhibitors are unlikely to increase the risk of testicular neoplasm. Additionally, the exact cause of testicular cancer is not fully understood, and researchers speculate that multiple factors are involved in its development.

Relevant Laboratory& Other Diagnostic Tests

[redacted] **20[redacted] AFP:** 2443 NG/ML (normal 0 to 16)

[redacted] **20[redacted] AFP:** 2125 NG/ML (normal 0 to 16)

[redacted] **20[redacted] BETA HCG:** 112.1 MIU/ML (normal 0.1 to 7.0)

[redacted] **20[redacted] BETA HCG:** 91.1 MIU/ML (normal 0.1 to 7.0)

[redacted] **20[redacted] CREATININE:** 1.2 mg/dL (normal 0.7 to 1.2)

[redacted] **20[redacted] HGB:** 13.8 G/DL (normal 13.9 to 17.7)

[redacted] **20[redacted] HISTOLOGY:** 70% embryonic carcinoma, 20% seminoma, 10% yolk sac tumor. PT2 L0 V1 R0

[redacted] **20[redacted] MRI NEOCRANIUM:** No presence of cerebral metastases

[redacted] **20[redacted] PLT:** 286 X10**3/MCL (normal 166 to 389)

[redacted] **20[redacted] POTASSIUM:** 4.6 MMOL/L (normal 3.4 to 5.4)

[redacted] **20[redacted] SODIUM:** 143 MMOL/L (normal 130 to 152)

[redacted] **20[redacted] SONOGRAPHY ABDOMINAL:** Testicular tumor malignancy suspected. Kidneys and bladder are normal.

[redacted] **20[redacted] SONOGRAPHY TESTIS:** Testicular tumor malignancy suspected. Right testicular microlithiasis. Doppler signs normal.

[redacted] **20[redacted] WBC:** 7.12 X10**3/MCL (normal 3.79 to 10.33)

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Hepatic enzyme increased: Asymptomatic. No alternative etiology.

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
結腸異形成		X		
精巣炎	X			X

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: ORCHITIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 182	125

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: EVERY 2 MONTH	Y-M: 20[redacted] / -350
SULFASALAZINE	4 g	QD	Y: 20[redacted]
ADALIMUMAB	NOT REPORTED	OTHER: EVERY 2 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
METHYLPREDNISOLONE	12 mg	QD	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 8
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 15
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / 77	Y-M: 20[redacted] / 83
CEFUROXIME	500 mg	BID	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 88
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 88	ONGOING
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 90
GENTAMICIN	16 mg	QD	Y-M: 20[redacted] / 89	ONGOING
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 98	ONGOING
SULFASALAZINE	4 g	QD	Y: 20[redacted]	ONGOING

Event #1: AE Leading to Discontinuation of Study Drug

Event Description	LOW GRADE COLONIC DYSPLAISA
Preferred term	結腸異形成
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 58 / 1
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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	YES
SAE Criteria	NONE

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

Event Description	ORCHITIS
Preferred term	精巣炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 140 / 83
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 91): URINE NPTST261-URINE MICROBIOLOGY TEST: Positive-E. COLI 10'5

SAE Supplemental Procedure

NOT REPORTED

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

Generated: [redacted]20[redacted]:06:46
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。本被験者はハンガリーの 3[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，精巣炎の事象を発現した。関連する病歴は，精巣炎，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140日後＊，被験者は精巣炎を発現した。

投与145日後＊，被験者は左精巣上体の過敏及び発熱があり，入院した。入院中の 投与148日後＊ ，尿培養検査で大腸菌が陽性であることも判明した。投与150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，シプロフロキサシン，xylamin plusz 及び zinnat であった。

Causality for ABT-494 (Open Label)

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1) Orchitis (10031064) (Orchitis (10031064)) [v.21.0] [10031064]

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Open Label)

Event of ORCHITIS

- Investigator: Bacterial infection

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] URINE MICROBIOLOGY TEST: Positive for E. coli 10'5

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

Reason for Narrative

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

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
ULCERATIV 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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 426	369
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 426		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
MESALAZINE	3000 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: ONCE A WEEK	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 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
MESALAZINE	3000 mg	QD	Y-M: 20[redacted]	Not reported
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 236
DEXAMETHASONE	6 mg	QD	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 239
ENOXAPARIN	0,4 mL	QD	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 249
DIHYDROCODEINE	10 mg	TID	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 238
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 239
FAVIPIRAVIR	1600 mg	BID	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 231
FAVIPIRAVIR	600 mg	BID	Y-M: 20[redacted] / 232	Y-M: 20[redacted] / 235
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 239

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

Event Description	WORSENING OF COVID 2019 INFECTION
Preferred term	COVID-19
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 653 / 228
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 228): CHEST X-RAY: 2 SIDED PNEUMONIA; [redacted]20[redacted] (RX DAY 238): CHEST X-RAY: FULL RADIOLOGICAL REGRESSION

AE Stopped Initial Rx Day / Rx Day	664 / 239
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

Generated: [redacted]20[redacted]:06:46

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。本被験者はハンガリーの 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 の感染の悪化の事象を発現した。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：

投与の約21ヵ月後＊，被験者は COVID-19 の感染（非重篤）を発現し始めた。

投与653日後＊，被験者は COVID-19 の感染の悪化を発現した。投与664日後＊，COVID-19 の感染の悪化は消失した。

投与653日後＊　，被験者は COVID-19 の症状悪化があり，入院した。症状には，発熱，脱力，咳嗽，及び酸素投与を必要とする息切れが含まれた。投与664日後＊，被験者は退院した。

本事象の危険因子は，被験者が看護師であることと考えられた。

The patient's past medications include:

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

METHYLPREDNISOLONE for ULCERATIVE COLITIS ([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 (10084268) (COVID-19 (10084268)) [v.24.0] [10084268]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF COVID 2019 INFECTION

- Investigator: Covid-19 infection.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** double sided pneumonia

[redacted] **20[redacted] CHEST X-RAY:** full radiological regression

[redacted] **20[redacted] COVID NASOPHARYNGEAL SWAB:** POSITIVE

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
耳帯状疱疹	X			X

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

Medical History	Onset Year
ANKYLOSING SPONDYLITIS	20[redacted]
LEFT SIDED UC	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53
M14-234 SS2 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 54	[redacted]20[redacted] / 112	59
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 113	[redacted]20[redacted] / 476	364
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 477		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	480 mg	QD	Y: 20[redacted]
FOLIC ACID	10MG OTHER: PILL	OTHER: WEEKLY	Y: 20[redacted]
METHOTREXATE	25 mg	OTHER: ONCE / WEEK	Y: 20[redacted]
VEDOLIZUMAB	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
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 24	Y-M: 20[redacted] / 31
ACICLOVIR	900 mg	TID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 36
CALCIUM CHLORIDE;CARMELLOSE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1 OTHER: DROP	OTHER: N/A	Y-M: 20[redacted] / 30	Not reported
RETINOL	1 OTHER: DROP	OTHER: NIGHTLY	Y-M: 20[redacted] / 30	Not reported
ACICLOVIR	1.00 g	TID	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 36
MESALAZINE	480 mg	QD	Y: 20[redacted]	Not reported
FOLIC ACID	10MG OTHER: PILL	OTHER: WEEKLY	Y: 20[redacted]	Y-M: 20[redacted] / 24
METHOTREXATE	25 mg	OTHER: ONCE / WEEK	Y: 20[redacted]	Y-M: 20[redacted] / 38

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

Event Description	RAMSAY HUNT SYNDROME
Preferred term	耳帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 500 / 24
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 29): Albumin: 48 [39 - 51] G/L; Alkaline Phosphatase: 66 [40 - 129] U/L; Aspartate Aminotransferase: 43 [0 - 40] U/L; Basophils: 0.04 [0 - 0.1] 10^9/L; Bilirubin: 12 [1 - 21] UMOL/L; Calcium: 2.39 [2.15 - 2.55] MMOL/L; Chloride: 98 [98 - 106] MMOL/L; Creatinine: 91 [64 - 104] UMOL/L; Eosinophils: 0.05 [0 - 0.5] 10^9/L; Erythrocytes: 3.9 [4.5 - 5.5] 10^12/L; Hematocrit: 0.356 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 128 [130 - 170] G/L; Leukocytes: 15.1 [4 - 10] 10^9/L; Lymphocytes: 1.8 [1 - 3] 10^9/L; Neutrophils: 12.32 [2 - 7] 10^9/L; Phosphate: 0.97 [0.87 - 1.45] MMOL/L; Platelets: 491 [150 - 400] 10^9/L; Potassium: 4.7 [3.3 - 5.1] MMOL/L; Protein: 72 [64 - 83] G/L;

Sodium: 135 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 31): Eosinophils: 0 [0.2 - 0.5] 10^9/L; Erythrocytes: 3.87 [4.5 - 5.5] 10^12/L; Hematocrit: 0.34 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 120 [130 - 170] G/L; Leukocytes: 17.4 [4 - 10] 10^9/L; Lymphocytes: 3.7 [1 - 3] 10^9/L; Neutrophils: 11.5 [2 - 7] 10^9/L; Platelets: 460 [150 - 400] 10^9/L; [redacted]20[redacted] (RX DAY 32): Albumin: 42 [39 - 51] G/L; Alkaline Phosphatase: 60 [40 - 129] U/L; Aspartate Aminotransferase: 46 [0 - 40] U/L; Bilirubin: 12 [1 - 21] UMOL/L; Calcium: 2.32 [2.15 - 2.55] MMOL/L; Chloride: 101 [98 - 106] MMOL/L; Creatinine: 85 [64 - 104] UMOL/L; Potassium: 4.1 [3.3 - 5.1] MMOL/L; Sodium: 137 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はアイルランドの 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，ラムゼーハント症候群の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），強直性脊椎炎，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与500日後＊，被験者はラムゼーハント症候群を発現した。

被験者は顔面麻痺を経験した。投与502日後＊　　，被験者は医学的評価を受け，当初はベル麻痺と診断され，ステロイドの経口投与を受けた。投与505日後＊，被験者は左耳の炎症及び腫脹があり，顔面左側の下垂が解消されないため，入院した。その他の症状及び徴候には，左耳の紅斑及び顔面神経麻痺が含まれた。前頭部での残存は認められなかった。感染症の可能性

が検討された。その他の神経経路は無傷であり，顔面の感覚も問題なかった。口腔や耳の小嚢は認められなかった。最終的な診断は，ラムゼーハント症候群であった。抗ウイルス薬の静脈内投与及び高用量のプレドニゾロンの投与が継続された。投与507日後＊ ，プレドニゾロンは8 日間の投与後に中止され，聴力検査では両耳とも正常であった。投与508日後＊ ，被験者は抗ウイルス薬を経口投与に切り替えられ，退院した。

投与された薬剤は，celluvisc drops，アシクロビル，プレドニゾロン及び vita pos eye drops であった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Ramsay-Hunt syndrome (10037834) (Herpes zoster oticus (10063491)) [v.23.1] [10037834]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of RAMSAY HUNT SYNDROME

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] COVID-19 NASOPHARYNGEAL SWAB: Negative for COVID-19

[redacted] **20**[redacted] **HEMATOCRIT:** 0.356 L/L (normal 0.4 to 0.5)

[redacted] **20**[redacted] **HEMOGLOBIN:** 12.8 G/DL (normal 13.0 to 17.0)

[redacted] **20**[redacted] **LYMPHOCYTES ABS:** 1.8 X10**9/L (normal 1 to 3)

[redacted] **20**[redacted] **NEUTROPHILS ABS:** 12.32 X10**9/L (normal 2 to 7)

[redacted] **20**[redacted] **PLATELET COUNT:** 491 X10**9/L (normal 150 to 400)

[redacted] **20**[redacted] **WHITE BLOOD CELLS:** 15.1 X10**9/L (normal 4 to 10)

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

Reason for Narrative

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

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

Medical History	Onset Year
ANEMIA: LOW HEMOGLOBIN	20[redacted]
LEFT SIDED UC	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 59	[redacted]20[redacted] / 96	38

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ADALIMUMAB	40 mg	OTHER: MONTHLY	Y-M: 20[redacted]
INFLIXIMAB	300 mg	OTHER: MONTHLY	Y-M: 20[redacted]
PREDNISONE	40 mg	OTHER: DAILY	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: 8 WEEKS	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]
PREDNISONE	2.5 mg	OTHER: DAILY	Y-M: 20[redacted]
PREDNISONE	30 mg	OTHER: DAILY	Y-M: 20[redacted]
MERCAPTOPURINE	50 mg	OTHER: DAILY	Y-M: 20[redacted] / -188
IRON	UNK	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
HYDROCORTISONE	100 mg	TID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 34
OMEPRAZOLE	20 mg	OTHER: DAILY	Y-M: 20[redacted] / 31	ONGOING
CALCIUM	1 OTHER: TABLET	OTHER: DAILY	Y-M: 20[redacted] / 35	ONGOING
PREDNISONE	40 mg	OTHER: DAILY	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 37
VITAMIN D NOS	2000 OTHER: UNITS	OTHER: DAILY	Y-M: 20[redacted] / 35	ONGOING
CICLOSPORIN	110 mg	OTHER: DAILY	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 63
HYDROCORTISONE	300 mg	TID	Y-M: 20[redacted] / 38	ONGOING
PREDNISONE	60 mg	OTHER: DAILY	Y-M: 20[redacted] / 38	ONGOING
IRON	UNK	NOT REPORTED	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	UC EXACBERATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 88 / 30
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 30): STOOL NPTST178-PARASITES: Negative

SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	92 / 34
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NO
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

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

Event Description	UC EXACBERATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 96 / 38
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	121 / 63 (25 DAYS AFTER LAST TREATMENT)
Duration of AE	26 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UC EXACBERATION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はイスラエルの 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，貧血，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88日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与92日後＊　，潰瘍性大腸炎の悪化は消失した。

投与88日後＊　，被験者は血便があり入院し，潰瘍性大腸炎の悪化と診断された。投与92日後＊，被験者は退院した。

投与された薬剤は，フラジール及びヒドロコルチゾンであった。

The patient's past medications include:

HUMIRA for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

PURINETHOL for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1)　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: rechallenge was done, reaction recurred

Alternative Etiology for ABT-494 (Open Label)

Event of UC EXACERBATION

- Investigator: Not reported.

- AbbVie: Event is more likely related to recurring flare of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] COLONOSCOPY:** Left sided ulcerative colitis

[redacted] **20[redacted] COLONOSCOPY:** demonstrated chronic disease

[redacted] **20[redacted] PARASITE STOOL TEST:** negative
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はイスラエルの 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，貧血，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 2 の臨床経過：

投与96日後＊，被験者は潰瘍性大腸炎の悪化を発現した。投与121日後＊，潰瘍性大腸炎の悪化は消失した。

投与96日後＊　，被験者は血性下痢及び腹痛の悪化のため入院し，潰瘍性大腸炎の悪化と診断された。投与121日後＊　，被験者は退院した。入院中の本事象の臨床経過に関する詳細な情報は入手しなかった。

被験者の治験薬投与は早期に，及び完全に中止された。

投与された薬剤は，シクロスポリン，prednisone 及びヒドロコルチゾンであった。

The patient's past medications include:

HUMIRA for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTIVYO for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

PURINITHOL for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.0] [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 UC EXACERBATION

- Investigator: UC EXACBERATION.

- AbbVie: RECURRING FLARE OF PRE-EXISTING ULCERATIVE COLITIS.

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

Reason for Narrative

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

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

Medical History	Onset Year
ANEMIA	20[redacted]
DEFICIT OF VITAMINE D	20[redacted]
EARLY MENOPAUSE	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HEARING LOSS	NOT REPORTED
HYPERTENSION	20[redacted]
RENAL COLIC	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 54	54

M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 55	[redacted]20[redacted] / 98	44
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 99		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	5 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]-[redacted]
MESALAZINE	2 g	QD	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]-[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]-[redacted]
OZANIMOD	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]-[redacted] / -160
BISOPROLOL;HYDROCHLOROTHIAZIDE	2.50 mg	QD	Y-M: 20[redacted]-[redacted] / -148
CICLOSPORIN	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
BISOPROLOL;HYDROCHLOROTHIAZIDE	2.50 mg	QD	Y-M: 20[redacted]-[redacted] / -148	Not reported
MESALAZINE	800 mg	TID	Y-M: 20[redacted]-[redacted] / 1	Not reported
ASCORBIC ACID;IRON	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted] / 66	Y-M: 20[redacted]-[redacted] / 157
AMOXICILLIN;CLAVULANIC ACID	875/125 mg	TID	Y-M: 20[redacted]-[redacted] / 143	Y-M: 20[redacted]-[redacted] / 149

Event #1: Serious Adverse Event

Event Description	KIDNEY STONES
Preferred term	腎結石症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 237 / 139
Age at AE Onset	5[redacted]
Laboratory Testing	

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 139): BILATERAL RENAL DOUBLE J-STENT PLACEMENT: REGULAR RECOVERY; LEFT PERCUTANEOUS NEPHROLITHOTRIPSY SURGERY: REGULAR RECOVERY; LEFT URETEROSCOPY: REGULAR RECOVERY

AE Stopped Initial Rx Day / Rx Day	246 / 148
Duration of AE	10 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SAE DUE TO KIDNEY STONES SURGERY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	KIDNEY STONE SURGERY
Preferred term	腎結石症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 310 / 212
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 202): URINE NPTST260-URINE CULTURE: Positive-E.COLI 1.000.000 UFC/ML

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 211): CHEST X-RAY: NORMAL; SARS COV 2 SWAB: NEGATIVE

AE Stopped Initial Rx Day / Rx Day	313 / 215
Duration of AE	4 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	KIDNEY STONES (COMORBIDITY)
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]:06:46

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。本被験者はイタリアの 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，腎結石の事象を発現した。関連する病歴は，早発閉経，高血圧，ビタミン D の欠乏，腎仙痛，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237日後＊，被験者は，腎結石を発現した。投与246日後＊，腎結石は消失した。

本事象発現前の 投与51日後＊，被験者は腎結石（非重篤）を経験した。

投与237日後＊　，被験者は血尿及び腎疝痛の徴候及び症状があり，左側の腎結石砕石術のために入院した。経皮的に左側の尿管鏡検査を行い，両側にダブル J ステントを留置した。投与240日後＊，被験者は左側の腎瘻造設を行い，退院した。投与245日後＊，腎瘻を抜去した。

投与された薬剤は，アモキシシリン・クラブラン酸合剤であった。

The patient's past medications include:

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

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

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

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

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

Causality for UPADACITINIB (Open Label)

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1)　Kidney stones (10023437)　(Nephrolithiasis (10029148))　[v.24.0]　[10023437]

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 KIDNEY STONES

- Investigator: SAE due to kidney stones surgery.

- AbbVie: The event is more likely related to pre-existing history of renal colic. Nephrolithiasis is relatively common problem with increased prevalence in Italy over the years with a rate of 9%.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はイタリアの 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，腎結石の手術の事象を発現した。関連する病歴は，早発閉経，ビタミンDの欠乏，腎仙痛，貧血，潰瘍性大腸炎，非喫煙者及び非飲酒者であった。

Event 2 の臨床経過：

投与310日後＊　，被験者は腎結石の手術を発現した。投与313日後＊，腎結石の手術は消失した。

投与310日後＊　，被験者は右側の尿管鏡検査及び右側のダブルJステントの抜去のために入院した。被験者は血尿の徴候及び症状があった。被験者は腎結石及び腎仙痛の病歴があった。投与313日後＊，被験者はダブルJステントを留置し，右側の腎瘻造設を行い，退院した。

被験者の危険因子には，尿路結石，尿路閉塞，尿路感染の再発及び高血圧の病歴が含まれた。

投与された薬剤は，cefiximina であった。

The patient's past medications include:

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

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

PENTACOL ([redacted] 20[redacted] - 20[redacted])

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

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

Causality for UPADACITINIB (Open Label)

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1) Kidney stone (10023436) (Nephrolithiasis (10029148)) [v.24.0] [10023436]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

Event of KIDNEY STONE SURGERY

- Investigator: KIDNEY STONES (COMORBIDITY)

- AbbVie: The event is more likely related to pre-existing history of renal colic. Nephrolithiasis is relatively common problem with increased prevalence in Italy over the years with a rate of 9%.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] 20[redacted] **SARS COV 2 SWAB:** negative

[redacted] 20[redacted] **URINE CULTURE:** Positive - E.coli 1.000.000 UFC/ml

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

Reason for Narrative

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

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

Medical History	Onset Year
ANEMIA: NOT APPLICABLE	20[redacted]
DRUG ALLERGIES/REACTIONS: NOT APPLICABLE	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HYPERLIPIDEMIA: NOT APPLICABLE	20[redacted]
NEPHROLITHIASIS: NOT APPLICABLE	20[redacted]
OTHER: CHRONIC RENAL FAILURE	20[redacted]
OTHER: HYPERURICEMIA	20[redacted]
OTHER: OVERACTIVE BLADDER	20[redacted]
PNEUMONIA: LATENT TUBERCULOSIS	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	10	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 161	104
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 162		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DIMETICONE	100 mg	OTHER: ONCE	Y-M: 20[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	15 mg	OTHER: UNKNOWN	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: KIT	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	25 mg	QD	Y-M: 20[redacted]
TACROLIMUS	NOT REPORTED	OTHER: UNK	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	1 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	250 mg	OTHER: WEEK0,2,6	Y-M: 20[redacted]
AMINO ACIDS NOS;CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;VITAMINS NOS	80 g	PRN	Y-M: 20[redacted]
BETAMETHASONE	1 g	QD	Y-M: 20[redacted]
OTHER THERAPEUTIC PRODUCTS	1 OTHER: KIT	NOT REPORTED	Y-M: 20[redacted]
TACROLIMUS	4 mg	BID	Y-M: 20[redacted]
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
TACROLIMUS	4 mg	BID	Y-M: 20[redacted]
MERCAPTOPURINE	10 mg	QD	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]

POLAPREZINC	75 mg	BID	Y-M: 20[redacted]
ARNICA MONTANA;CONVALLARIA MAJALIS;ECHINACEA ANGUSTIFOLIA;EQUISETUM ARVENSE;MAGNESIUM PHOSPHATE;RUBIA TINCTORUM;SOLIDAGO VIRGAUREA	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -187
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / -187
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS	2 OTHER: TABLETS	TID	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
DIMETICONE	100 mg	OTHER: ONCE	Y-M: 20[redacted]	Y-M: 20[redacted] / 1011
AMINO ACIDS NOS;CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;VITAMINS NOS	80 g	PRN	Y-M: 20[redacted]	ONGOING
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]	ONGOING
POLAPREZINC	75 mg	BID	Y-M: 20[redacted]	ONGOING
ARNICA MONTANA;CONVALLARIA MAJALIS;ECHINACEA ANGUSTIFOLIA;EQUISETUM ARVENSE;MAGNESIUM PHOSPHATE;RUBIA TINCTORUM;SOLIDAGO VIRGAUREA	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / -187	Y-M: 20[redacted] / 660
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
DIMETICONE	100 mg	QD	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 337
LACTULOSE	90 mL	QD	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 337
LIDOCAINE	15 mL	QD	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 337
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	10 mL	QD	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 337
SODIUM PICOSULFATE	75 mg	OTHER: ONCE	Y-M: 20[redacted] / 443	Y-M: 20[redacted] / 443
DIMETICONE	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 444

HYOSCINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 444
LACTULOSE	58500 mg	OTHER: ONCE	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 444
LIDOCAINE	15 mL	OTHER: ONCE	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 444
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	OTHER: ONCE	Y-M: 20[redacted] / 444	Y-M: 20[redacted] / 444
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 589	Y-M: 20[redacted] / 591
LIDOCAINE	10 mL	QD	Y-M: 20[redacted] / 589	Y-M: 20[redacted] / 589
CEFACLOR	250 mg	TID	Y-M: 20[redacted] / 591	Y-M: 20[redacted] / 595
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 631	Y-M: 20[redacted] / 631
CEFOTIAM	1 g	OTHER: ONCE	Y-M: 20[redacted] / 631	Y-M: 20[redacted] / 631
DICLOFENAC	25 mg	OTHER: ONCE	Y-M: 20[redacted] / 631	Y-M: 20[redacted] / 631
GLYCEROL	120 mL	OTHER: ONCE	Y-M: 20[redacted] / 631	Y-M: 20[redacted] / 631
HYDROXYZINE	25 mg	OTHER: ONCE	Y-M: 20[redacted] / 631	Y-M: 20[redacted] / 631
PENTAZOCINE	15 mg	OTHER: ONCE	Y-M: 20[redacted] / 631	Y-M: 20[redacted] / 631
CEFACLOR	250 mg	TID	Y-M: 20[redacted] / 632	Y-M: 20[redacted] / 632
SENNOSIDE A+B	24 mg	OTHER: ONCE	Y-M: 20[redacted] / 1197	Y-M: 20[redacted] / 1197
SODIUM PICOSULFATE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / 1198	Y-M: 20[redacted] / 1198
DIMETICONE	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 1199	Y-M: 20[redacted] / 1199
LACTULOSE	58500 mg	OTHER: ONCE	Y-M: 20[redacted] / 1199	Y-M: 20[redacted] / 1199
LIDOCAINE	15 mL	OTHER: ONCE	Y-M: 20[redacted] / 1199	Y-M: 20[redacted] / 1199
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	OTHER: ONCE	Y-M: 20[redacted] / 1199	Y-M: 20[redacted] / 1199
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted] / 1228	Not reported
VALSARTAN	80 mg	QD	Y-M: 20[redacted] / 1228	Not reported
CALCIUM CHLORIDE;NEOSTIGMINE;POTASSIUM ASPARTATE;SODIUM BICARBONATE;SODIUM CHLORIDE	2-3 OTHER: DROPS	QID	Y-M: 20[redacted] / 1318	Not reported
PIRENOXINE	1-2 OTHER: DROPS	QID	Y-M: 20[redacted] / 1318	Not reported

SENNOSIDE A+B	24 mg	OTHER: ONCE	Y-M: 20[redacted] / 1345	Y-M: 20[redacted] / 1345
SODIUM PICOSULFATE	75 mg	OTHER: ONCE	Y-M: 20[redacted] / 1345	Y-M: 20[redacted] / 1345
DIMETICONE	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 1346	Y-M: 20[redacted] / 1346
LACTULOSE	58500 mg	OTHER: ONCE	Y-M: 20[redacted] / 1346	Y-M: 20[redacted] / 1346
LIDOCAINE	15 mL	OTHER: ONCE	Y-M: 20[redacted] / 1346	Y-M: 20[redacted] / 1346
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	OTHER: ONCE	Y-M: 20[redacted] / 1346	Y-M: 20[redacted] / 1346
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS	2 OTHER: TABLETS	TID	Y: 20[redacted]	ONGOING

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

Event Description	HIGH CPK
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] / 484 / 323
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	498 / 337
Duration of AE	15 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: Serious Adverse Event

Event Description	COLONIC POLYP
Preferred term	大腸ポリープ
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 498 / 337
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 444): COLONIC POLYPECTOMY: COMPLETE; PATHOLOGICAL EXAMINATION: RECTUM(BIOPSY),ACTIVE STAGE OF ULCERATIVE COLITIS RECTUM(EMR),TUBULAR ADENOMA	
AE Stopped Initial Rx Day / Rx Day	611 / 450
Duration of AE	114 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SPORADIC LESION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	CALCULOUS PYELONEPHRITIS
Preferred term	腎結石症，腎盂腎炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 750 / 589
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	757 / 596
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NEPHROLITHIASIS

Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #4: Serious Adverse Event

Event Description	WORSENING OF NEPHROLITHIASIS(RIGHT)
Preferred term	腎結石症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 792 / 631
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	794 / 633
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	TREATMENT FOR ADVERSE EVENT "WORSENING OF NEPHROLITHIASIS(RIGHT)".
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #5: Serious Adverse Event

Event Description	COLON POLYP
Preferred term	大腸ポリープ
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1360 / 1199
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 1077): ENDOSCOPIC MUCOUSAL RESECTION: COMPLETE	

AE Stopped Initial Rx Day / Rx Day	1360 / 1199
Duration of AE	1 DAY
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NONE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #6: Serious Adverse Event

Event Description	COLON POLYP
Preferred term	大腸ポリープ
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1507 / 1346
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 1346): ENDOSCOPIC MUCOUSAL RESECTION: COMPLETE

AE Stopped Initial Rx Day / Rx Day	1507 / 1346
Duration of AE	1 DAY
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NONE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

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。本被験者は日本の 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，大腸ポリープの事象を発現した。

Event 2 の臨床経過：

投与498日後＊ ，被験者は大腸ポリープを発現した。投与611日後＊ ，大腸ポリープは消失した。

投与604日後＊，被験者は 投与605日後＊に実施の大腸ポリープ切除術のために入院した。
投与606日後＊，被験者は退院した。

Causality for ABT-494 (Open Label)

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1) Colonic polyp (10010003) (Large intestine polyp (10051589)) [v.21.0] [10010003]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of COLONIC POLYP

- Investigator: Sporadic lesion.

- AbbVie: Risk factors include male gender, age and pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] COLONOSCOPY:** clear demarcation between normal and inflamed colonic mucosa seen; distance of demarcation from the anal verge 20.

[redacted] **20[redacted] HYSTOLOGY:** Rectum(biopsy),active stage of ulcerative colitis Rectum(EMR),tubular adenoma

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は日本の 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，結石性腎盂腎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 10 年間），腎結石症，慢性腎不全，高脂血症，高尿酸血症，広範囲な潰瘍性大腸炎（全大腸炎型），過活動性膀胱及び少量の元飲酒者（1 日 2 杯未満）であった。

Event 3 の臨床経過：

投与750日後＊　，被験者は結石性腎盂腎炎を発現した。投与757日後＊　　，結石性腎盂腎炎は消失した。

投与750日後＊　，被験者は結石性腎盂腎炎と診断された右側の腹痛のために入院した。同日，尿管ステントが留置された。投与757日後＊，被験者は退院した。

投与された薬剤は，セフトリアキソンナトリウム及びケフラールであった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

LEUKERIN POWDER for ULCERATIVE COLITIS ([redacted])

LCAP during hemodialysis for ULCERATIVE COLITIS ([redacted])

GCAP during hemodialysis for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1) Pyelonephritis (10037596) (Pyelonephritis (10037596)) [v.21.1] [10037596]

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) Renal calculus (10038386) (Nephrolithiasis (10029148)) [v.21.1] [10038386]

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 CALCULOUS PYELONEPHRITIS

- Investigator: Nephrolithiasis

- AbbVie: Event more likely related to pre-existing history of nephrolithiasis. Additional risk factor is pre-existing hyperuricemia.
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は日本の成人男性であり，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，腎結石症の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 10 年間），腎結石症，慢性腎不全，高脂血症，高尿酸血症，潰瘍性大腸炎及

び元飲酒者（1 日 2 杯未満）であった。

Event 4 の臨床経過：

投与792日後＊　，被験者は腎結石症の悪化を発現した。投与794日後＊　，腎結石症の悪化は消失した。

投与792日後＊に被験者は入院し，投与794日後＊に退院した。

投与された薬剤は，ソルアセトＦ輸液，セフォチアム塩酸塩，アタラックス-P 及びソセゴンであった。

The patient's past medications include:

CEFTRIAXONE SODIUM HYDRATE for CALCULOUS PYELONEPHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LIDOCAINE HYDROCHLORIDE INJ for URETER STENT PLACEMENT ([redacted] 20[redacted] - [redacted] 20[redacted])

KEFRAL for CALCULOUS PYELONEPHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABT-494 (Open Label)

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1) Nephrolithiasis (10029148) (Nephrolithiasis (10029148)) [v.21.1] [10029148]

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 WORSENING OF NEPHROLITHIASIS

- Investigator: TREATMENT FOR ADVERSE EVENT "WORSENING OF NEPHROLITHIASIS(RIGHT)".

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は日本の 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，大腸ポリープの事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 10 年間），高脂血症，広範囲な潰瘍性大腸炎（全大腸炎型），内視鏡下での粘膜切除術及び元飲酒者（1 日 2 杯未満）であった。

Event 5 の臨床経過：

投与1360日後＊ ，被験者は大腸ポリープを発現した。投与1360日後＊ ，大腸ポリープは消失した。

本事象発現前に，被験者は大腸ポリープの事象を複数回経験していた。投与の39ヵ月後＊，被験者は大腸ポリープ（非重篤）を発現した。

投与1360日後＊ ，被験者は結腸内視鏡検査のために入院した。同日，被験者は結腸内視鏡検査及び内視鏡下での粘膜切除術を受けた。投与1361日後＊，被験者は退院した。

The patient's past medications include:

ASACOL TABLETS for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

GCAP for ULCERATIVE COLITIS ([redacted])

PENTASA TAB for ULCERATIVE COLITIS ([redacted])

PROGRAF CAPSULES for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE FOR I.V. INFUSION100 for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

LCAP for ULCERATIVE COLITIS ([redacted])

PENTASA SUPPOSITORIES for ULCERATIVE COLITIS ([redacted])

LEUKERIN POWDER 10% for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Colonic polyp (10010003) (Large intestine polyp (10051589)) [v.23.1] [10010003]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of COLON POLYP

- Investigator: None

- AbbVie: Colon polyps are common in the general population and in men between age 65-69, there was a 34% prevalence on routine colonoscopy.
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は日本の成人男性であり，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，大腸ポリープの事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 10 年間），高脂血症，潰瘍性大腸炎及び元飲酒者（1 日 2 杯未満）であった。

Event 6 の臨床経過：

投与1507日後＊，被験者は大腸ポリープを発現した。投与1507日後＊ ，大腸ポリープは消失した。

投与1507日後＊，被験者は結腸内視鏡検査のために入院した。同日，ポリープが発見され，被験者は内視鏡下での粘膜切除術を受けた。投与1508日後＊，被験者は退院した。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

GCAP for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

RINDERON for ULCERATIVE COLITIS ([redacted])

LCAP for ULCERATIVE COLITIS ([redacted])

LEUKERIN for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Colonic polyp (10010003) (Large intestine polyp (10051589)) [v.23.1] [10010003]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of COLON POLYP

- Investigator: Not reported

- AbbVie: Colon polyps are common in the general population and in men between age 65-69, there was a 31% prevalence on routine colonoscopy.

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			
γ-グルタミルトランスフェラーゼ増加				X
肝機能異常				X
骨壊死	X			
尿管結石症	X			

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

Medical History	Onset Year
ANEMIA: ANEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: CLAVICLE FRACTURE	19[redacted]
OTHER: DORSI MANUS FRACTURE	19[redacted]
OTHER: HUMERUS FRACTURE	20[redacted]
OTHER: LUMBER FRACTURE	20[redacted]
OTHER: SILENT CALCULUS URETERIC	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	20	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 99	43
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 100	[redacted]20[redacted] / 1043	944

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	PRN	Y-M: 20[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: 1 TIME PER 2WEEKS	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: KIT	NOT REPORTED	Y-M: 20[redacted]
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted]
ENTEROCOCCUS FAECALIS	6 mg	NOT REPORTED	Y-M: 20[redacted]
LACTOMIN	1 g	NOT REPORTED	Y-M: 20[redacted]
MEROPENEM	0.5 g	TID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
CLOSTRIDIUM BUTYRICUM	20 mg	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
TACROLIMUS	0.5 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted] / -346
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -353
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -361
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -322
INFLIXIMAB	300 mg	OTHER: 1 TIME PER 8WEEKS	Y-M: 20[redacted] / -328
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -333
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted] / -284

PREDNISOLONE	2.5 mg	BID	Y-M: 20[redacted] / -300
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -307
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -256
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -229
MESALAZINE	1 g	PRN	Y-M: 20[redacted] / -235
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -207
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -183
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -122
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -14
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM INFANTIS	2 g	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
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 951
ALENDRONIC ACID	35 mg	OTHER: ONCE AWEEK	Y-M: 20[redacted] / 173	ONGOING
PREDNISOLONE	25 mg	QD	Y-M: 20[redacted] / 214	Y-M: 20[redacted] / 226
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 227	Y-M: 20[redacted] / 240
PREDNISOLONE	17.5 mg	QD	Y-M: 20[redacted] / 241	Y-M: 20[redacted] / 254
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted] / 246	Y-M: 20[redacted] / 296
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 259
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 259
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / 255	Y-M: 20[redacted] / 268
PREDNISOLONE	12.5 mg	QD	Y-M: 20[redacted] / 269	Y-M: 20[redacted] / 282
MECOBALAMIN	500 ug	TID	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 296
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 283	Y-M: 20[redacted] / 296
HYALURONIC ACID	25 mg	OTHER: ONCE A WEEK	Y-M: 20[redacted] / 296	Y-M: 20[redacted] / 327
LIDOCAINE	1 mL	OTHER: ONCE A WEEK	Y-M: 20[redacted] / 296	Y-M: 20[redacted] / 327
PREDNISOLONE	9 mg	QD	Y-M: 20[redacted] / 297	Y-M: 20[redacted] / 317
PREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 318	Y-M: 20[redacted] / 339
SODIUM PICOSULFATE	10 mL	PRN	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 339
LIDOCAINE	15 mL	PRN	Y-M: 20[redacted] / 340	Y-M: 20[redacted] / 340
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	2 L	PRN	Y-M: 20[redacted] / 340	Y-M: 20[redacted] / 340

PREDNISOLONE	25 mg	QD	Y-M: 20[redacted] / 340	Y-M: 20[redacted] / 363
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted] / 342	Y-M: 20[redacted] / 886
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / 385	Y-M: 20[redacted] / 830
EFINACONAZOLE	PROPER AMOUNT OTHER: PROPER AMOUNT	QD	Y-M: 20[redacted] / 418	Y-M: 20[redacted] / 652
VANCOMYCIN	0.25 g	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / 474	Y-M: 20[redacted] / 494
BUDESONIDE	2 mg	BID	Y-M: 20[redacted] / 508	Y-M: 20[redacted] / 562
ATROPINE	0.5 mg	PRN	Y-M: 20[redacted] / 521	Y-M: 20[redacted] / 521
HYDROXYZINE	25 mg	PRN	Y-M: 20[redacted] / 521	Y-M: 20[redacted] / 521
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 521	Y-M: 20[redacted] / 521
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 521	Y-M: 20[redacted] / 522
REBAMIPIDE	100 mg	PRN	Y-M: 20[redacted] / 521	Y-M: 20[redacted] / 521
TRAMADOL	100 mg	PRN	Y-M: 20[redacted] / 521	Y-M: 20[redacted] / 522
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 522	Y-M: 20[redacted] / 525
CEFTERAM	100 mg	TID	Y-M: 20[redacted] / 560	Y-M: 20[redacted] / 564
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted] / 560	Y-M: 20[redacted] / 560
GUALENIC ACID	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 560	Y-M: 20[redacted] / 566
MICONAZOLE	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 560	Y-M: 20[redacted] / 564
TRANEXAMIC ACID	250 mg	TID	Y-M: 20[redacted] / 560	Y-M: 20[redacted] / 564
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 562	Y-M: 20[redacted] / 567
PIPERACILLIN;TAZOBACTAM	4.5 g	QD	Y-M: 20[redacted] / 564	Y-M: 20[redacted] / 567
CEFCAPENE	100 mg	TID	Y-M: 20[redacted] / 567	Y-M: 20[redacted] / 574
GENTAMICIN	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 567	Y-M: 20[redacted] / 582
POVIDONE-IODINE	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 567	Y-M: 20[redacted] / 595
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / 567	Y-M: 20[redacted] / 574

DEXTROMETHORPHAN	30 mg	TID	Y-M: 20[redacted] / 571	Y-M: 20[redacted] / 601
HEPARINOID	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 581	Y-M: 20[redacted] / 583
BUDESONIDE	2 mg	BID	Y-M: 20[redacted] / 583	Y-M: 20[redacted] / 606
BUDESONIDE	2 mg	BID	Y-M: 20[redacted] / 645	Y-M: 20[redacted] / 646
VANCOMYCIN	0.25 g	QID	Y-M: 20[redacted] / 647	Y-M: 20[redacted] / 657
VANCOMYCIN	0.25 g	BID	Y-M: 20[redacted] / 658	Y-M: 20[redacted] / 664
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 666	Y-M: 20[redacted] / 676
LOPERAMIDE	1 mg	TID	Y-M: 20[redacted] / 672	Y-M: 20[redacted] / 676
LOXOPROFEN	300 mg	BID	Y-M: 20[redacted] / 865	Y-M: 20[redacted] / 917
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 866	Y-M: 20[redacted] / 906
PREDNISOLONE	9 mg	QD	Y-M: 20[redacted] / 882	Y-M: 20[redacted] / 951
PREGABALIN	50 mg	BID	Y-M: 20[redacted] / 886	Y-M: 20[redacted] / 906
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 907	Y-M: 20[redacted] / 917
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted] / 919	ONGOING
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM CITRATE	1800 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
CALCIUM GLUCONATE;GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE;SODIUM CITRATE	900 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
CEFAZOLIN	1 g	TID	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 939
CLOSTRIDIUM BUTYRICUM	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 951
DESFLURANE	40.89 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
DROPERIDOL	0.5 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
FENTANYL	100 ug	BID	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
FLURBIPROFEN	5 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
HEPARIN	5 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
HYDROCORTISONE	100 mg	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
LEVOBUPIVACAINE	30 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
LIDOCAINE	20 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
NICARDIPINE	0.2 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938

PARACETAMOL	1000 mg	BID	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
PROPOFOL	9 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
REMIFENTANIL	1.8 mg	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
ROCURONIUM	1 mL	TID	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
ROCURONIUM	5 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
SUGAMMADEX	2 mL	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
TRANEXAMIC ACID	10 mL	TID	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 938
CELECOXIB	300 mg	BID	Y-M: 20[redacted] / 939	Y-M: 20[redacted] / 939
DEXMEDETOMIDINE	50 mL	QD	Y-M: 20[redacted] / 939	Y-M: 20[redacted] / 939
EDOXABAN	30 mg	QD	Y-M: 20[redacted] / 939	Y-M: 20[redacted] / 945
ELECTROLYTES NOS	500 mL	QD	Y-M: 20[redacted] / 939	Y-M: 20[redacted] / 939
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 939	Y-M: 20[redacted] / 939
CELECOXIB	200 mg	BID	Y-M: 20[redacted] / 940	Y-M: 20[redacted] / 945
PREDNISOLONE	9 mg	QD	Y-M: 20[redacted] / 954	Y-M: 20[redacted] / 956
PREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / 957	Y-M: 20[redacted] / 967
PREDNISOLONE	7 mg	QD	Y-M: 20[redacted] / 968	Y-M: 20[redacted] / 977

Event #1: Event of Interest - Hepatic Disorder

Event Description	GAMMA GTP INCREASE
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] / 344 / 245
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	439 / 340
Duration of AE	96 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 #2: Serious Adverse Event

Event Description	DETERIORATION OF CALCULUS URETERIC
Preferred term	尿管結石症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 620 / 521
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 368): NPTST259-URINARY OCCULT BLOOD: 3+ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 438): NPTST259-URINARY OCCULT BLOOD: 3+ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 445): NPTST259-URINARY OCCULT BLOOD: 3+ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 459): NPTST259-URINARY OCCULT BLOOD: 3+ [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 494): Leukocytes: 1-4 [0 - 0] /HPF; NPTST210-RED BLOOD CELL: 1-4 [0 - 0] /HPF; NPTST259-URINARY OCCULT BLOOD: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 536): NPTST259-URINARY OCCULT BLOOD: NEGATIVE [NOT REPORTED - NOT REPORTED] NOT APPLICABLE

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 438): CT: REMAINING STONE WAS SHOWN ON CT; CYSTOSCOPY: NO ABNORMAL FINDINGS; [redacted]20[redacted] (RX DAY 494): ULTRASONOGRAPHY: ULTRASONOGRAPHY WAS PERFORMED AND STONE REMARINED IN THA SAME POSITION.; [redacted]20[redacted] (RX DAY 522): X-RAY: [redacted]/[redacted]/20[redacted]:REMAINING STONE WAS SHOWN ON THE X-RAY IMAGE.; [redacted]20[redacted] (RX DAY 536): RENAL ECHOGRAPHY: HYDRONEPHROSIS OF EITHER KIDNEY WAS NOT ILLUSTRATED AT RENAL ECHOGRAPHY.; X-RAY: NO STONE WAS ILLUSTRATED ON THE X-RAY IMAGE.

AE Stopped Initial Rx Day / Rx Day	635 / 536
Duration of AE	16 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THE PATIENT WAS FOUND TO HAVE ASYMPTOMATIC CALCULUS BEFORE THE STUDY TREATMENT.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #3: Event of Interest - Hepatic Disorder

Event Description	HEPATIC FUNCTION ABNORMAL
Preferred term	肝機能異常
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 663 / 564
Age at AE Onset	4[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	771 / 672
Duration of AE	109 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 #4: Serious Adverse Event

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] / 1020 / 921
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 956): NPTST016-ACTH: 47.1 [7.2 - 63.3] PG/ML; NPTST080-CORTISOL: 10.4 [4.4 - 21.1] UG/DL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 952): LAPAROSCOPIC TOTAL COLECTOMY: THE COLON WAS COMPLETELY REMOVED AND THE ILEUM WAS PLACED IN THE STOMA

AE Stopped Initial Rx Day / Rx Day	1066 / 967 (23 DAYS AFTER LAST TREATMENT)
Duration of AE	47 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DUE TO LONG-TERM USE OF STEROIDS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #5: Serious Adverse Event

Event Description	AVASCULAR NECROSIS FEMORAL HEAD
Preferred term	骨壊死
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1020 / 921
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 917): X-RAY EXAMINATION ON THE HIP: [redacted]/[redacted]/20[redacted]:DIAGNOSIS OF NECROSIS OF FEMORAL HEAD IN THE LEFT; [redacted]20[redacted] (RX DAY 945): CT SCAN: NORMAL AFTER JOINT REPLACEMENT	
AE Stopped Initial Rx Day / Rx Day	1076 / 977 (33 DAYS AFTER LAST TREATMENT)
Duration of AE	57 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DUE TO LONG TERM USE OF STEROIDS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者は日本の 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，尿管結石の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 20 年間），貧血，無症候性の尿管結石，潰瘍性大腸炎及び少量の現飲酒者であった。

Event 2 の臨床経過：

投与620日後＊，被験者は尿管結石の悪化を発現した。投与635日後＊，尿管結石の悪化は消失した。

投与439日後＊　及び 投与467日後＊　，被験者は尿潜血が陽性であった。投与537日 後＊，被験者は 2 日前から肉眼的血尿があると訴え，泌尿器科を紹介された。膀胱鏡検査が行われ，異常所見は認められなかった。CT スキャン検査の結果，8.5 mm の尿管結石が確認された。泌尿器科医は，被験者に十分な量の水分を摂取するように指示した。投与593日後＊　，再度 CT スキャン検査を行ったところ，尿管結石が同じ位置に残っており，体外衝撃波結石破砕術が予定された。投与620日後＊　，被験者は腰痛があり入院し，同日，予定されていた体外衝撃波結石破砕術が行われた。被験者は術後の痛みに対し，鎮痛薬の静脈内投与を受けた。X 線検査で結石の残存が確認され，被験者は引き続き十分な量の水分を摂取するように指示された。 投与621日後＊，被験者は退院した。

投与624日後＊　，退院後も激しい痛みが続いていたが，その後痛みが消えたため，鎮痛薬の服用を中止した。投与635日後＊ ，被験者は泌尿器科を再び受診し，超音波検査及び X 線検査が行われた。腎結石は消失していることが確認された。

投与された薬剤は，カロナール，アセリオ及びトラマールであった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1) Ureteral calculus (10046383) (Ureterolithiasis (10077989)) [v.21.1] [10046383]

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 DETERIORATION OF CALCULUS URETERIC

- Investigator: The patient was found to have asymptomatic calculus before the study treatment.

- AbbVie: The investigator reports asymptomatic calculus was present before the study treatment. Pre-existing ulcerative colitis is an additional risk factor.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は日本の 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，大腿骨頭の虚血性骨壊死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，背側の手骨骨折，鎖骨骨折，上腕骨骨折，腰椎骨折，元喫煙者（1 日 1 箱を 20 年間），潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

<u>Event 4 及び 5 の臨床経過：</u>

投与1020日後＊，被験者は大腿骨頭の虚血性骨壊死及び潰瘍性大腸炎の悪化を発現した。投与1066日後＊ ，潰瘍性大腸炎の悪化は消失した。投与1076日後＊ ，大腿骨頭の虚血性骨壊死は消失した。

本事象発現前，被験者は 投与950日後＊ に MRI 検査を受け，腰椎椎間板ヘルニア（非重篤）と診断された。

入院前の 投与964日後＊ ，被験者は整形外科を受診し，仕事で重いものを持ち上げた後，投与962日後＊ より左臀部から左下肢のしびれ感及び痛みが始まったと訴えた。X 線検査が行われ，骨頭の明らかな壊死は認められなかった。投与985日後＊ ，被験者は左臀部から左下肢

のしびれ感及び痛みが改善しないため，再び整形外科を受診し，リリカが処方された。投与1016日後＊，被験者は腰椎の治療のために専門医を訪れた。左股関節及び膝の X 線検査が行われ，左大腿骨頭の壊死の疑いが認められた。被験者は股関節及び膝関節の治療のため，別の専門医を紹介された。投与1020日後＊，被験者は関節の専門医を受診し，大腿骨頭（左）の壊死と診断された。投与1030日後＊，治験薬の投与は中止された。

投与1036日後＊，被験者は予定された手術のために入院した。投与1037日後＊，被験者は人工骨移植を伴う左股関節の人工関節及び靭帯の置換術を受けた。術後，被験者は集中治療室に入った。投与1038日後＊，被験者は集中治療室から一般病棟に移った。術後経過では，合併症は認められなかった。しかし，被験者の大腿骨頭の壊死を引き起こしたと考えられるため，治験薬投与と併用した副腎皮質ステロイド療法は継続できなかった。投与1046日後＊ ，潰瘍性大腸炎が悪化したため，結腸切除術のために後日再入院する予定で退院した。

投与1049日後＊，被験者は予定された結腸切除術のために入院した。投与1051日後＊ ，回腸瘻造設を伴う，腹腔鏡下での直腸結腸全摘術が行われた。投与1053日後＊，被験者は副腎皮質ステロイド療法を再開した。投与1054日後＊ ，被験者は通常の食事を再開した。術後，回腸瘻からの排液量が増加した。投与1057日後＊，排液量は減少した。投与1066日後＊，被験者は退院した。

潰瘍性大腸炎が悪化したため，治験薬の投与は完全に中止された。

投与された薬剤は，セファメジン，ミヤ BM 及びセレコックスであった。

The patient's past medications include:

LAC-B GRANULAR POWDER N for ULCERATIVE COLITIS (20[redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

BIOFERMIN-R for ULCERATIVE COLITIS ([redacted])

CEFTRIAXONE SODIUM HYDRATE for ULCERATIVE COLITIS ([redacted])

ADACOLUMN for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

MEROPEN for ULCERATIVE COLITIS ([redacted])

BIOFERMIN for ULCERATIVE COLITIS ([redacted])

MIYA-BM for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

PREDONEMA for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

RECTABUL for ULCERATIVE COLITIS ([redacted])

LOXONIN for LUMBAR DISC HERNIATION ([redacted])

LYRICA OD for LUMBAR DISC HERNIATION ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Avascular necrosis femoral head (10003860) (Osteonecrosis (10031264)) [v.23.0] [10003860]

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) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.0] [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 UPADACITINIB (Open Label)

Event of AVASCULAR NECROSIS FEMORAL HEAD

- Investigator: Due to long term use of steroids

- AbbVie: Risk factor includes long term and current use of corticosteroids.

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Due to long-term use of steroids

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ACTH:** 47.1 PG/ML (normal 7.2 to 63.3)

[redacted] **20[redacted] CORTISOL: 10**.4 MCG/DL (normal 4.4 to 21.1)

[redacted] **20[redacted] CT SCAN:** Normal after joint replacement.

[redacted] **20[redacted] HIP X-RAY:** no apparent necrosis of the bone head

[redacted] **20[redacted] HIP X-RAY:** diagnosis of necrosis of femoral head in the left made on [redacted] 20[redacted]

[redacted] **20[redacted] MRI:** lumbar disc herniation

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Gamma-glutamyltransferase: Asymptomatic. Alcohol Use 20% alcohol 400 ml/Day
Hepatic function abnormal: Asymptomatic. No Alcohol Use.

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
帯状疱疹	X			X

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
GOUT	20[redacted]
HYPERTENSION	20[redacted]
OTHER: CHICKENPOX	NOT REPORTED
OTHER: HYPOKALEMIA	20[redacted]
OTHER: LEFT RIB FRACTURE	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 174	117
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 175		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BIFIDOBACTERIUM LACTIS	1 OTHER: TAB	NOT REPORTED	Y-M: 20[redacted]
POLYCARBOPHIL	500 mg	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
OTHER THERAPEUTIC PRODUCTS	1 OTHER: KIT	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted]
OTHER THERAPEUTIC PRODUCTS	1 OTHER: KIT	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	2.5 mg	OTHER: EVERY TWO DAYS	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted] / -342
CLOSTRIDIUM BUTYRICUM	1 g	TID	Y-M: 20[redacted] / -315
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -220
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / -146
HYDROCHLOROTHIAZIDE;LOSARTAN	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -146

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
CLOSTRIDIUM BUTYRICUM	1 g	TID	Y-M: 20[redacted] / -315	ONGOING
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -220	ONGOING
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / -146	ONGOING
HYDROCHLOROTHIAZIDE;LOSARTAN	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -146	ONGOING
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 140
RABBIT VACCINIA EXTRACT	2 OTHER: TABLET	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 140
REBAMIPIDE	100 mg	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 140
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 126
SODIUM PICOSULFATE	10 mg	QD	Y-M: 20[redacted] / 347	Y-M: 20[redacted] / 347
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 348	Y-M: 20[redacted] / 348

MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	2 L	QD	Y-M: 20[redacted] / 348	Y-M: 20[redacted] / 348
SODIUM PICOSULFATE	10 mg	QD	Y-M: 20[redacted] / 681	Y-M: 20[redacted] / 681
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 682	Y-M: 20[redacted] / 682
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	2 L	QD	Y-M: 20[redacted] / 682	Y-M: 20[redacted] / 682
ACETAZOLAMIDE	250 mg	BID	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 900
ACICLOVIR	ADEQUATE DOSE OTHER: APPLICATION	OTHER: 5 TIMES IN A DAY	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 920
AMENAMEVIR	400 mg	QD	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 896
FLUOROMETHOLONE	1 gtt	QID	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 896
MOXIFLOXACIN	1 gtt	QID	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 920
PARACETAMOL	600 mg	TID	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 900
POTASSIUM ASPARTATE	600 mg	BID	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 900
FLUOROMETHOLONE	1 gtt	BID	Y-M: 20[redacted] / 897	ONGOING
ACETAZOLAMIDE	125 mg	BID	Y-M: 20[redacted] / 901	Y-M: 20[redacted] / 917
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / 901	ONGOING
POTASSIUM ASPARTATE	300 mg	BID	Y-M: 20[redacted] / 901	Y-M: 20[redacted] / 917
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] / 901	Y-M: 20[redacted] / 920
ACETAZOLAMIDE	250 mg	BID	Y-M: 20[redacted] / 918	ONGOING
POTASSIUM ASPARTATE	600 mg	BID	Y-M: 20[redacted] / 918	ONGOING
ACICLOVIR	ADEQUATE DOSE OTHER: APPLICATION	TID	Y-M: 20[redacted] / 921	Y-M: 20[redacted] / 935
CARTEOLOL	1 gtt	QD	Y-M: 20[redacted] / 921	Y-M: 20[redacted] / 935
ACICLOVIR	ADEQUATE DOSE OTHER: APPLICATION	QD	Y-M: 20[redacted] / 936	Y-M: 20[redacted] / 941
AMENAMEVIR	400 mg	QD	Y-M: 20[redacted] / 936	Y-M: 20[redacted] / 942
CARTEOLOL	1 gtt	BID	Y-M: 20[redacted] / 936	ONGOING
ACICLOVIR	ADEQUATE DOSE OTHER: APPLICATION	TID	Y-M: 20[redacted] / 942	ONGOING

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

Event Description	CPK INCREASED
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] / 200 / 26
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
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 - Herpes Zoster

Event Description	ZOSTER HERPES
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 291 / 117
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	329 / 155
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: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1045 / 871
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
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	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者は日本の 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，帯状疱疹の事象を発現した。関連する病歴は，高血圧，潰瘍性大腸炎，水痘，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

この被験者は，先行の M14-234 試験では，被験者番号 [redacted] であり，20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで盲検化された治験薬を投与された。

Event 3 の臨床経過：

投与1045日後＊，被験者は帯状疱疹を発現した。

本事象発現前の 投与の約9ヵ月後＊，被験者は帯状疱疹（非重篤）を経験していた。

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，幼少期の水痘の病歴であった。

投与1045日後＊　，被験者は帯状疱疹の症状を発現した。被験者は 1 つの皮膚分節の病変及び眼の病変を有していた。被験者は，帯状疱疹ワクチンを受けていなかった。投与1064日後＊，被験者は，左三叉神経第一枝の帯状疱疹，左目の帯状疱疹性角結膜炎/眼瞼炎，及び左眼の高眼圧と診断された。投与1162日後＊，被験者は眼圧を下げるための眼球の手術のために入院した。投与1163日後＊，被験者は退院した。

投与された薬剤は，アメナリーフ，アセトアミノフェン，ミケラン LA，アスパラカリウム，フルメトロン，ベガモックス，ゾビラックス眼軟膏及びダイアモックスであった。

The patient's past medications include:

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

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

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

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

Causality for UPADACITINIB (Open Label)

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1)　Herpes zoster (10019974)　(Herpes zoster (10019974))　[v.24.0]　[10019974]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Open Label)

Event of HERPES ZOSTER

- Investigator: Not Applicable

- AbbVie: Not Applicable

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Herpes zoster ([redacted]20[redacted]): One dermatone. 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
腹痛	X			
貧血				X
肝機能異常		X		X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ANEMIA: ANEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: ASTHENOPIA	20[redacted]
OTHER: CHRONIC COUGH	20[redacted]
OTHER: PRIMARY SCLEROSING CHOLANGITIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 384	327

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
URSODEOXYCHOLIC ACID	300 mg	TID	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: KIT	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	1 g	BID	Y-M: 20[redacted]
INFLIXIMAB	300 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -233
TACROLIMUS	2 mg	BID	Y-M: 20[redacted] / -248
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -217
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -175
MERCAPTOPURINE	20 mg	QD	Y-M: 20[redacted] / -196
MESALAZINE	1200 mg	TID	Y-M: 20[redacted] / -105
PRANLUKAST	225 mg	BID	Y-M: 20[redacted] / -105
RABEPRAZOLE	10 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
URSODEOXYCHOLIC ACID	300 mg	TID	Y-M: 20[redacted]	ONGOING
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -175	ONGOING
PRANLUKAST	225 mg	BID	Y-M: 20[redacted] / -105	ONGOING
NAPHAZOLINE;POLYSORBATE 80	APPROPRIATE AMOUNT	PRN	Y-M: 20[redacted] / 22	ONGOING
BORIC ACID;EPHEDRINE;MAFENIDE;TAURINE;ZINC	APPROPRIATE AMOUNT	PRN	Y-M: 20[redacted] / 29	ONGOING
DESLORATADINE	5 mg	QD	Y-M: 20[redacted] / 57	ONGOING

ASCORBIC ACID;CAFFEINE;CHLORPHENAMINE;DIHYDROCODEINE;GLYCYRRHIZIC ACID;METHYLEPHEDRINE;PARACETAMOL;PROPYPHENAZONE;RIBOFLAVIN	2 OTHER: CAP	BID	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 69
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 70
BERBERINE;GERANIUM THUNBERGII	1 OTHER: TAB	QD	Y-M: 20[redacted] / 99	Y-M: 20[redacted] / 112
IRON	50 mg	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 168
IRON	80 mg	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 322
CEFMETAZOLE	1 g	OTHER: ONCE	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 322
HYOSCINE	1 g	OTHER: ONCE	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 322
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 324
CEFMETAZOLE	1 g	TID	Y-M: 20[redacted] / 323	Y-M: 20[redacted] / 326
CEFMETAZOLE	1 g	QD	Y-M: 20[redacted] / 327	Y-M: 20[redacted] / 327
RABEPRAZOLE	10 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Event of Interest - Anemia

Event Description	WORSING OF ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 156 / 99
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	226 / 169
Duration of AE	71 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 #2: Serious Adverse Event

Event Description	ABDOMINAL PAIN
Preferred term	腹痛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 378 / 321
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 177): Creatinine: 68.954543 [31.825174 - 93.707456] UMOL/L; NPTST207-RDW-CV: 15.5 [0 - 35] NOT APPLICABLE; [redacted]20[redacted] (RX DAY 180): Alkaline Phosphatase: 441 [115 - 359] U/L; NPTST024-AMYLASE: 74 [33 - 120] U/L; NPTST090-DIRECT BILIRUBIN: 3.2 [0 - 0.4] MG/DL; [redacted]20[redacted] (RX DAY 322): Alanine Aminotransferase: 88 [8 - 42] U/L; Albumin: 39 [40 - 52] G/L; Alkaline Phosphatase: 455 [115 - 359] U/L; Aspartate Aminotransferase: 69 [13 - 33] U/L; Basophils/Leukocytes: 0.8 [0 - 1] %; Bilirubin: 2+ [NOT REPORTED - NOT REPORTED] N/A; Blood Urea Nitrogen: 6.42546 [2.85576 - 7.1394] MMOL/L; Chloride: 105 [99 - 109] MMOL/L; Creatine Kinase: 125 [62 - 287] U/L; Creatinine: 60.114217 [31.825174 - 93.707456] UMOL/L; Eosinophils/Leukocytes: 3.2 [2 - 7] %; Erythrocytes: 1~4 [NOT REPORTED - NOT REPORTED] /HIGH POWER FIELD; Erythrocytes: 4.95 [4.1 - 5.5] 10^12/L; Glucose: 0.00 [NOT REPORTED - 0.05] g/dL; Glucose: - [NOT REPORTED - NOT REPORTED] N/A; Hematocrit: 0.405 [0.39 - 0.51] FRACTION OF 1; Ketones: - [NOT REPORTED - NOT REPORTED] N/A; Leukocytes: 5-9 [NOT REPORTED - NOT REPORTED] /HPF; Leukocytes: 7.24 [4 - 9] 10^9/L; Leukocytes: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Lymphocytes/Leukocytes: 12.2 [26 - 47] %; Monocytes/Leukocytes: 5.4 [3 - 8] %; NPTST024-AMYLASE: 92 [33 - 120] U/L; NPTST037-BACTERIA: - [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST085-CRP: 0.16 [NOT REPORTED - 0.3] mg/dL; NPTST090-DIRECT BILIRUBIN: 1.4 [0 - 0.4] MG/DL; NPTST091-EGFR: 114 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST112-GAMMA GLUTAMYLTRANSFERASE: 245 [11 - 58] U/L; NPTST121-GLASS COLUMN: 0-1 [NOT REPORTED - NOT REPORTED] /LPF; NPTST129-HEMOGLOBIN: 12.6 [13 - 17] G/DL; NPTST134-IG%: 0.3 [NOT REPORTED - NOT REPORTED] %; NPTST144-LACTATE DEHYDROGENASE: 232 [119 - 229] U/L; NPTST155-MAGNESIUM: 2.0 [1.9 - 2.5] MG/DL; NPTST157-MCH: 25.5 [28 - 34] PG; NPTST158-MCHC: 31.1 [32 - 36] G/DL; NPTST159-MCV: 81.8 [83 - 100] FL; NPTST207-RDW-CV: 14.9 [0 - 15] %; NPTST211-RED BLOOD CELL SEDIMENTATION RA: 31 [1 - 10] MM; NPTST212-RED BLOOD CELL SEDIMENTATION RA: 61 [NOT REPORTED - NOT REPORTED] MM; NPTST213-RED BLOOD CELL SEDIMENTATION RA: 11 [NOT REPORTED - NOT REPORTED] MM; NPTST215-RENAL TUBULAR EPITHELIAL CELLS: 1-4 [NOT REPORTED - NOT REPORTED] /HPF; NPTST234-SQUAMOUS CELL: 0-1 [NOT REPORTED - NOT REPORTED] /HPF; NPTST240-TOTAL BILIRUBIN: 1.8 [0.2 - 1.2] MG/DL; NPTST242-TOTAL PROTEIN: 8.0 [6.6 - 8.7] G/DL; NPTST245-TRANSITIONAL CELL: 0-1 [NOT REPORTED - NOT REPORTED] /HPF; NPTST255-TURBIDITY: - [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils/Leukocytes: 78.4 [38 - 58] %; Nitrite: - [NOT REPORTED - NOT REPORTED] N/A; Occult Blood: - [NOT REPORTED - NOT REPORTED] N/A; Platelets: 290 [150 - 350] 10^9/L; Potassium: 3.7 [3.6 - 4.9] MMOL/L; Protein: 100 [NOT REPORTED - 30] mg/dL; Protein: 2+ [NOT REPORTED - NOT REPORTED] N/A; Sodium: 139 [138 - 146] MMOL/L; Specific Gravity: 1.038 [1.005 - 1.03] UNIT NOT REPORTED; Urobilinogen: 2.0 [NOT REPORTED - NOT REPORTED] mg/dL; [redacted]20[redacted] (RX DAY 323): Alanine Aminotransferase: 115 [8 - 42] U/L; Alanine Aminotransferase: 114 [8 - 42] U/L; Albumin: 34 [40 - 52] G/L; Albumin: 35 [40 - 52] G/L; Alkaline Phosphatase: 474 [115 - 359] U/L; Alkaline Phosphatase: 473 [115 - 359] U/L; Aspartate Aminotransferase: 89 [13 - 33] U/L; Aspartate Aminotransferase: 89 [13 - 33] U/L; Basophils/Leukocytes: 0.3 [0 - 1] %; Bilirubin: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Blood Urea Nitrogen: 3.92667 [2.85576 - 7.1394] MMOL/L; Blood Urea Nitrogen: 3.92667 [2.85576 - 7.1394] MMOL/L; Calcium: 2.120835 [2.021031 - 2.594904] MMOL/L; Chloride: 103 [99 - 109] MMOL/L; Chloride: 104 [99 - 109] MMOL/L; Creatine Kinase: 104 [62 - 287] U/L; Creatine Kinase: 106 [62 - 287] U/L; Creatinine: 55.694054 [31.825174 - 93.707456] UMOL/L; Creatinine: 58.346152 [31.825174 - 93.707456] UMOL/L; Eosinophils/Leukocytes: 1.4 [2 - 7] %; Erythrocytes: 4.66 [4.1 - 5.5] 10^12/L; Erythrocytes: 4.66 [4.1 - 5.5] 10^12/L; Glucose: 0 [NOT REPORTED -

0.05] g/dL; Glucose: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Hematocrit: 0.374 [0.39 - 0.51] FRACTION OF 1; Hematocrit: 0.379 [0.39 - 0.51] FRACTION OF 1; Hemoglobin: 121 [130 - 170] G/L; Hemoglobin: 120 [130 - 170] G/L; Ketones: NA [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Leukocytes: 11.11 [4 - 9] 10^9/L; Leukocytes: 11.18 [4 - 9] 10^9/L; Leukocytes: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Lymphocytes/Leukocytes: 7.7 [26 - 47] %; Monocytes/Leukocytes: 5.8 [3 - 8] %; NPTST024-AMYLASE: 59 [33 - 120] U/L; NPTST024-AMYLASE: 60 [33 - 120] U/L; NPTST072-CHOLINESTERASE: 212 [168 - 470] U/L; NPTST085-CRP: 2.51 [NOT REPORTED - 0.3] mg/dL; NPTST090-DIRECT BILIRUBIN: 2.7 [0 - 0.4] MG/DL; NPTST090-DIRECT BILIRUBIN: 2.7 [0 - 0.4] MG/DL; NPTST091-EGFR: 124 [NOT REPORTED - NOT REPORTED] ML/MIN/1.73M2; NPTST091-EGFR: 117 [NOT REPORTED - NOT REPORTED] ML/MIN/1.73M2; NPTST112-GAMMA GLUTAMYLTRANSFERASE: 230 [11 - 58] U/L; NPTST112-GAMMA GLUTAMYLTRANSFERASE: 229 [11 - 58] U/L; NPTST134-IG%: 0.6 [NOT REPORTED - NOT REPORTED] %; NPTST144-LACTATE DEHYDROGENASE: 207 [119 - 229] U/L; NPTST144-LACTATE DEHYDROGENASE: 230 [119 - 229] U/L; NPTST155-MAGNESIUM: 1.9 [1.9 - 2.5] MG/DL; NPTST157-MCH: 25.8 [28 - 34] PG; NPTST157-MCH: 26.0 [28 - 34] PG; NPTST158-MCHC: 31.9 [32 - 36] G/DL; NPTST158-MCHC: 32.1 [32 - 36] G/DL; NPTST159-MCV: 80.3 [83 - 100] FL; NPTST159-MCV: 81.3 [83 - 100] FL; NPTST184-PHOSPHORUS: 3.0 [2.5 - 4.5] MG/DL; NPTST192-PROCALCITONIN: 0.23 [NOT REPORTED - 0.05] ng/mL; NPTST195-PROTHROMBIN RATIO: 1.01 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST200-PT-%: 99.0 [70 - 120] %; NPTST201-PT-INR: 1.01 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST202-PT-SEC: 11.5 [NOT REPORTED - NOT REPORTED] sec; NPTST207-RDW-CV: 15.3 [0 - 15] NOT APPLICABLE; NPTST207-RDW-CV: 15.5 [0 - 15] NOT APPLICABLE; NPTST211-RED BLOOD CELL SEDIMENTATION RA: 41 [1 - 10] MM; NPTST211-RED BLOOD CELL SEDIMENTATION RA: 75 [NOT REPORTED - NOT REPORTED] MM; NPTST213-RED BLOOD CELL SEDIMENTATION RA: 15 [NOT REPORTED - NOT REPORTED] MM; NPTST240-TOTAL BILIRUBIN: 3.3 [0.2 - 1.2] MG/DL; NPTST240-TOTAL BILIRUBIN: 3.3 [0.2 - 1.2] MG/DL; NPTST242-TOTAL PROTEIN: 7.5 [6.6 - 8.7] G/DL; NPTST242-TOTAL PROTEIN: 7.6 [6.6 - 8.7] G/DL; NPTST255-TURBIDITY: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Neutrophils/Leukocytes: 85 [38 - 58] %; Nitrite: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Occult Blood: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Platelets: 255 [150 - 350] 10^9/L; Platelets: 251 [150 - 350] 10^9/L; Potassium: 3.4 [3.6 - 4.9] MMOL/L; Potassium: 3.3 [3.6 - 4.9] MMOL/L; Protein: 0 [NOT REPORTED - 30] mg/dL; Protein: - [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; Sodium: 138 [138 - 146] MMOL/L; Sodium: 138 [138 - 146] MMOL/L; Specific Gravity: 1.003 [1.005 - 1.03] UNIT NOT REPORTED; Urate: 249.835782 [202.248014 - 416.39297] UMOL/L; Urobilinogen: NORMAL [NOT REPORTED - NOT REPORTED] mg/dL; pH: 7.0 [5 - 7.5] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 326): Alanine Aminotransferase: 179 [8 - 42] U/L; Albumin: 30 [40 - 52] G/L; Alkaline Phosphatase: 470 [115 - 359] U/L; Aspartate Aminotransferase: 123 [13 - 33] U/L; Blood Urea Nitrogen: 3.92667 [2.85576 - 7.1394] MMOL/L; Chloride: 103 [99 - 109] MMOL/L; Creatine Kinase: 102 [62 - 287] U/L; Creatinine: 63.650347 [31.825174 - 93.707456] UMOL/L; Erythrocytes: 4.5 [4.1 - 5.5] 10^12/L; Hematocrit: 0.37 [0.39 - 0.51] FRACTION OF 1; Hemoglobin: 116 [130 - 170] G/L; Leukocytes: 4.39 [4 - 9] 10^9/L; NPTST024-AMYLASE: 74 [33 - 120] U/L; NPTST072-CHOLINESTERASE: 180 [168 - 470] U/L; NPTST085-CRP: 3.18 [NOT REPORTED - 0.3] mg/dL; NPTST090-DIRECT BILIRUBIN: 2.7 [0 - 0.4] MG/DL; NPTST091-EGFR: 107 [NOT REPORTED - NOT REPORTED] ML/MIN/1.73M2; NPTST112-GAMMA GLUTAMYLTRANSFERASE: 165 [11 - 58] U/L; NPTST144-LACTATE DEHYDROGENASE: 164 [119 - 229] U/L; NPTST157-MCH: 25.8 [28 - 34] PG; NPTST158-MCHC: 31.4 [32 - 36] G/DL; NPTST159-MCV: 82.2 [83 - 100] FL; NPTST192-PROCALCITONIN: 0.05 [NOT REPORTED - 0.05] ng/mL; NPTST195-PROTHROMBIN RATIO: 1.03 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST200-PT-%: 95.9 [70 - 120] %; NPTST201-PT-INR: 1.03 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST202-PT-SEC: 11.7 [NOT REPORTED - NOT REPORTED] sec; NPTST207-RDW-CV: 15.5 [0 - 15] NOT APPLICABLE; NPTST240-TOTAL BILIRUBIN: 3.1 [0.2 - 1.2] MG/DL; NPTST242-TOTAL PROTEIN: 7.1 [6.6 - 8.7] G/DL; Platelets: 275 [150 - 350] 10^9/L; Potassium: 3.7 [3.6 - 4.9] MMOL/L; Sodium: 138 [138 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 328): Alanine Aminotransferase: 180 [8 - 42] U/L; Albumin: 34 [40 - 52] G/L; Alkaline Phosphatase: 513 [115 - 359] U/L; Aspartate Aminotransferase: 95 [13 - 33] U/L; Blood Urea Nitrogen: 2.85576 [2.85576 - 7.1394] MMOL/L; Chloride: 104 [99 - 109] MMOL/L; Creatine Kinase: 93 [62 - 287] U/L; Erythrocytes: 5.23 [4.1 - 5.5] 10^12/L; Hematocrit: 0.426 [0.39 - 0.51] FRACTION OF 1; Hemoglobin: 136 [130 - 170] G/L; Leukocytes: 5.39 [4 - 9] 10^9/L; NPTST024-AMYLASE: 130 [33 - 120] U/L; NPTST072-CHOLINESTERASE: 211 [168 - 470] U/L; NPTST085-

CRP: 1.35 [NOT REPORTED - 0.3] mg/dL; NPTST090-DIRECT BILIRUBIN: 3.3 [0 - 0.4] MG/DL; NPTST091-EGFR: 98 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST112-GAMMA GLUTAMYLTRANSFERASE: 157 [11 - 58] U/L; NPTST144-LACTATE DEHYDROGENASE: 169 [119 - 229] U/L; NPTST157-MCH: 26.0 [28 - 34] PG; NPTST158-MCHC: 31.9 [32 - 36] G/DL; NPTST159-MCV: 81.5 [83 - 100] FL; NPTST192-PROCALCITONIN: 0.04 [NOT REPORTED - 0.05] ng/mL; NPTST195-PROTHROMBIN RATIO: 1.15 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST200-PT-%: 78.0 [70 - 120] %; NPTST201-PT-INR: 1.16 [NOT REPORTED - NOT REPORTED] NOT APPLICABLE; NPTST202-PT-SEC: 13.1 [NOT REPORTED - NOT REPORTED] fmol; NPTST240-TOTAL BILIRUBIN: 3.8 [0.2 - 1.2] MG/DL; NPTST242-TOTAL PROTEIN: 8.1 [6.6 - 8.7] G/DL; Platelets: 356 [150 - 350] 10^9/L; Potassium: 4.1 [3.6 - 4.9] MMOL/L; Sodium: 138 [138 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 331): Alanine Aminotransferase: 87 [8 - 42] U/L; Albumin: 31 [40 - 52] G/L; Aspartate Aminotransferase: 37 [13 - 33] U/L; Blood Urea Nitrogen: 3.92667 [2.85576 - 7.1394] MMOL/L; Chloride: 105 [99 - 109] MMOL/L; Creatine Kinase: 47 [62 - 287] U/L; Creatinine: 67.186478 [31.825174 - 93.707456] UMOL/L; Erythrocytes: 4.78 [4.1 - 5.5] 10^12/L; Hematocrit: 0.394 [0.39 - 0.51] FRACTION OF 1; Hemoglobin: 123 [130 - 170] G/L; Leukocytes: 6.03 [4 - 9] 10^9/L; NPTST072-CHOLINESTERASE: 175 [168 - 470] U/L; NPTST085-CRP: 0.43 [NOT REPORTED - 0.3] mg/dL; NPTST091-EGFR: 101 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST112-GAMMA GLUTAMYLTRANSFERASE: 100 [11 - 58] U/L; NPTST144-LACTATE DEHYDROGENASE: 189 [119 - 229] U/L; NPTST157-MCH: 25.7 [28 - 34] PG; NPTST158-MCHC: 31.2 [32 - 36] G/DL; NPTST159-MCV: 82.4 [83 - 100] FL; NPTST195-PROTHROMBIN RATIO: 1.14 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST200-PT-%: 78.6 [70 - 120] %; NPTST201-PT-INR: 1.15 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST202-PT-SEC: 13.1 [NOT REPORTED - NOT REPORTED] sec; NPTST207-RDW-CV: 16.2 [0 - 15] NOT APPLICABLE; NPTST240-TOTAL BILIRUBIN: 3.8 [0.2 - 1.2] MG/DL; NPTST242-TOTAL PROTEIN: 7.1 [6.6 - 8.7] G/DL; Platelets: 329 [150 - 350] 10^9/L; Potassium: 4 [3.6 - 4.9] MMOL/L; Sodium: 138 [138 - 146] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 322): ABDOMINAL ECHO: SUSPICION OF CHOLECYTITIS

AE Stopped Initial Rx Day / Rx Day	391 / 334 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MEDICAL HISTORY OF PRIMARY SCLEROSING CHDANGITIS AND GALLBLADDER ENLARGEMENT WAS FOUND.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: AE Leading to Discontinuation of Study Drug, Event of Interest - Hepatic Disorder

Event Description	LIVER DYSFUNCTION
Preferred term	肝機能異常
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 379 / 322
Age at AE Onset	2[redacted]

Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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	YES
SAE Criteria	NONE

Generated: [redacted]20[redacted]:06:46
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。本被験者は日本の 2[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，腹痛の事象を発現した。関連する病歴は，原発性硬化性胆管炎，貧血，潰瘍性大腸炎，非喫煙者及び少量の現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与378日後＊，被験者は腹痛を発現した。投与391日後＊，腹痛は消失した。

投与378日後＊，被験者は右上腹部痛があった。投与379日後＊，被験者は圧痛のある胆嚢肥大があり，入院した。肝酵素の軽度の上昇（肝機能異常［非重篤］）があり，口から何も摂取しないように指示された。投与383日後＊　，被験者は腹痛から回復し，食事を再開した。投与384日後＊，被験者は腹痛がなかった。投与391日後＊　，全身状態が安定していることが確認され，被験者は退院した。

投与された薬剤は，ブチルスコポラミン臭化物，セフメタゾールナトリウム，ロキソニン及びロキソプロフェン Na であった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS ([redacted])

PREDONISOLONE for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

ADACOLUM for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

LEUKERIN for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

LOXONINS for ABDOMONAL PAIN and HEADACHE ([redacted])

Causality for ABT-494 (Open Label)

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1) Abdominal pain (10000081) (Abdominal pain (10000081)) [v.21.1] [10000081]

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 ABDOMINAL PAIN

- Investigator: MEDICAL HISTORY OF PRIMARY SCLEROSING CHOLANGITIS AND GALLBLADDER ENLARGEMENT WAS FOUND.

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS AND PRIMARY SCLEROSING CHOLANGITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ECHO:** Suspicion of cholecytitis

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 88 U/L (normal 8 to 42)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 115 U/L (normal 8 to 42)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 179 U/L (normal 8 to 42)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 180 U/L (normal 8 to 42)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 87 U/L (normal 8 to 42)

[redacted] **20[redacted] ALBUMIN:** 3.9 G/DL (normal 4.0 to 5.2)

[redacted] **20[redacted] ALBUMIN:** 3.4 G/DL (normal 4.0 to 5.2)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 455 U/L (normal 115 to 359)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 473 U/L (normal 115 to 359)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 470 U/L (normal 115 to 359)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 513 U/L (normal 115 to 359)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 441 U/L (normal 115 to 359)

[redacted] **20[redacted] AMYLASE:** 92 U/L (normal 33 to 120)

[redacted] **20[redacted] AMYLASE:** 59 U/L (normal 33 to 120)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 69 U/L (normal 13 to 33)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 89 U/L (normal 13 to 33)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 123 U/L (normal 13 to 33)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 95 U/L (normal 13 to 33)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 37 U/L (normal 13 to 33)

[redacted] 20[redacted] **BASOPHILS:** 0.8 % (normal 0.0 to 1.0)

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 18 mg/dL (normal 8 to 20)

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 11 mg/dL (normal 8 to 20)

[redacted] 20[redacted] **CREATINE KINASE:** 125 U/L (normal 62 to 287)

[redacted] 20[redacted] **CREATINE KINASE:** 106 U/L (normal 62 to 287)

[redacted] 20[redacted] **CREATININE:** 0.68 mg/dL (normal 0.36 to 1.06)

[redacted] 20[redacted] **CREATININE:** 0.63 mg/dL (normal 0.36 to 106)

[redacted] 20[redacted] **CRP:** 0.16 mg/dL (normal >0.03)

[redacted] 20[redacted] **DIRECT BILIRUBIN:** 1.4 mg/dL (normal 0.0 to 0.4)

[redacted] 20[redacted] **DIRECT BILIRUBIN:** 2.7 mg/dL (normal 0 to 0.4)

[redacted] 20[redacted] **EGFR:** 114 ML/MIN/1.73M2

[redacted] 20[redacted] **EGFR:** 117 (ML/MIN/1.73M2

[redacted] 20[redacted] **EOSINOPHILS:** 3.2 % (normal 2.0 to 7.0)

[redacted] 20[redacted] **GLUTAMYLTRANSFERASE:** 245 U/L (normal 11 to 58)

[redacted] 20[redacted] **GLUTAMYLTRANSFERASE:** 229 U/L (normal 11 to 58)

[redacted] 20[redacted] **GLUTAMYLTRANSFERASE:** 157 U/L (normal 11 to 58)

[redacted] 20[redacted] **HEMATOCRIT:** 40.5 % (normal 39 to 51)

[redacted] 20[redacted] **HEMATOCRIT:** 39.4 % (normal 39 to 51)

[redacted] 20[redacted] **HEMOGLOBIN:** 12.6 G/DL (normal 13 to 17)

[redacted] 20[redacted] **HEMOGLOBIN:** 12.3 G/DL (normal 13 to 17)

[redacted] 20[redacted] **INR:** 1.15 no unit

[redacted] 20[redacted] **LACTATE DEHYDROGENASE:** 232 U/L (normal 119 to 229)

[redacted] **20[redacted] LYMPHOCYTES:** 12.2 % (normal 26.0 to 47.0)

[redacted] **20[redacted] MCH:** 25.5 PG (normal 28 to 34)

[redacted] **20[redacted] MCH:** 26 PG (normal 28 to 34)

[redacted] **20[redacted] MCHC:** 31.1 G/DL (normal 32.0 to 36.0)

[redacted] **20[redacted] MCHC:** 31.9 G/DL (normal 32.0 to 36.0)

[redacted] **20[redacted] MCV:** 81.8 FL (normal 83 to 100)

[redacted] **20[redacted] MCV:** 81.5 FL (normal 83 to 100)

[redacted] **20[redacted] MONOCYTES:** 5.4 % (normal 3.0 to 8.0)

[redacted] **20[redacted] NEUTROPHILS:** 78.4 % (normal 38.0 to 58.0)

[redacted] **20[redacted] PLATELET COUNT:** 290 No unit (normal 150 to 350)

[redacted] **20[redacted] PLATELET COUNT:** 329 10^3/uL (normal 150 to 350)

[redacted] **20[redacted] PROTHROMBIN RATIO:** 1.14 no unit

[redacted] **20[redacted] PT:** 13.1 SEC

[redacted] **20[redacted] RED BLOOD CELL SEDIMENTATION RATE 1HOUR:** 31 MM (normal 1 to 10)

[redacted] **20[redacted] RED BLOOD CELL SEDIMENTATION RATE 2HOUR:** 61 MM

[redacted] **20[redacted] RED BLOOD CELL SEDIMENTATION RATE 30MIN:** 11 MM

[redacted] **20[redacted] RED BLOOD CELLS:** 4.95 No unit (normal 4.10 to 5.50)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.78 No unit (normal 4.10 to 5.50)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 1.8 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] TOTAL BILIRUBIN:** 3.3 mg/dL (normal 0.2 to 1.2)

[redacted] **20[redacted] TOTAL PROTEIN:** 8.0 G/DL (normal 6.6 to 8.7)

[redacted] **20[redacted] URIC ACID:** 4.2 mg/dL (normal 3.4 to 7.0)

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

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

[redacted] **URINE KETONES:** NEGATIVE

[redacted] **URINE PROTEIN:** 100 mg/dL (normal 0 to 30)

[redacted] **URINE RED BLOOD CELLS:** 1-4 HPF

[redacted] **URINE SQUAMOUS CELL:** 0-1 HPF

[redacted] **URINE UROBILINOGEN:** 2.0 mg/dL

[redacted] **URINE WHITE BLOOD CELLS:** 5-9 HPF

[redacted] **WHITE BLOOD CELLS:** 7.24 10^3/uL (normal 4.0 to 9.0)

[redacted] **WHITE BLOOD CELLS:** 5.39 No unit (normal 4.0 to 9.0)

[redacted] **WHITE BLOOD CELLS:** 6.03 10^3/uL (normal 4.0 to 9.0)

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Hepatic function abnormal: Abdomial pain.

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

Reason for Narrative

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

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

Medical History	Onset Year
DERMATITIS ATOPIC	19[redacted]
LEFT SIDED UC	20[redacted]
MIGRAINE	20[redacted]
POLLINOSIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 54	[redacted]20[redacted] / 412	359

M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 413	[redacted]20[redacted] / 746	334

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	NOT REPORTED	OTHER: UNK	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	20 mg	PRN	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	25 mg	OTHER: 2 TIME PAR WEEK	Y-M: 20[redacted]
MESALAZINE	1500 mg	BID	Y-M: 20[redacted]
USTEKINUMAB	130 mg	OTHER: 1TIME PAR 8WEEKS	Y-M: 20[redacted]
RIZATRIPTAN	10 mg	PRN	Y-M: 20[redacted]
MESALAZINE	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
MESALAZINE	1500 mg	BID	Y-M: 20[redacted]	ONGOING
RIZATRIPTAN	10 mg	PRN	Y-M: 20[redacted]	ONGOING
MIDAZOLAM	2.0 mg	OTHER: ONCE	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 50
PETHIDINE	35 mg	OTHER: ONCE	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 50
ACICLOVIR	250 mg	BID	Y-M: 20[redacted] / 155	Y-M: 20[redacted] / 155
DOMPERIDONE	10 mg	PRN	Y-M: 20[redacted] / 155	Y-M: 20[redacted] / 189
PARACETAMOL	400 mg	BID	Y-M: 20[redacted] / 155	Y-M: 20[redacted] / 189
PARACETAMOL;TRAMADOL	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / 155	Y-M: 20[redacted] / 189
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 161
MESALAZINE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]	Not reported

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] / 462 / 50
Age at AE Onset	4[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	655 / 243
Duration of AE	194 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 of Interest - Herpes Zoster

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted] / 566 / 154
Age at AE Onset	[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	614 / 202
Duration of AE	49 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

Generated: [redacted]

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。本被験者は日本の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，帯状疱疹の事象を発現した。関連する病歴は，アトピー性皮膚炎，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566日後＊，被験者は帯状疱疹を発現した。投与614日後＊，帯状疱疹は消失した。

投与566日後＊ ，被験者は頚部痛を感じ始め，発疹が現れた。激しい頚部痛のため，救急科を受診したが，原因は不明であった。投与567日後＊ ，被験者は皮膚科医を受診し，帯状疱疹と診断された。同日，頚部の発疹に伴う左肩部，左胸部及び左頚部の激しい痛みのため，被験者は入院した。帯状疱疹の治療が開始された。投与574日後＊，被験者は退院した。

被験者に帯状疱疹ワクチン接種歴はなかった。

投与された薬剤は，トアラセット，アセトアミノフェン及びドンペリドンであった。

The patient's past medications include:

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

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.23.1] [10019974]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of HERPES ZOSTER

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BODY WEIGHT: 4[redacted] KG

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
頭痛	X			
帯状疱疹	X			X
リンパ球減少症				X
好中球減少症				X

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

Medical History	Onset Year
ANEMIA: ANEMIA	20[redacted]
DRUG ABUSE: AZATHIOPRINE	20[redacted]
LEFT SIDED UC	19[redacted]
MIGRAINE HEADACHE: SOMETIME	19[redacted]
OTHER: CERVICAL DISC HERNIATION	NOT REPORTED
OTHER: CHICKENPOX	NOT REPORTED
OTHER: CRP INCREASED	20[redacted]
OTHER: DEHYDRATION	20[redacted]
OTHER: ILIOTIBIAL BAND FRICTION SYNDROME	NOT REPORTED
OTHER: LYMPHOPENIA	20[redacted]
OTHER: NEUTROPHILIA	20[redacted]
OTHER: POLLINOSIS	20[redacted]
OTHER: THROMOBOCYTOSIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: FOR APPENDICITIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 56		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	40 mg	OTHER: ONE TIME PER TWO WEEKS	Y-M: 20[redacted]-[redacted]
ALENDRONIC ACID	35 mg	OTHER: ONE TIME PER A WEEK	Y-M: 20[redacted]-[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]-[redacted]
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted]-[redacted]
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted]
TACROLIMUS	2 mg	BID	Y-M: 20[redacted]-[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted]-[redacted]
ALUMINIUM HYDROXIDE;BISMUTH;CALCIUM CARBONATE;MAGNESIUM TRISILICATE;SODIUM BICARBONATE	3 g	NOT REPORTED	Y-M: 20[redacted]-[redacted]
BETAMETHASONE	1 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]-[redacted]
SULFASALAZINE	2000 mg	BID	Y-M: 20[redacted]-[redacted]
BETAMETHASONE	1 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	260 mg	OTHER: ONE TIME PER SIX WEEKS	Y-M: 20[redacted]-[redacted]

METHOTREXATE	3 mg	OTHER: TWO DAYS PER A WEEK	Y-M: 20[redacted]
PREDNISOLONE	7.5 mg	QD	Y-M: 20[redacted]
CLOSTRIDIUM BUTYRICUM	2 OTHER: TABLET	QD	Y-M: 20[redacted]
ALUMINIUM HYDROXIDE;BISMUTH;CALCIUM CARBONATE;MAGNESIUM TRISILICATE;SODIUM BICARBONATE	2 g	NOT REPORTED	Y-M: 20[redacted]
BECLOMETASONE	20 mg	QD	Y-M: 20[redacted]
BETAMETHASONE	3 mg	QD	Y-M: 20[redacted] / -303
MERCAPTOPURINE	10 mg	QD	Y-M: 20[redacted] / -259
MESALAZINE	3600 mg	QD	Y-M: 20[redacted] / -243
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -243
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -251
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -65
PARACETAMOL	200 mg	PRN	Y: 19[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 OTHER: KIT	NOT REPORTED	Y: 20[redacted]
PREDNISOLONE	5 mg	OTHER: ONE TIME PER TWO DAYS	Y: 20[redacted]
AZATHIOPRINE	NOT REPORTED	OTHER: UNK	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
ALENDRONIC ACID	35 mg	OTHER: ONE TIME PER A WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 169
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted]	ONGOING
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 114
CLOSTRIDIUM BUTYRICUM	2 OTHER: TABLET	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 676
MESALAZINE	3600 mg	QD	Y-M: 20[redacted] / -243	Y-M: 20[redacted] / 326
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -65	Y-M: 20[redacted] / 86
PREDNISOLONE	7.5 mg	QD	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 128
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / 129	Y-M: 20[redacted] / 176
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	PRN	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 169

CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 167
GLUCOSE	20 mL	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 167
LOXOPROFEN	60 mg	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 170
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 167
METOCLOPRAMIDE	5 mg	TID	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 170
ALENDRONIC ACID	35 mg	OTHER: ONE TIME PER A WEEK	Y-M: 20[redacted] / 170	Y-M: 20[redacted] / 326
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted] / 177	Y-M: 20[redacted] / 211
DEXAMETHASONE	PROPER DOSE OTHER: PROPER DOSE	BID	Y-M: 20[redacted] / 200	Y-M: 20[redacted] / 202
ASCORBIC ACID;PANTOTHENIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 204	ONGOING
TRANEXAMIC ACID	250 mg	TID	Y-M: 20[redacted] / 246	Y-M: 20[redacted] / 253
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 252
CEFDITOREN	100 mg	TID	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 252
CHLORPHENAMINE;DIHYDROCODEINE;METHYLEPHEDRINE	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 252
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 252
TULOBUTEROL	2 mg	QD	Y-M: 20[redacted] / 248	Y-M: 20[redacted] / 252
AMBROXOL	15 mg	TID	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 256
GARENOXACIN	400 mg	BID	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 256
TRANEXAMIC ACID	500 mg	TID	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 256
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 281
GARENOXACIN	200 mg	BID	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 260
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 260
CLARITHROMYCIN	200 mg	QD	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 281
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 L	PRN	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 326
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 326
RISEDRONIC ACID	75 mg	OTHER: ONCE A MONTH	Y-M: 20[redacted] / 326	ONGOING
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 326
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 331	Y-M: 20[redacted] / 331
BEPOTASTINE	10 mg	BID	Y-M: 20[redacted] / 332	Y-M: 20[redacted] / 336

CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 332	Y-M: 20[redacted] / 338
CEFDITOREN	100 mg	BID	Y-M: 20[redacted] / 332	Y-M: 20[redacted] / 336
CLOPERASTINE	20 mg	TID	Y-M: 20[redacted] / 332	Y-M: 20[redacted] / 336
DEXTROMETHORPHAN	15 mg	TID	Y-M: 20[redacted] / 332	Y-M: 20[redacted] / 336
AMOXICILLIN;CLAVULANIC ACID	375 mg	TID	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 338
AMBROXOL	15 mg	TID	Y-M: 20[redacted] / 338	Y-M: 20[redacted] / 345
MESALAZINE	1200 mg	BID	Y-M: 20[redacted] / 339	ONGOING
DEXAMETHASONE	PROPER DOSE OTHER: PROPER DOSE	PRN	Y-M: 20[redacted] / 424	ONGOING
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted] / 430	Y-M: 20[redacted] / 676
BEPOTASTINE	100 mg	BID	Y-M: 20[redacted] / 462	Y-M: 20[redacted] / 469
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 462	Y-M: 20[redacted] / 469
CEFDITOREN	100 mg	TID	Y-M: 20[redacted] / 462	Y-M: 20[redacted] / 469
CLOPERASTINE	100 mg	TID	Y-M: 20[redacted] / 462	Y-M: 20[redacted] / 469
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 529	Y-M: 20[redacted] / 535
CEFCAPENE	100 mg	TID	Y-M: 20[redacted] / 529	Y-M: 20[redacted] / 535
GUALENIC ACID	PROPERDOSE OTHER: PROPERDOSE	PRN	Y-M: 20[redacted] / 529	Y-M: 20[redacted] / 680
DIAZEPAM	10 mg	QD	Y-M: 20[redacted] / 585	Y-M: 20[redacted] / 585
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 585	Y-M: 20[redacted] / 585
LIDOCAINE	PROPER DOSE OTHER: PROPER DOSE	PRN	Y-M: 20[redacted] / 585	Y-M: 20[redacted] / 615
MIDAZOLAM	3 mg	QD	Y-M: 20[redacted] / 585	Y-M: 20[redacted] / 585
PARACETAMOL	200 mg	PRN	Y-M: 20[redacted] / 585	ONGOING
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 675	Y-M: 20[redacted] / 675
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 676	Y-M: 20[redacted] / 676
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted] / 677	ONGOING
MECOBALAMIN	500 ug	TID	Y-M: 20[redacted] / 840	Y-M: 20[redacted] / 851
VALACICLOVIR	1000 ug	TID	Y-M: 20[redacted] / 841	Y-M: 20[redacted] / 846
CALCIUM CHLORIDE;GLUCOSE;POTASSIUM;SODIUM ACETATE	500 mL	PRN	Y-M: 20[redacted] / 842	Y-M: 20[redacted] / 843
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	PRN	Y-M: 20[redacted] / 842	Y-M: 20[redacted] / 842

METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 842	Y-M: 20[redacted] / 844
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	PRN	Y-M: 20[redacted] / 843	Y-M: 20[redacted] / 847
PREGABALIN	25 mg	QD	Y-M: 20[redacted] / 848	Y-M: 20[redacted] / 848
PREGABALIN	25 mg	BID	Y-M: 20[redacted] / 953	Y-M: 20[redacted] / 955
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 L	PRN	Y-M: 20[redacted] / 1005	Y-M: 20[redacted] / 1005
HYOSCINE	20 mg	PRN	Y-M: 20[redacted] / 1005	Y-M: 20[redacted] / 1005
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 1005	Y-M: 20[redacted] / 1005
ALLIUM SATIVUM;BIOTIN;LIVER EXTRACT;THIAMINE	1 mL	OTHER: ONCE A WEEK	Y-M: 20[redacted] / 1131	ONGOING
HYOSCINE	10 mg	QD	Y-M: 20[redacted] / 1248	Y-M: 20[redacted] / 1248
PARACETAMOL	200 mg	PRN	Y: 19[redacted]	ONGOING

Event #1: Event of Interest - Lymphopenia

Event Description	LYMPHOCYTOPENIA
Preferred term	リンパ球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 124 / 69
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
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 Description	HEADACHE
Preferred term	頭痛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 222 / 167
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 167): HEAD CT: NO ABNORMAL FINDINGS.	
AE Stopped Initial Rx Day / Rx Day	224 / 169
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SHE HAS A HISTORY OF SEVERE HEADACHE WITH VOMITING. IN ADDITION, TIME HAS PASSED SINCE THE START OF THE INVESTIGATIONAL AGENT. SO I THINK THAT THE SYMPTOMS ARE NOT DUE TO INVESTIGATIONAL AGENT.
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] / 489 / 434
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
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, Event of Interest - Serious Infections, 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] / 893 / 838
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	906 / 851
Duration of AE	14 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, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:06:46
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。本被験者は日本の 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，頭痛の事象を発現した。関連する病歴は，花粉症，貧血，

脱水，非喫煙者，現飲酒者（1 日 2 杯未満）及び片頭痛であった。

Event 2 の臨床経過：

投与222日後＊，被験者は頭痛を発現した。投与224日後＊，頭痛は消失した。

投与221日後＊ ，被験者は，悪寒及び嘔吐を伴う頭痛を発現し始めた。投与222日後＊，症状が改善しなかったため，被験者は救急治療室を受診した。頭部 CT 検査では，異常所見は認められなかった。対症療法及び点滴注入で治療を行い，投与222日後＊ ，被験者は経過観察のために入院した。入院後，補液及び制吐薬を投与したところ，頭痛が改善し始めた。被験者は夕方には食事を摂ることができた。投与224日後＊，症状が安定し，被験者は退院した。

投与された薬剤は，プリンペランであった。

The patient's past medications include:

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

Causality for ABT-494 (Open Label)

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1) Headache (10019211) (Headache (10019211)) [v.21.0] [10019211]

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 HEADACHE

- Investigator: She has a history of severe headache with vomiting. In addition, time has passed since the start of the investigational agent, so I think the symptoms are not due to investigational agent but functional headaches.

- AbbVie: Event more likely related to pre-existing history of migraine headache.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] HEAD CT:** no abnormal findings
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は日本の 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，帯状疱疹の事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者，現飲酒者（1 日 2 杯未満）及び水痘であった。

Event 4 の臨床経過：

投与893日後＊，被験者は帯状疱疹を発現した。投与906日後＊，帯状疱疹は消失した。

投与893日後＊　，被験者は右後頚部及び右後頭部の皮膚の痛みを発現した。投与896日後＊，症状が改善しないため，外来を受診した。発疹は認められなかったが，帯状疱疹が疑われ，バラシクロビルが処方された。被験者は摂氏 38°C の発熱と，右後頭部及び後頚部を含む 2 つの皮膚分節に限局した発疹を発現した。投与897日後＊ ，被験者は入院した。投与906日後＊，被験者は退院した。

投与された薬剤は，リリカ，プリンペラン注射液，ソリューゲン F，ソリューゲン G，バラシクロビル粒状錠，メチコバール及びソルデム 3A であった。

The patient's past medications include:

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

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

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

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

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

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

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

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

BECLOMETASONE DIPROPIONATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

Causality for UPADACITINIB (Open Label)

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1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.23.1] [10019974]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

Event of HERPES ZOSTER

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

20[redacted] BODY TEMPERATURE: 38 Degrees C

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
背部痛	X			
椎間板突出	X			
腰部脊柱管狭窄症	X			

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

Medical History	Onset Year
ASTHMA	NOT REPORTED
HYPERTENSION	NOT REPORTED
LEFT SIDED UC	19[redacted]
OSTEOPOROSIS	NOT REPORTED
OTHER: HEADACHE	20[redacted]
OTHER: INSOMNIA	NOT REPORTED
OTHER: LATENT TUBERCULOSIS INFECTION	20[redacted]
OTHER: LUMBAR DISC HERNIATION	20[redacted]
OTHER: SHOULDER STIFFNESS	NOT REPORTED

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	0.2 PACK	0.3	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 55	55
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 56	[redacted] / 329	274
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 330		

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: 19[redacted]
INFLIXIMAB	5 mg/kg	QD	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: EVERY TWO WEEKS	Y-M: 20[redacted]
TACROLIMUS	8 mg	QD	Y-M: 20[redacted]
MINODRONIC ACID	50 mg	OTHER: ONCE PER 4WEEKS	Y-M: 20[redacted]
ISONIAZID	250 mg	QD	Y-M: 20[redacted] / -350
OLMESARTAN	20 mg	QD	Y-M: 20[redacted] / -301
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted] / -301
LOXOPROFEN	1 OTHER: SHEET	QD	Y-M: 20[redacted] / -314
FELBINAC	PROPER AMOUNT g	PRN	Y-M: 20[redacted] / -226
PREGABALIN	25 mg	BID	Y-M: 20[redacted] / -214
ETIZOLAM	0.5 mg	PRN	Y-M: 20[redacted] / -185
GLYCYRRHIZIC ACID	2 OTHER: TABLET	TID	Y-M: 20[redacted] / -190
URSODEOXYCHOLIC ACID	200 mg	TID	Y-M: 20[redacted] / -190
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / -132
CAMPHOR;CAPSICUM SPP.;SALICYLIC ACID	1 OTHER: SHEET	PRN	Y-M: 20[redacted] / -24
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -9
AZATHIOPRINE	50 mg	QD	Y: 19[redacted]
MESALAZINE	3000 mg	QD	Y: 19[redacted]
BETAMETHASONE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y: 20[redacted]

MESALAZINE	1 g	BID	Y: 20[redacted]
MESALAZINE	3000 mg	QD	Y: 20[redacted]
PREDNISOLONE	15 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
MINODRONIC ACID	50 mg	OTHER: ONCE PER 4WEEKS	Y-M: 20[redacted]	ONGOING
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted] / -301	ONGOING
LOXOPROFEN	1 OTHER: SHEET	QD	Y-M: 20[redacted] / -314	ONGOING
FELBINAC	PROPER AMOUNT g	PRN	Y-M: 20[redacted] / -226	ONGOING
ETIZOLAM	0.5 mg	PRN	Y-M: 20[redacted] / -185	ONGOING
GLYCYRRHIZIC ACID	2 OTHER: TABLET	TID	Y-M: 20[redacted] / -190	Not reported
URSODEOXYCHOLIC ACID	200 mg	TID	Y-M: 20[redacted] / -190	Not reported
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / -132	ONGOING
CAMPHOR;CAPSICUM SPP.;SALICYLIC ACID	1 OTHER: SHEET	PRN	Y-M: 20[redacted] / -24	Not reported
HYALURONIC ACID	1 OTHER: GTT.	OTHER: 6 TIMES PER DAY	Y-M: 20[redacted] / 155	ONGOING
OLMESARTAN	40 mg	QD	Y-M: 20[redacted] / 240	ONGOING
TRICHLORMETHIAZIDE	1 mg	QD	Y-M: 20[redacted] / 310	Y-M: 20[redacted] / 474
BUDESONIDE;FORMOTEROL	2 OTHER: PUFF	BID	Y-M: 20[redacted] / 386	Y-M: 20[redacted] / 553
LOXOPROFEN	1 OTHER: SHEET	QD	Y-M: 20[redacted] / 400	Y-M: 20[redacted] / 531
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 407	Y-M: 20[redacted] / 563
METOCLOPRAMIDE	5 mg	TID	Y-M: 20[redacted] / 456	Y-M: 20[redacted] / 462
TRAMADOL	25 mg	BID	Y-M: 20[redacted] / 456	Y-M: 20[redacted] / 531
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 483	Y-M: 20[redacted] / 483
LOXOPROFEN	1 OTHER: SHEET	QD	Y-M: 20[redacted] / 532	ONGOING
METOCLOPRAMIDE	5 mg	TID	Y-M: 20[redacted] / 532	Y-M: 20[redacted] / 545
PARACETAMOL;TRAMADOL	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 532	Y-M: 20[redacted] / 569
DULOXETINE	20 mg	QD	Y-M: 20[redacted] / 553	Y-M: 20[redacted] / 594
METOCLOPRAMIDE	5 mg	TID	Y-M: 20[redacted] / 553	Y-M: 20[redacted] / 566
BUDESONIDE;FORMOTEROL	1 OTHER: PUFF	BID	Y-M: 20[redacted] / 554	Y-M: 20[redacted] / 822
PREGABALIN	150 mg	BID	Y-M: 20[redacted] / 564	Y-M: 20[redacted] / 786
PARACETAMOL;TRAMADOL	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 570	Y-M: 20[redacted] / 570
PARACETAMOL;TRAMADOL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 571	Y-M: 20[redacted] / 602

IOHEXOL	10 mL	QD	Y-M: 20[redacted] / 573	Y-M: 20[redacted] / 573
LIDOCAINE	3 mL	QD	Y-M: 20[redacted] / 573	Y-M: 20[redacted] / 573
DULOXETINE	40 mg	QD	Y-M: 20[redacted] / 595	Y-M: 20[redacted] / 602
DULOXETINE	60 mg	QD	Y-M: 20[redacted] / 603	Y-M: 20[redacted] / 786
LIDOCAINE	3 mL	QD	Y-M: 20[redacted] / 608	Y-M: 20[redacted] / 608
GUALENIC ACID	1 OTHER: PUSH	PRN	Y-M: 20[redacted] / 617	ONGOING
MAGNESIUM OXIDE	330 mg	PRN	Y-M: 20[redacted] / 642	ONGOING
PARACETAMOL;TRAMADOL	1(TRAMADOL YDROCHLORIDE 37.5MG,ACETAMINO PHEN 325MG OTHER: TABLETS	TID	Y-M: 20[redacted] / 642	Y-M: 20[redacted] / 822
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted] / 663	Y-M: 20[redacted] / 663
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QID	Y-M: 20[redacted] / 663	Y-M: 20[redacted] / 663
RIBOFLAVIN	20 mg	QD	Y-M: 20[redacted] / 663	Y-M: 20[redacted] / 663
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 663	Y-M: 20[redacted] / 663
THIAMINE	10 mg	QD	Y-M: 20[redacted] / 663	Y-M: 20[redacted] / 663
DIMETICONE	10 mL	QD	Y-M: 20[redacted] / 664	Y-M: 20[redacted] / 664
GLUCAGON	1 mg	QD	Y-M: 20[redacted] / 664	Y-M: 20[redacted] / 664
LIDOCAINE	5 mL	QD	Y-M: 20[redacted] / 664	Y-M: 20[redacted] / 664
POTASSIUM;SODIUM BICARBONATE;SODIUM SULFATE	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 664	Y-M: 20[redacted] / 664
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE	500 mL	BID	Y-M: 20[redacted] / 671	Y-M: 20[redacted] / 671
IOHEXOL	10 mL	QD	Y-M: 20[redacted] / 671	Y-M: 20[redacted] / 671
LIDOCAINE	3 mL	QD	Y-M: 20[redacted] / 671	Y-M: 20[redacted] / 671
IOHEXOL	10 mL	QD	Y-M: 20[redacted] / 722	Y-M: 20[redacted] / 722
LIDOCAINE	3 mL	QD	Y-M: 20[redacted] / 722	Y-M: 20[redacted] / 722
PROCATEROL	10 ug	PRN	Y-M: 20[redacted] / 734	ONGOING
DIPHENHYDRAMINE	PROPER AMOUNT g	PRN	Y-M: 20[redacted] / 787	Y-M: 20[redacted] / 790
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / 787	Y-M: 20[redacted] / 790
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	500 mL	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 789

CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE	500 mL	BID	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
CALCIUM GLUCONATE;GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE;SODIUM CITRATE	500 mL	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
CARBAZOCHROME	100 mg	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
CEFAZOLIN	1 g	TID	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 789
EPHEDRINE	40 mg	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
EPINEPHRINE	UNK mg	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
FENTANYL	0.6 mg	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
GLYCEROL	120 mL	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
HYDROCORTISONE	300 mg	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
KETAMINE	40 mL	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
MAGNESIUM CHLORIDE;MALTOSE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
PROPOFOL	50 mL	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
REMIFENTANIL	2 mg	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
TRANEXAMIC ACID	500 mg	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
VECURONIUM	5 mg	QD	Y-M: 20[redacted] / 788	Y-M: 20[redacted] / 788
HYDROCORTISONE	100 mg	QD	Y-M: 20[redacted] / 789	Y-M: 20[redacted] / 789
GLYCEROL	120 mL	QD	Y-M: 20[redacted] / 790	Y-M: 20[redacted] / 790
PARACETAMOL;TRAMADOL	1 OTHER: TAB	TID	Y-M: 20[redacted] / 792	Y-M: 20[redacted] / 801
PARACETAMOL;TRAMADOL	1 OTHER: TAB	BID	Y-M: 20[redacted] / 802	Y-M: 20[redacted] / 822
SUMATRIPTAN	50 mg	PRN	Y-M: 20[redacted] / 803	ONGOING
BUDESONIDE;FORMOTEROL	2 OTHER: PUFF	BID	Y-M: 20[redacted] / 823	Y-M: 20[redacted] / 878
CHLORPHENAMINE;DIHYDROCODEINE;METHYLEPHEDRINE	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / 823	Y-M: 20[redacted] / 852
BUDESONIDE;FORMOTEROL	3 OTHER: PUFF	BID	Y-M: 20[redacted] / 879	Y-M: 20[redacted] / 983

CHLORPHENAMINE;DIHYDROCODEINE;METHYLEPHEDRINE	2 OTHER: TABLETS	PRN	Y-M: 20[redacted] / 879	ONGOING
BUDESONIDE;FORMOTEROL	4 OTHER: PUFF	BID	Y-M: 20[redacted] / 984	Not reported
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 984	Not reported
GARENOXACIN	400 mg	QD	Y-M: 20[redacted] / 984	Y-M: 20[redacted] / 989
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / 1000	Y-M: 20[redacted] / 1003
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 1008	Y-M: 20[redacted] / 1008
DIMETICONE	10 mL	QD	Y-M: 20[redacted] / 1009	Y-M: 20[redacted] / 1009
GLUCAGON	1 mg	QD	Y-M: 20[redacted] / 1009	Y-M: 20[redacted] / 1009
LIDOCAINE	5 mL	QD	Y-M: 20[redacted] / 1009	Y-M: 20[redacted] / 1009
POTASSIUM;SODIUM BICARBONATE;SODIUM SULFATE	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / 1009	Y-M: 20[redacted] / 1009
POTASSIUM;SODIUM BICARBONATE;SODIUM SULFATE	PROPER AMOUNT OTHER: PROPER AMOUNT	QD	Y-M: 20[redacted] / 1009	Y-M: 20[redacted] / 1009
INFLUENZA VACCINE	0.5 mL	QD	Y-M: 20[redacted] / 1012	Y-M: 20[redacted] / 1012
TRIAMCINOLONE	PROPER AMOUNT g	PRN	Y-M: 20[redacted] / 1027	Y-M: 20[redacted] / 1047
TIOTROPIUM	2 OTHER: PUFF	QD	Y-M: 20[redacted] / 1103	Not reported

Event #1: Serious Adverse Event

Event Description	LUMBAGO
Preferred term	背部痛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 812 / 483
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
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	MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, PERSISTENT OR SIGNIFICANT DISABILITY/INCAPACITY

Event #2: Serious Adverse Event

Event Description	LUMBAR SPINAL CANAL STENOSIS
Preferred term	腰部脊柱管狭窄症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1000 / 671
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 763): CT MYELOGRAPHY: L4/5 STENOSIS(LUMBAR SPINAL CANAL STENOSIS)

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	MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	EXACERBATION OF LUMBAR DISC HERNIATION
Preferred term	椎間板突出
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1117 / 788
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 763): MRI: L4/5 STENOSIS(LUMBAR SPINAL CANAL STENOSIS) LEFT L4/5 LEVEL HERNIA EXCLUSION IN L5 NERVE ROOT	
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	MORE LIKELY SPORADIC AND COMMON MECHANICAL CAUSATION.
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]:06:46
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。本被験者は日本の 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，腰痛症の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.2 箱を 0.3 年間），骨粗鬆症及び中程度の現飲酒者（1 日 2–4 杯）であった。

Event 1 の臨床経過：

投与812日後＊，被験者は腰痛症を発現した。

本事象発現前の 投与の10ヵ月後＊，被験者は軽度の腰痛症（非重篤）を経験していた。

投与812日後＊　，被験者は整形外科を受診した。身体所見から，仙腸骨炎及び脊椎炎の徴候は認められなかった。歩行障害及び下背部痛があり，同日，重症度が中等度の腰痛症のために入院した。被験者は鎮痛薬を投与され，安静を指示された。被験者は歩行訓練及び運動を行い，日ごとに改善した。投与822日後＊，被験者は退院した。

投与された薬剤は，トラマール OD であった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted])

IMURAN for ULCERATIVE COLITIS (Started 19[redacted], Stopped [redacted] [redacted] 20[redacted])

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted] [redacted] 19[redacted] - 19[redacted])

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

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

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

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

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

ISONIAZID for TB PROPHYLAXIS ([redacted] [redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Lumbago (10024988) (Back pain (10003988)) [v.23.1] [10024988]

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 LUMBAGO

- Investigator: More likely sporadic and common mechanical causation.

- AbbVie: Risk factors include history of lumbar disc herniation and pre-existing osteoporosis.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は日本の 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，腰部脊柱管狭窄症及び腰椎椎間板ヘルニアの悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎，腰椎椎間板ヘルニア，元喫煙者（1 日 0.2 箱を 0.3 年間），高血圧，骨粗鬆症，喘息及び現飲酒者（1 日 2–4 杯）であった。

Event 2 及び 3 の臨床経過：

投与1000日後＊，被験者は腰部脊柱管狭窄症を発現した。投与1117日後＊，被験者は腰椎椎間板ヘルニアの悪化を発現した。

入院前，被験者は投与の約3年前＊に腰椎椎間板ヘルニアと診断されていた（病歴）。被験者は，腰痛症を経験していた。

投与1088日後＊，被験者は腰痛，下肢痛及びしびれ感のために入院した。入院中，合併症として腰椎椎間板ヘルニアが確認された。

投与1114日後＊，被験者は手術のために入院した。被験者は，歩行に支障をきたすほどの下背部痛のため，手術を選択した。整形外科医が腰部脊柱管狭窄症の手術中に，必要に応じて椎間板切除を行う予定であった。投与1117日後＊，腰部脊柱管狭窄症及び腰椎椎間板ヘルニアの悪化の診断により，椎間板切除を伴う手術を行った。整形外科医は，手術中に腰椎椎間板ヘルニアの悪化を確認した。

腰椎椎間板ヘルニアが腰部脊柱管狭窄症に影響していたため，腰椎椎間板ヘルニアに対して椎間板切除術を行った。摘出したヘルニアの量は 0.6 g であった。被験者は，傷口の痛みに対して鎮痛薬を服用した。

投与1124日後＊，整形外科医は傷口が感染していないことを確認した。治験責任医師は，血液検査データがほぼ正常であること，問題がないことを確認した。治験薬投与が再開された。投与1127日後＊，被験者は独力で安定して歩けた。投与1133日後＊　，被験者は改善し，退院した。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS (19[redacted] - [redacted] 20[redacted])

IMURAN for ULCERATIVE COLITIS (19[redacted] - [redacted] [redacted] 20[redacted])

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted] 19[redacted] - 19[redacted])

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

PREDONINE for ULCERATIVE COLITIS (20[redacted] - 20[redacted], 20[redacted] - [redacted] 20[redacted], Started [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

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

ISONIAZID for TB PROPHYLAXIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Lumbar spinal stenosis (10025005) (Lumbar spinal stenosis (10025005)) [v.23.0] [10025005]

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

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

Dechallenge: Not Applicable

2) Lumbar disc herniation (10066256) (Intervertebral disc protrusion (10050296)) [v.23.0] [10066256]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Open Label)

Event of LUMBAR SPINAL CANAL STENOSIS

- Investigator: More likely sporadic and common mechanical causation

- AbbVie: Event is more likely related to pre-existing history of lumbar disc herniation.

Event of EXACERBATION OF LUMBAR DISC HERNIATION

- Investigator: More likely sporadic and common mechanical causation

- AbbVie: Event is more likely related to pre-existing history of lumbar disc herniation.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT MYELOGRAPHY:** L4/5 STENOSIS(LUMBAR SPINAL CANAL STENOSIS.

[redacted] **20[redacted] MRI:** L4/5 stenosis (lumbar spinal canal stenosis) Left L4/5 level hernia Exclusion in L5 nerve root

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
アラニンアミノトランスフェラーゼ増加				X
アスパラギン酸アミノトランスフェラーゼ増加				X
γ-グルタミルトランスフェラーゼ増加				X
胃食道逆流性疾患	X			
好中球数減少				X

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

Medical History	Onset Year
HEARING DISORDER: HIGH FREQUENCY BILATERAL DEAFNESS	20[redacted]
LEFT SIDED UC	20[redacted]
OSTEOARTHRITIS: RIGHT ANKLE ARTHRALGIA	20[redacted]
OTHER: APPENDICITIS	19[redacted]
OTHER: DRUGINESS PANCREATITIS	20[redacted]
OTHER: EPIGASTRIC PAIN	20[redacted]
OTHER: FOLLICULITIS	20[redacted]
OTHER: HEADACHE	NOT REPORTED
OTHER: NUMBNESS OF THE RIGHT HAND	NOT REPORTED
OTHER: PALPITATION	20[redacted]
OTHER: PHARYNGITIS	NOT REPORTED
OTHER: POLLINOSIS	NOT REPORTED
TUBERCULOSIS: PLEURAL TUBERCULOSIS	20[redacted]

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

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	2 PACK	15	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 54	54
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 55	[redacted]20[redacted] / 364	310
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 365		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
OTHER THERAPEUTIC PRODUCTS	1 OTHER: KIT	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: 1 TIME PER WEEK	Y-M: 20[redacted]
PYRIDOXAL	30 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted]
TACROLIMUS	7 mg	BID	Y-M: 20[redacted]
THIAMINE	50 mg	BID	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: 1 TIME PER 2 WEEKS	Y-M: 20[redacted]
INFLIXIMAB	300 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	300 mg	QD	Y-M: 20[redacted]
ASCORBIC ACID;PANTOTHENIC ACID	2 OTHER: TABLET	BID	Y-M: 20[redacted]
FLAVINE ADENINE DINUCLEOTIDE	20 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	300 mg	QD	Y-M: 20[redacted]
TRANEXAMIC ACID	500 mg	BID	Y-M: 20[redacted]

ALUMINIUM HYDROXIDE;BISMUTH;CALCIUM CARBONATE;MAGNESIUM TRISILICATE;SODIUM BICARBONATE	3 OTHER: TABLET	NOT REPORTED	Y-M: 20[redacted]
INFLIXIMAB	300 mg	QD	Y-M: 20[redacted]
MECOBALAMIN	500 ug	TID	Y-M: 20[redacted]
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted]
CAMPHOR;CAPSAICIN;SALICYLIC ACID	20 g	PRN	Y-M: 20[redacted]
BACTERIA NOS;HYDROCORTISONE	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted]
GENTAMICIN	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted]
CEFCAPENE	100 mg	TID	Y-M: 20[redacted] / -364
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / -364
HEPARINOID	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / -14
SULFASALAZINE	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
MESALAZINE	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
DIMEMORFAN	NOT REPORTED	NOT REPORTED	Not reported	Not reported
PARACETAMOL	NOT REPORTED	NOT REPORTED	Not reported	Not reported
PYRIDOXAL	30 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 924
THIAMINE	50 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 924
ASCORBIC ACID;PANTOTHENIC ACID	2 OTHER: TABLET	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 924
FLAVINE ADENINE DINUCLEOTIDE	20 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 924
TRANEXAMIC ACID	500 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 924
MECOBALAMIN	500 ug	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 924
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 414
CAMPHOR;CAPSAICIN;SALICYLIC ACID	20 g	PRN	Y-M: 20[redacted]	ONGOING

BACTERIA NOS;HYDROCORTISONE	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted]	ONGOING
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / -364	Y-M: 20[redacted] / 249
HEPARINOID	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / -14	ONGOING
LORATADINE	10 mg	QD	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 82
MOMETASONE	100 ug	BID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 82
OLOPATADINE	PROPER QUANTITY OTHER: PROPER QUANTITY	BID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 82
MINOCYCLINE	100 mg	BID	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 61
MINOCYCLINE	100 mg	BID	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 71
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 140	Y-M: 20[redacted] / 145
CHLORPHENAMINE	0.01 %	PRN	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 147
CHONDROITIN	0.3 %	PRN	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 147
GUALENIC ACID	0.02 %	PRN	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 147
SULFAMETHOXAZOLE	4.0 %	PRN	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 147
AMOXICILLIN;CLAVULANIC ACID	1 OTHER: TAB	TID	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 147
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 145	Y-M: 20[redacted] / 147
DEXTROMETHORPHAN	15 mg	TID	Y-M: 20[redacted] / 145	Y-M: 20[redacted] / 147
AZULENE	PRN mL	PRN	Y-M: 20[redacted] / 266	Not reported
ELETRIPTAN	20 mg	PRN	Y-M: 20[redacted] / 268	Not reported
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 271	Y-M: 20[redacted] / 417
LOXOPROFEN	100 mg	PRN	Y-M: 20[redacted] / 274	Y-M: 20[redacted] / 417
CARBOCISTEINE	500 mg	PRN	Y-M: 20[redacted] / 286	Y-M: 20[redacted] / 937
DEXTROMETHORPHAN	15 mg	PRN	Y-M: 20[redacted] / 286	Y-M: 20[redacted] / 937
LOXOPROFEN	100 mg	PRN	Y-M: 20[redacted] / 307	Y-M: 20[redacted] / 314
LOPERAMIDE	1 mg	PRN	Y-M: 20[redacted] / 314	Y-M: 20[redacted] / 314
RAMOSETRON	5 ug	PRN	Y-M: 20[redacted] / 314	Y-M: 20[redacted] / 636
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 326	Y-M: 20[redacted] / 326
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2000 mL	PRN	Y-M: 20[redacted] / 327	Y-M: 20[redacted] / 327
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 329	Y-M: 20[redacted] / 331

PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 338	Y-M: 20[redacted] / 344
OSELTAMIVIR	75 mg	BID	Y-M: 20[redacted] / 342	Y-M: 20[redacted] / 346
FLUOROMETHOLONE	1 OTHER: DROP	QID	Y-M: 20[redacted] / 408	Y-M: 20[redacted] / 421
LEVOFLOXACIN	1 OTHER: DROP	QID	Y-M: 20[redacted] / 408	Y-M: 20[redacted] / 421
METHYLPREDNISOLONE;NEOMYCIN	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / 408	Y-M: 20[redacted] / 412
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted] / 415	Not reported
LORATADINE	10 mg	PRN	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 447
OLOPATADINE	1 OTHER: DROP	PRN	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 447
TEPRENONE	150 mg	TID	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 636
SULPIRIDE	50 mg	TID	Y-M: 20[redacted] / 432	Y-M: 20[redacted] / 636
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	2000 mL	QD	Y-M: 20[redacted] / 449	Y-M: 20[redacted] / 453
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	QD	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 454
LOXOPROFEN	100 mg	PRN	Y-M: 20[redacted] / 468	Y-M: 20[redacted] / 501
FLUOROMETHOLONE	1 OTHER: DROP	PRN	Y-M: 20[redacted] / 486	Y-M: 20[redacted] / 501
LEVOFLOXACIN	1 OTHER: DROP	PRN	Y-M: 20[redacted] / 486	Y-M: 20[redacted] / 501
FLUOROMETHOLONE	1 OTHER: DROP	PRN	Y-M: 20[redacted] / 533	Y-M: 20[redacted] / 571
OFLOXACIN	1 OTHER: DROP	PRN	Y-M: 20[redacted] / 533	Y-M: 20[redacted] / 537
AZITHROMYCIN	250 mg	BID	Y-M: 20[redacted] / 557	Y-M: 20[redacted] / 559
LOXOPROFEN	PROPER QUANTITY mg	PRN	Y-M: 20[redacted] / 634	Y-M: 20[redacted] / 695
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 665	Y-M: 20[redacted] / 665
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2000 mL	PRN	Y-M: 20[redacted] / 666	Y-M: 20[redacted] / 666
DIMETICONE	10 mL	QD	Y-M: 20[redacted] / 666	Y-M: 20[redacted] / 666
POVIDONE-IODINE	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / 673	Not reported
LORATADINE	10 mg	QD	Y-M: 20[redacted] / 755	Y-M: 20[redacted] / 837
MOMETASONE	100 ug	BID	Y-M: 20[redacted] / 755	Y-M: 20[redacted] / 837

OLOPATADINE	PROPER QUANTITY OTHER: PROPER QUANTITY	BID	Y-M: 20[redacted] / 755	Y-M: 20[redacted] / 837
TERBINAFINE	PROPER QUANTITY OTHER: PROPER QUANTITY	QD	Y-M: 20[redacted] / 755	Y-M: 20[redacted] / 847
TERBINAFINE	PROPER QUANTITY OTHER: PROPER QUANTITY	QD	Y-M: 20[redacted] / 755	Y-M: 20[redacted] / 1112
AZITHROMYCIN	1000 mg	BID	Y-M: 20[redacted] / 838	Y-M: 20[redacted] / 840
ASCORBIC ACID;PANTOTHENIC ACID	2 OTHER: TABLET	PRN	Y-M: 20[redacted] / 938	Not reported
FLAVINE ADENINE DINUCLEOTIDE	20 mg	PRN	Y-M: 20[redacted] / 938	Not reported
MECOBALAMIN	500 ug	PRN	Y-M: 20[redacted] / 938	Not reported
PYRIDOXAL	30 mg	PRN	Y-M: 20[redacted] / 938	Not reported
THIAMINE	50 mg	PRN	Y-M: 20[redacted] / 938	Not reported
TRANEXAMIC ACID	500 mg	PRN	Y-M: 20[redacted] / 938	Not reported
VONOPRAZAN	20 mg	PRN	Y-M: 20[redacted] / 938	Not reported
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 1000	Y-M: 20[redacted] / 1000
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	QD	Y-M: 20[redacted] / 1001	Y-M: 20[redacted] / 1001
DIMETICONE	10 mL	QD	Y-M: 20[redacted] / 1001	Y-M: 20[redacted] / 1001
FLUMAZENIL	0.5 mg	QD	Y-M: 20[redacted] / 1001	Y-M: 20[redacted] / 1001
MIDAZOLAM	10 mg	QD	Y-M: 20[redacted] / 1001	Y-M: 20[redacted] / 1001
HYALURONIC ACID	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / 1015	Not reported
LOXOPROFEN	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / 1015	Not reported

LOXOPROFEN	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / 1017	Y-M: 20[redacted] / 1064
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 1055	Y-M: 20[redacted] / 1057
LOXOPROFEN	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / 1101	Y-M: 20[redacted] / 1127
LOXOPROFEN	PROPER QUANTITY OTHER: PROPER QUANTITY	PRN	Y-M: 20[redacted] / 1104	Y-M: 20[redacted] / 1127
CEFCAPENE	100 mg	TID	Y-M: 20[redacted] / 1125	Y-M: 20[redacted] / 1133

Event #1: Event of Interest - Hepatic Disorder

Event Description	ALT INCREASED
Preferred term	アラニンアミノトランスフェラーゼ増加
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 440 / 76
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	461 / 97
Duration of AE	22 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 #2: Event of Interest - Hepatic Disorder

Event Description	AST INCREASED
Preferred term	アスパラギン酸アミノトランスフェラーゼ増加
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 440 / 76

Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	461 / 97
Duration of AE	22 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 #3: Event of Interest - Hepatic Disorder

Event Description	GGT INCREASED
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] / 440 / 76
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	509 / 145
Duration of AE	70 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 #4: Event of Interest - Neutropenia

Event Description	NEUTROPHIL COUNT DECREASED
Preferred term	好中球数減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 706 / 342
Age at AE Onset	4[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	713 / 349
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 #5: Serious Adverse Event

Event Description	REFLUX ESOPHAGITIS
Preferred term	胃食道逆流性疾患
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 779 / 415
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 432): Hemoglobin: 147 [137 - 168] G/L; NPTST024-AMYLASE: 76 [44 - 132] U/L; NPTST153-LIPASE: 47 [13 - 49] IU/L; [redacted]20[redacted] (RX DAY 448): Blood Urea Nitrogen: 3.676791 [2.85576 - 7.1394] MMOL/L; Hemoglobin: 149 [137 - 168] G/L; NPTST024-AMYLASE: 86 [44 - 132] U/L; NPTST153-LIPASE: 37 [13 - 49] IU/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 432): CT SCAN: NOT PARTICULAR; [redacted]20[redacted] (RX DAY 449): CT SCAN: NOT PARTICULAR; UPPER ENDOSCOPY: REFLUX ESOPHAGITIS (GRADED), HIATAL HERNIA; [redacted]20[redacted] (RX DAY 450): ABDOMINAL ULTRASOUND: LIVER: NOT PARTICULAR　PANCREAS: NOT PARTICULR　SPLEEN: NOT PARTICULR　GALBLADDER: NOT PARTICULR　RRIGHT KIDNEY: STONE 5MM　LEFT KIDNEY: NOT PARTICULAR　GI TRACT: NOT PARTICULR　PARAAORTIC LYMPH NODE: SWELLING(-), AAA(-), ASCITES(-)

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	REFLUX ESOPHAGITIS　WAS OCCUERED BY DIETARY DISORDER AND ESOPHAGEAL HERNIA.THUS,IT WAS CONSIDERED TO HAVE NO RELATIONSHIP WITH THE INVESTIGATIONAL AGENT.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #6: Event of Interest - Neutropenia

Event Description	NEUTROPHIL COUNT DECREASED
Preferred term	好中球数減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1119 / 755
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1211 / 847
Duration of AE	93 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

Generated: [redacted]20[redacted]:06:46
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。本被験者は日本の 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，逆流性食道炎の事象を発現した。関連する病歴は，潰瘍

性大腸炎（左側），心窩部痛，元喫煙者（1 日 2 箱を 15 年間），咽頭炎及び現飲酒者（1 日 2 杯未満）であった。

Event 5 の臨床経過：

投与779日後＊，被験者は逆流性食道炎を発現した
。

投与790日後＊　，被験者は投与 60 週時の定期的な来院を行い，本事象は継続していた。被験者はテプレノンの服用を開始した。投与796日後＊　，被験者は本事象に変化がないことを報告した。被験者は痛みを感じ，その痛みを過去に経験した急性膵炎に似ていると説明した。CT 検査及び検体検査が行われた。異常な所見は報告されなかった。被験者は急性胃炎と診断され，スルピリドを服用し，3 週間後に追跡調査を行うと告げられた。投与812日後＊ ，黒い嘔吐物及び黒い便があり，本事象は悪化していた。被験者は上腹部の圧痛があった。外来での検査及び診断は可能と考えられたが，被験者の不安が非常に強かったため，投与813日後＊ に入院することとなった。被験者は追加の検査及び静脈内投与での治療を受けた。投与817日後＊　，被験者は経口摂取を再開し，軽度の心窩部痛のみが認められた。投与818日後＊　，被験者は静脈内投与での治療を終了した。投与821日後＊，食事の際に軽度の心窩部痛のみはあるものの，食事を摂ることができるようになり，被験者は退院した。本事象は改善したと判断された。

投与された薬剤は，スルピリド，テプレノン及びソルデム 3A であった。

The patient's past medications include:

CEFDINIR for PHARYNGITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ZITHROMAC SR for PHARYNGITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Reflux esophagitis (10038262) (Gastrooesophageal reflux disease (10017885)) [v.22.1] [10038262]

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 REFLUX ESOPHAGITIS

- Investigator: Reflux espohagitis was occurred by dietary disorder and esophageal hernia. Thus, it was considered to have no relationship with the investigational agent.

- AbbVie: Event is more likely related to pre-existing epigastric pain since [redacted] 20[redacted].

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** No abnormal findings

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Liver: No particular findings; Pancreas: No particular findings; Spleen: No particular findings; Gallbladder: No particular findings; Right kidney: Stone 5mm; Left kidney: No particular findings; GI tract: No particular findings; Paraortic lymph node: Swelling (-), AAA (-), Ascites (-)

[redacted] **20[redacted] AMYLASE:** 76 U/L (normal 44 to 132)

[redacted] **20[redacted] AMYLASE:** 86 U/L (normal 44 to 132)

[redacted] **20[redacted] BUN:** 10.3 mg/dL (normal 8 to 20)

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

[redacted] **20[redacted] CT ABDOMINAL:** No abnormal findings; acute gastritis

[redacted] **20[redacted] CT ABDOMINAL:** No abnormal findings

[redacted] **20[redacted] CT SCAN:** No particular findings

[redacted] **20[redacted] CT SCAN:** No particular findings

[redacted] **20[redacted] ENDOSCOPY:** Reflux esophagitis (Grade D), hiatal hernia

[redacted] **20[redacted] HB:** 14.7 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] HB:** 14.9 G/DL (normal 13.7 to 16.8)

[redacted] **20[redacted] LIPASE:** 47 IU/L (normal 13 to 49)

[redacted] **20[redacted] LIPASE:** 37 U/L (normal 13 to 49)

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Alanine aminotransferase increased: Asymptomatic.
Aspartate aminotransferase increased: Asymptomatic.
Gamma-glutamyltransferase increased: Asymptomatic.

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	5[redacted]	MALE	ASIAN

Medical History	Onset Year
COLON POLYP	20[redacted]
GASTRIC ULCER	20[redacted]
HEADACHE	19[redacted]
HEMORRHAGIC DUODENAL ULCER	20[redacted]
LEFT SIDED UC	20[redacted]
LUMBAGO	19[redacted]
REFLUX ESOPHAGITIS	20[redacted]
STIFF SHOULDER	19[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: POLYPECTOMY	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	26	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 54	54
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 55	[redacted]20[redacted] / 413	359
M14-533 Placebo (LTE)		QD	[redacted]20[redacted] / 414		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2250 mg	TID	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
MESALAZINE	2250 mg	TID	Y-M: 20[redacted]
MESALAZINE	2400 mg	TID	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / -190

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
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]	Not reported
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / -190	Not reported
GUAIAZULENE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 108
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 97
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 97	Not reported
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 144
CAMPHOR;CAPSICUM SPP.;SALICYLIC ACID	20 g	QD	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 101

Event #1: 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] / 504 / 91
Age at AE Onset	5[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	509 / 96
Duration of AE	6 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, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster

Event Description	WORSENING OF HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 510 / 97
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	582 / 169
Duration of AE	73 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

Generated: [redacted]20[redacted]:06:46

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。本被験者は日本の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，帯状疱疹の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 26 年間），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510日後＊　，被験者は，帯状疱疹の悪化を発現した。投与582日後＊，帯状疱疹の悪化は消失した。

入院前，被験者は帯状疱疹（非重篤）を経験していた。被験者は右上背部の発疹を発見し，バラシクロビルを服用し，アズノール軟膏を塗布していた。

投与510日後＊　，被験者は帯状疱疹の悪化のため入院した。徴候及び症状には，右上背部の発疹，並びに胸部痛及び背部痛が含まれた。投与513日後＊　，被験者は快方に向かっていたため，退院した。転帰は回復と考えられた。帯状疱疹が痂皮化した後，治験薬の投与を再開する予定である。

被験者の帯状疱疹は，1 つの皮膚分節に発現した。詳細不明な診察が行われ，被験者は保存的局所療法，抗ウイルス薬，非麻薬性及び/又は麻薬性鎮痛薬で治療された。

投与された薬剤は，リリカ及びアシクロビルであった。

The patient's past medications include:

PENTASA for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

LIALDA for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Herpes zoster (10019974)　(Herpes zoster (10019974))　[v.23.1]　[10019974]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF HERPES ZOSTER

- Investigator: Not applicable.

- AbbVie: Not applicable.

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Herpes zoster ([redacted]20[redacted]): History of chicken pox. One dermatone. 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
アラニンアミノトランスフェラーゼ増加				X
アスパラギン酸アミノトランスフェラーゼ増加				X
腓骨骨折	X			
肝障害				X
脛骨骨折	X			

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

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OTHER: GASTRITIS	20[redacted]
OTHER: NONORGANIC INSOMNIA	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 54	54
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 55	[redacted] / 218	164
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 219		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	50 mg	QD	Y-M: [redacted]
FOLIC ACID	1 mg	QD	Y-M: [redacted]
LACTOBACILLUS ACIDOPHILUS	300 mg	TID	Y-M: [redacted]
MESALAZINE	1200 mg	TID	Y-M: [redacted]
PREDNISOLONE	10 mg	QD	Y-M: [redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: [redacted]
MESALAZINE	4800 mg	QD	Y-M: [redacted] / -268
ZOLPIDEM	6.25 mg	PRN	Y-M: [redacted] / -79

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	1 mg	QD	Y-M: [redacted]	ONGOING
LACTOBACILLUS ACIDOPHILUS	300 mg	TID	Y-M: [redacted]	Y-M: [redacted] / 761
MESALAZINE	4800 mg	QD	Y-M: [redacted] / -268	ONGOING
ZOLPIDEM	6.25 mg	PRN	Y-M: [redacted] / -79	ONGOING
ACHILLEA MILLEFOLIUM;ACONITUM SPP.;ARNICA SPP.;ATROPA BELLADONNA;BELLIS PERENNIS;CALENDULA SPP.;ECHINACEA ANGUSTIFOLIA;ECHINACEA PURPUREA;HAMAMELIS SPP.;HERBAL NOS;HYPERICUM SPP.;SULFURATED POTASH;SY	1 OTHER: AMPOULE	BID	Y-M: [redacted] / 133	Y-M: [redacted] / 136

ASCORBIC ACID;BIOTIN;CYANOCOBALAMIN;DEXPANTHENOL;ERGOCALCIFEROL;FOLIC ACID;NICOTINAMIDE;PYRIDOXINE;RETINOL;RIBOFLAVIN;THIAMINE;TOCOPHEROL	1 OTHER: VIAL	QD	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 136
GALLAMINE	10 mg	BID	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 136
KETOROLAC	30 mg	QD	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 135
SODIUM CHLORIDE	1 L	QD	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 136
ATROPINE	1 mL	OTHER: ONCE	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 134
BUPIVACAINE	4 mL	OTHER: ONCE	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 134
BUPRENORPHINE	5 ug	OTHER: ONCE A WEEK	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 136
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	1 L	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 134
CEFAZEDONE	2 g	BID	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 140
DEXMEDETOMIDINE	2 mL	OTHER: ONCE	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 134
FENTANYL	2 mL	PRN	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 136
GLYCOPYRRONIUM	0.2 mg	OTHER: ONCE	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 134
NEFOPAM	10 mg	BID	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 136
NEFOPAM	2 mL	PRN	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 136
RAMOSETRON	0.3 mg	QD	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 135
BENZOCAINE;POTASSIUM CHLORATE;SODIUM BICARBONATE	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 154
CITRULLINE	1 mL	TID	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 138
EPERISONE	75 mg	BID	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 154
MELOXICAM	7.5 mg	BID	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 154
METOCLOPRAMIDE	4.231 mg	QD	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 136
PARACETAMOL;TRAMADOL	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 135	Y-M: 20[redacted] / 154
PREDNICARBATE	0.1 g	OTHER: ONCE	Y-M: 20[redacted] / 139	Y-M: 20[redacted] / 139
CEFALEXIN	500 mg	TID	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 146
ISONIAZID	300 mg	QD	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 618
PYRIDOXINE	50 mg	QD	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 618
URSODEOXYCHOLIC ACID	100 mg	TID	Y-M: 20[redacted] / 379	Y-M: 20[redacted] / 407
URSODEOXYCHOLIC ACID	100 mg	BID	Y-M: 20[redacted] / 408	Y-M: 20[redacted] / 618

ACHILLEA MILLEFOLIUM;ACONITUM SPP.;ARNICA SPP.;ATROPA BELLADONNA;BELLIS PERENNIS;CALENDULA SPP.;ECHINACEA ANGUSTIFOLIA;ECHINACEA PURPUREA;HAMAMELIS SPP.;HERBAL NOS;HYPERICUM SPP.;SULFURATED POTASH;SY	1 OTHER: AMPOULE	BID	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 514
ASCORBIC ACID;BIOTIN;CYANOCOBALAMIN;DEXPANTHENOL;ERGOCALCIFEROL;FOLIC ACID;NICOTINAMIDE;PYRIDOXINE;RETINOL;RIBOFLAVIN;THIAMINE;TOCOPHEROL	1 OTHER: VIAL	QD	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 514
ATROPINE	0.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
BUPIVACAINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
CALCIUM CHLORIDE;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1 L	OTHER: ONCE	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
CEFAZEDONE	2 g	BID	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 518
DEXMEDETOMIDINE	236 ug	OTHER: ONCE	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
GLYCOPYRRONIUM	0.1 mg	OTHER: ONCE	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
METHOCARBAMOL	500 mg	BID	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 514
METOCLOPRAMIDE	4.231 mg	QD	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
MIDAZOLAM	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
NEFOPAM	10 mg	BID	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 514
SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 514
SODIUM CHLORIDE	2 L	QD	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
SODIUM CHLORIDE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 512
TRAMADOL	50 mg	QD	Y-M: 20[redacted] / 512	Y-M: 20[redacted] / 514
CITRULLINE	1 mL	TID	Y-M: 20[redacted] / 513	Y-M: 20[redacted] / 519
EPERISONE	75 mg	BID	Y-M: 20[redacted] / 513	Y-M: 20[redacted] / 519
NIZATIDINE	150 mg	BID	Y-M: 20[redacted] / 513	Y-M: 20[redacted] / 519
PARACETAMOL	650 mg	BID	Y-M: 20[redacted] / 513	Y-M: 20[redacted] / 519
HYALURONIC ACID	2 OTHER: DROP	TID	Y-M: 20[redacted] / 736	ONGOING
PIRENOXINE	2 OTHER: DROP	TID	Y-M: 20[redacted] / 736	ONGOING
FISH OIL	1200 mg	QD	Y-M: 20[redacted] / 762	ONGOING
PROBIOTICS NOS	2000 mg	QD	Y-M: 20[redacted] / 762	ONGOING

BORON;CALCIUM;CALCIUM CARBONATE;CALCIUM GLUCONATE;MAGNESIUM;MAGNESIUM CITRATE;MAGNESIUM OXIDE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 789	ONGOING
VITAMIN B12 NOS	1000 OTHER: MCG	QD	Y-M: 20[redacted] / 789	ONGOING
IBANDRONIC ACID	3.375 mg	OTHER: EVERY 3 MONTH	Y-M: 20[redacted] / 834	ONGOING

Event #1: Serious Adverse Event

Event Description	LEFT DISTAL TIBIOFIBULA FRACTURE
Preferred term	腓骨骨折，脛骨骨折
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 350 / 132
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 134): OPEN REDUCTION AND INTERNAL FIXATION: REMOVED SUTURE ON [redacted]20[redacted]; [redacted]20[redacted] (RX DAY 512): LEFT DISTAL TIBIOFIBULA IMPLANT REMOVE: REMOVED SUTURE ON [redacted]20[redacted]	
AE Stopped Initial Rx Day / Rx Day	365 / 147
Duration of AE	16 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FELL DOWN THE STAIRS.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Hepatic Disorder

Event Description	アラニンアミノトランスフェラーゼ増加
Preferred term	Alanine aminotransferase increased
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 597 / 379
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	779 / 561
Duration of AE	183 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 #3: Event of Interest - Hepatic Disorder

Event Description	ASPARTATE AMINOTRANSFERASE INCREASED
Preferred term	アスパラギン酸アミノトランスフェラーゼ増加
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 597 / 379
Age at AE Onset	5[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	779 / 561
Duration of AE	183 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 #4: Event of Interest - Hepatic Disorder

Event Description	CHRONIC LIVER DISEASE
Preferred term	肝障害
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1185 / 967
Age at AE Onset	6[redacted]

Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
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]:06:46
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。本被験者は韓国の 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，左遠位脛腓骨骨折の事象を発現した。関連する病歴は，広範囲な潰瘍性大腸炎（全大腸炎型），非器質性不眠症，非喫煙者及び禁酒であった。

Event 1 の臨床経過：

投与350日後＊ ，被験者は左遠位脛腓骨骨折を発現した。投与365日後＊ ，左遠位脛腓骨骨折は消失した。

投与350日後＊ ，被験者は階段から転落し，足首の痛み及び浮腫があり，入院した。左遠位脛腓骨骨折と診断された。投与352日後＊ ，観血的整復及び内固定の手術を受けた。被験者は軽度の足首の痛みがあったが，日常生活に影響はなかった。投与730日後＊ ，被験者は退院した。

投与729日後＊，被験者は予定された左遠位脛腓骨のインプラント除去のために入院した。投与730日後＊，手術が行われた。投与737日後＊ ，被験者は退院した。投与745日後＊，抜糸が行われ，合併症は認められなかった。

投与された薬剤は，nefopam hydrochloride，citrulline malate，ブプレノルフィン，taracet semi，メロキシカム，methylol cefalexin lysinate，gallamine triethiodide，s-multi vita，グリコピロニウム臭化物，ketorolac tromethamine，エペリゾン及び prednicarbate cream 0.25%であった。

The patient's past medications include:

ASACOL DR for ULCERATIVE COLITIS ([redacted])

IMMUTHERA for ULCERATIVE COLITIS ([redacted])

SOLONDO for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Fibula fracture (10016667)　(Fibula fracture (10016667))　[v.22.1]　[10016667]

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)　Tibia fracture (10043827)　(Tibia fracture (10043827))　[v.22.1]　[10043827]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

Event of LEFT DISTAL TIBIOFIBULA FRACTURE

- Investigator: Fell down on the stairs.

- AbbVie: Event is more likely related to trauma when the subject fell down the stairs.

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Liver disorder: Asymptomatic.

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
挫傷	X			
椎間板障害	X			
脊柱変形	X			

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

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
OTHER: DERMATITIS	20[redacted]
OTHER: NUMMULAR DERMATITIS	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 161	106

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 162

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1200 mg	BID	Y-M: 20[redacted]
MESALAZINE	1200 mg	BID	Y-M: 20[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
BLINDED THERAPY	225 mg	OTHER: Q4WEEKS	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -237
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -238
DESOGESTREL;ETHINYLESTRADIOL	0.17 mg	OTHER: QD IN 21 DAYS OF EVERY 28 DAYS MENSTRUATION CYCLE	Y-M: 20[redacted] / -137

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
DESOGESTREL;ETHINYLESTRADIOL	0.17 mg	OTHER: QD IN 21 DAYS OF EVERY 28 DAYS MENSTRUATION CYCLE	Y-M: 20[redacted] / -137	ONGOING
MESALAZINE	2400 mg	QD	Y-M: 20[redacted] / 85	ONGOING
CLEBOPRIDE;SIMETICONE	1 OTHER: CAP.	TID	Y-M: 20[redacted] / 647	Y-M: 20[redacted] / 649
CODEINE;PARACETAMOL	25 mg	TID	Y-M: 20[redacted] / 647	Y-M: 20[redacted] / 649
GALLAMINE	2 mL	QD	Y-M: 20[redacted] / 647	Y-M: 20[redacted] / 649
GLUCOSE	500 mL	QD	Y-M: 20[redacted] / 647	Y-M: 20[redacted] / 649
PIROXICAM	50 mg	TID	Y-M: 20[redacted] / 647	Y-M: 20[redacted] / 649
TRAMADOL	50 mg	QD	Y-M: 20[redacted] / 647	Y-M: 20[redacted] / 649

Event #1: Serious Adverse Event

Event Description	DISTORTION OF THE LUMBAR VERTEBRA., CONTUSION OF THE LEFT KNEE, CONTUSION OF THE BOTH SHOULDER AND UPPER ARM, TENSION OF THE LUMBAR VERTEBRA
Preferred term	挫傷，挫傷，椎間板障害，脊柱変形
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 808 / 647
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	810 / 649
Duration of AE	3 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	TRAFFIC ACCIDENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者は韓国の 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，腰椎の歪み，左膝の挫傷，両肩部及び両上腕部の挫傷，並びに腰椎の緊張の事象を発現した。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808日後＊　，被験者は腰椎の歪み，左膝の挫傷，両肩部及び両上腕部の挫傷，並びに腰椎の緊張を発現した。投与810日後＊　，腰椎の歪み，左膝の挫傷，両肩部及び両上腕部の挫傷，並びに腰椎の緊張は消失した。

投与808日後＊　，被験者は交通事故に遭い，入院した。被験者は頭痛，左膝及び背部の痛み，並びに全身の脱力感があった。X 線検査及び血液検査を行ったが，結果は提供されなかった。投与810日後＊，被験者は退院した。

投与された薬剤は，erexin，gastin，gallonin，depain，トラマドール及び dextrose 5%であった。

The patient's past medications include:

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Spinal deformity (10058907) (Spinal deformity (10058907)) [v.24.0] [10058907]

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

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

Dechallenge: Not Applicable

2) Contusion of knee (10010860) (Contusion (10050584)) [v.24.0] [10010860]

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

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

Dechallenge: Not Applicable

3) Contusion (10050584) (Contusion (10050584)) [v.24.0] [10050584]

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

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

Dechallenge: Not Applicable

4) Intervertebral disc disorder (10061521) (Intervertebral disc disorder (10061521)) [v.24.0] [10061521]

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 DISTORTION OF THE LUMBAR VERTEBRA

- Investigator: Traffic accident.

- AbbVie: Event is more likely related to trauma sustained from a traffic accident.

Event of CONTUSION OF THE LEFT KNEE

- Investigator: Traffic accident.

- AbbVie: Event is more likely related to trauma sustained from a traffic accident.

Event of CONTUSION OF THE BOTH SHOULDER AND UPPER ARM

- Investigator: Traffic accident.

- AbbVie: Event is more likely related to trauma sustained from a traffic accident.

Event of TENSION OF THE LUMBAR VERTEBRA

- Investigator: Traffic accident.

- AbbVie: Event is more likely related to trauma sustained from a traffic accident.

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
異形成	X	X		

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

Medical History	Onset Year
BENIGN PROSTATIC HYPERPLASIA: NA	20[redacted]
EYE DISEASE/DISORDER: UVEITIS	20[redacted]
EYE DISEASE/DISORDER: VITREOUS OPACITY	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ADENOMA OF STOMACH WITH HG-DYSPLASIA	20[redacted]
OTHER: CHORONIC ATROPHIC GASTRITIS	20[redacted]
OTHER: EROSIVE GASTRITIS	20[redacted]
OTHER: HERNIATED NUCLEUS PULPOSUS	20[redacted]
OTHER: L-STENOSIS(L4-5)	20[redacted]
OTHER: TUBULAR ADENOMA	20[redacted]
OTHER: TUBULAR ADENOMA	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	FORMER			
CIGARETTES	FORMER	1 PACK	20	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted] / 1	[redacted] / 57	57
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 58	[redacted] / 253	196
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 253	[redacted] / 1291	1039

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FOLIC ACID	1 mg	QD	Y-M: [redacted]
MESALAZINE	500 mg	QD	Y-M: [redacted]
PREDNISOLONE	5 mg	QD	Y-M: [redacted]
SULFASALAZINE	3 OTHER: TABLET	TID	Y-M: [redacted]
SULFASALAZINE	3 OTHER: TABLET	TID	Y-M: [redacted]
SULFASALAZINE	2 OTHER: TABLET	TID	Y-M: [redacted]
MESALAZINE	1 g	QD	Y-M: [redacted]
PREDNISOLONE	30 mg	QD	Y-M: [redacted]
SULFASALAZINE	3 OTHER: TABLET	TID	Y-M: [redacted]
PREDNISOLONE	10 mg	QD	Y-M: [redacted]
BUDESONIDE;SODIUM CHLORIDE	1 OTHER: EA	QD	Y-M: [redacted]
PREDNISOLONE	15 mg	QD	Y-M: [redacted]
AZATHIOPRINE	25 mg	QD	Y-M: [redacted]
PREDNISOLONE	10 mg	QD	Y-M: [redacted]
MESALAZINE	4 g	QD	Y-M: [redacted]
INFLIXIMAB	400 mg	OTHER: EVERY 8 WEEKS	Y-M: [redacted]
PREDNISOLONE	5 mg	QD	Y-M: [redacted]
BECLOMETASONE	5 mg	QD	Y-M: [redacted]
BUDESONIDE;SODIUM CHLORIDE	1 OTHER: EA	QD	Y-M: [redacted]
GOLIMUMAB	100 mg	OTHER: EVERY 4WEEKS	Y-M: [redacted]
SULFASALAZINE	2000 mg	TID	Y-M: [redacted]
MESALAZINE	1 g	QD	Y-M: [redacted]
IRON;PROTEASE NOS	256.26 mg	BID	Y-M: [redacted] / -20

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	
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]	ONGOING
SULFASALAZINE	2000 mg	TID	Y-M: 20[redacted]	ONGOING
TAMSULOSIN	0.2 mg	QD	Y-M: 20[redacted] / 240	Y-M: 20[redacted] / 1030
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	170 mL	QD	Y-M: 20[redacted] / 1002	Y-M: 20[redacted] / 1003
LACTULOSE	60 mL	QD	Y-M: 20[redacted] / 1002	Y-M: 20[redacted] / 1002
MIDAZOLAM	4 mg	QD	Y-M: 20[redacted] / 1003	Y-M: 20[redacted] / 1003
PETHIDINE	25 mg	QD	Y-M: 20[redacted] / 1003	Y-M: 20[redacted] / 1003
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 L	QD	Y-M: 20[redacted] / 1031	Y-M: 20[redacted] / 1032
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / 1031	ONGOING
MIDAZOLAM	3 mg	QD	Y-M: 20[redacted] / 1032	Y-M: 20[redacted] / 1032
PETHIDINE	25 mg	QD	Y-M: 20[redacted] / 1032	Y-M: 20[redacted] / 1032

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

Event Description	HIGH GRADE DYSPLASIA
Preferred term	異形成
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1256 / 1004
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 1032): ENDOSCOPIC SUBMUCOSAL DISSECTION: TUBULAR ADENOMA WAS REMOVED COMPLETELY.

AE Stopped Initial Rx Day / Rx Day	1285 / 1033
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

Generated: [redacted]20[redacted]:06:46
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。本被験者は韓国の 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，高度異形成の事象を発現した。関連する病歴は，高度異形成を伴う胃腺腫，元喫煙者（1 日 1 箱を 20 年間），慢性萎縮性胃炎，びらん性胃炎，潰瘍性大腸炎，管状腺腫，噛みタバコの元喫煙者及び元飲酒者（1 日 2–4 杯）であった。

Event 1 の臨床経過：

投与1256日後＊ ，被験者は高度異形成を発現した。投与1285日後＊ ，高度異形成は消失した。

入院前の投与1255日後＊ ，被験者は結腸内視鏡検査を受けた。ポリープが確認され，S 状結腸で生検が行われた。生検の結果は管状腺腫であったが，完全には除去されなかった。

投与1283日後＊ ，被験者は内視鏡下での粘膜下層剥離術のため入院し，直腸 S 状結腸移行部の残存病変の除去を受けた。投与1285日後＊，被験者は退院した。

本事象により，治験薬の投与は完全に中止された。

The patient's past medications include:

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

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

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

PENTASA for ULCERATIVE COLITIS ([redacted])

ENTOCORT for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

CLIPPER SR for ULCERATIVE COLITIS ([redacted])

GOLIMUMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Dysplasia (10058314) (Dysplasia (10058314)) [v.24.0] [10058314]

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 HIGH GRADE DYSPLASIA

- Investigator: Ulcerative colitis.

- AbbVie: Risk factors for gastrointestinal dysplasia include pre-existing tubular adenomas in 20[redacted] and 20[redacted], advanced age and pre-existing ulcerative colitis.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
手根管症候群	X			
胃腸炎	X			X
変形性脊椎症	X			

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

Medical History	Onset Year
ASTHMA	20[redacted]
DIABETES MELLITUS	20[redacted]
HEARING DISORDER: SENSORINEURAL HEARING LOSS	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ENTEROPATHIC ARTHRITIS SECONDARY TO UC	20[redacted]
OTHER: HYPERCHOLESTEROLEMIA	20[redacted]
OTHER: THALASSAEMIA TRAIT	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	CURRENT	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 59		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted] / -351
INFLIXIMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted] / -344
AMLODIPINE	10 mg	QD	Y: 20[redacted]
GLICLAZIDE	30 mg	QD	Y: 20[redacted]
METFORMIN	250 mg	BID	Y: 20[redacted]
SIMVASTATIN	20 mg	QD	Y: 20[redacted]
SULFASALAZINE	1500 mg	TID	Y: 20[redacted]
PREDNISOLONE	5 mg	QD	Y: 20[redacted]
LATANOPROST	1 OTHER: DROP	QD	Y: 20[redacted] / -318

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted] / -351	ONGOING
CALCIUM	600 mg	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 840
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 143	ONGOING
DICLOFENAC	75 mg	OTHER: STAT	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143
DICLOFENAC	75 mg	OTHER: STAT	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 147
NAPROXEN	550 mg	OTHER: 1 DOSE	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 147
CELECOXIB	200 mg	BID	Y-M: 20[redacted] / 148	ONGOING
SALICYLIC ACID	1 OTHER: APPLICATION	TID	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 149
DICLOFENAC	50 mg	OTHER: STAT	Y-M: 20[redacted] / 150	Y-M: 20[redacted] / 150
GABAPENTIN	300 mg	QD	Y-M: 20[redacted] / 150	Y-M: 20[redacted] / 152

PARACETAMOL	1000 mg	QID	Y-M: 20[redacted] / 150	Y-M: 20[redacted] / 163
TRAMADOL	25 mg	OTHER: TDS WHEN REQUIRED	Y-M: 20[redacted] / 150	Y-M: 20[redacted] / 156
PARACETAMOL	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 172
PARACETAMOL;TRAMADOL	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 172
PERINDOPRIL	4 mg	QD	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 201
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 191	Y-M: 20[redacted] / 197
TELMISARTAN	40 mg	QD	Y-M: 20[redacted] / 202	Y-M: 20[redacted] / 246
ALPRAZOLAM	500 ug	QD	Y-M: 20[redacted] / 210	Y-M: 20[redacted] / 292
FLUNARIZINE	5 OTHER: MG	QD	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 221
MECOBALAMIN	500 OTHER: MCG	OTHER: UNKNOWN	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 259
PARACETAMOL;TRAMADOL	PARACETAMOL 325MG + TRAMADOL HCL 37.5MG mg	OTHER: UNKNOWN	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 221
PREGABALIN	50 mg	OTHER: UNKNOWN	Y-M: 20[redacted] / 217	Y-M: 20[redacted] / 221
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 410
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 410
CEFOPERAZONE	2 g	OTHER: STAT	Y-M: 20[redacted] / 411	Y-M: 20[redacted] / 411
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	1 OTHER: TAB	QD	Y-M: 20[redacted] / 412	Y-M: 20[redacted] / 418
MAGNESIUM TRISILICATE	15 mL	TID	Y-M: 20[redacted] / 412	Y-M: 20[redacted] / 418
CEFUROXIME	250 mg	BID	Y-M: 20[redacted] / 413	Y-M: 20[redacted] / 418
AMLODIPINE	10 mg	QD	Y: 20[redacted]	ONGOING
GLICLAZIDE	30 mg	QD	Y: 20[redacted]	ONGOING
METFORMIN	250 mg	BID	Y: 20[redacted]	Y-M: 20[redacted] / 1197
SIMVASTATIN	20 mg	QD	Y: 20[redacted]	ONGOING
LATANOPROST	1 OTHER: DROP	QD	Y: 20[redacted] / -318	ONGOING

Event #1: Serious Adverse Event

Event Description	WORSENING SYMPTOMS OF CARPAL TUNNEL SYNDROME
Preferred term	手根管症候群
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 229 / 171
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	230 / 172
Duration of AE	2 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ENTEROPATHIC ARTHRITIS SECONDARY TO UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	CERVICAL SPONDYLOSIS
Preferred term	変形性脊椎症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 275 / 217
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 218): CERVICAL SPINE MRI: CERVICAL SPONDYLOSIS WITH C5/6 POST DISC HERNIATION; SPINE LUMBAR MRI: LUMBAR SPONDYLOSIS. L4/5 AND L5/S1 MINOR DISC PROLAPSE WITH L5/S1 ANNULAR TEAR

AE Stopped Initial Rx Day / Rx Day	279 / 221
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	OLD AGE, UNDERLYING RHEUMATOID ARTHRITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: 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] / 467 / 409
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 411): Alanine Aminotransferase: 104 [10 - 49] U/L; Albumin: 36 [32 - 48] G/L; Alkaline Phosphatase: 85 [45 - 129] U/L; Aspartate Aminotransferase: 125 [NOT REPORTED - 34] U/L; Bilirubin: 21 [NOT REPORTED - 17] umol/L; Creatinine: 64 [44 - 71] UMOL/L; Erythrocytes: 4.66 [3.8 - 4.8] 10^12/L; Hematocrit: 0.28 [0.36 - 0.46] FRACTION OF 1; Hemoglobin: 90 [120 - 150] G/L; Leukocytes: 9.6 [4 - 10] 10^9/L; Lymphocytes: 0.78 [1 - 3] 10^9/L; NPTST025-AMYLASE (SERUM): 57 [30 - 118] U/L; NPTST085-CRP: 1.2 [NOT REPORTED - 0.3] mg/dL; NPTST111-G-GLUTAMYL TRANSFERASE: 37 [NOT REPORTED - 38] U/L; NPTST157-MCH: 19.3 [27 - 32] PG; NPTST158-MCHC: 326 [315 - 345] G/L; NPTST159-MCV: 59 [77 - 97] FL; NPTST204-RDW: 16 [11.6 - 14] %; NPTST257-UREA (SERUM): 5.5 [3.2 - 8.2] MMOL/L; Neutrophils: 8.17 [2 - 7] 10^9/L; Platelets: 328 [150 - 400] 10^9/L; Potassium: 4.1 [3.6 - 5.2] MMOL/L; Sodium: 135 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 412): NPTST075-CLOSTRIDIUM DIFFICILE TOXIN AND: NOT DETECTED [NOT REPORTED - NOT REPORTED] NOT DETECTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 411): PHYSICAL EXAMINATION: LUNG, CARDIOVASCULAR AND ABDOMEN EXAMINATION : NORMAL

AE Stopped Initial Rx Day / Rx Day	476 / 418
Duration of AE	10 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MOST PROBABLY CAUSED BY FOOD POISONING FOLLOWING A CHRISTMAS PARTY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

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。本被験者はマレーシアの 6[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，頚椎症の事象を発現した。関連する病歴は，糖尿病，潰瘍性大腸炎，潰瘍性大腸炎に続発する腸疾患性関節炎，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275日後＊　，被験者は頚椎症の事象を発現した。投与279日後＊　，頚椎症は消失した。

投与275日後＊　　，被験者は顔面のしびれ感，頚部痛及び両手のしびれ感があり，入院した。危険因子には，年齢及び基礎疾患である腸疾患性関節炎が含まれた。投与279日後＊　，被験者は退院した。

投与された薬剤は，ultracet，フルナリジン，プレガバリン及びメコバラミンであった。

Causality for UPADACITINIB (Open Label)

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1)　Cervical spondylosis (10008315)　(Spinal osteoarthritis (10041591))　[v.23.0]　[10008315]

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 CERVICAL SPONDYLOSIS

- Investigator: OLD AGE, UNDERLYING RHEUMATOID ARTHRITIS

- AbbVie: RISK FACTOR　INCLUDES　SUBJECT'S AGE. ADDITIONALLY PER PI SUBJECT HAS UNDERLYING　RHEUMATOID ARTHIRTIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **CERVIAL SPINE MRI:** CERVICAL SPONDYLIOSIS WITH C5/6 POST DISC HERNIATION

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

[redacted] **SPINE LUMBAR MRI:** LUMBAR SPONDYLOSIS. L54/5 AND L5/S1 MINOR DISC PROLAPSE WITHL5/S1 ANNULAR TEAR
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はマレーシアの 6[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，急性胃腸炎の事象を発現した。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，及び潰瘍性大腸炎に続発する腸疾患性関節炎であった。

Event 3 の臨床経過：

投与467日後＊　，被験者は急性胃腸炎を発現した。投与467日後＊　，急性胃腸炎は消失した。

投与469日後＊　，被験者はクリスマスパーティーの後の 3 日間，下痢及び嘔吐があり，入院した。入院時の身体検査では，両肺，心血管及び腹部は正常であった。被験者は 投与470日後＊に退院した。

投与された薬剤は，ネキシウム，maxolon，セフロキシム，セフォペラゾン，三ケイ酸マグネシウム化合物及びビタミン B 化合物であった。

Causality for ABT-494 (Open Label)

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1)　Acute gastroenteritis (10066762)　(Gastroenteritis (10017888))　[v.21.1]　[10066762]

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 ACUTE GASTROENTERITIS

- Investigator: Most probably caused by food poisoning following a Christmas party.

- AbbVie: Event is common in the general population. Additionally, risk factor includes probable food consumption at Christmas party per PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 104 U/L (normal 10 to 49)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 125 U/L (normal <34)

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

[redacted] **20[redacted] COLONOSCOPY:** Was a clear demarcation between normal and inflamed colonic mucosa seen.

[redacted] **20[redacted] CRP:** 1.2 mg/dL (normal <0.3)

[redacted] **20[redacted] HEMOGLOBIN:** 90 G/L (normal 120 to 150)

[redacted] **20[redacted] LYMPHOCYTES ABS:** 0.78 X10**9/L (normal 1.00 to 3.00)

[redacted] **20[redacted] NEUTROPHILS ABS:** 8.17 X10**9/L (normal 2.00 to 7.00)

[redacted] **20[redacted] STOOL CULTURE:** Clostridium difficile, Not detected, Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.6 X10**9/L (normal 4.0 to 10.0)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はマレーシアの 6[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，手根管症候群の症状の悪化の事象を発現した。関連する病歴は，糖尿病，潰瘍性大腸炎（左側），潰瘍性大腸炎に続発する腸疾患性関節炎，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229日後＊　，被験者は手根管症候群の症状の悪化を発現した。投与230日後＊　，手根管症候群の症状の悪化は消失した。

本事象発現前の 投与197日後＊　，被験者は手根管症候群（非重篤）を経験した。

投与229日後＊　，被験者は軽傷を負い，右中指を骨折した。この症状が悪化し，右手首及び右手のしびれ感及び疼痛が発現した。同日，被験者は疼痛管理のために入院した。投与230日後＊，被験者は症状が改善し，退院した。

投与された薬剤は，dynacet 及び ultracet であった。

The patient's past medications include:

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

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

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

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

VOLTAREN for CARPAL TUNNEL SYNDROME AND PRONATOR TERES SYNDROME and CARPAL TUNNEL SYNDROME AND PRONATOR TERES SYNDROME ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

NAPROXEN for CARPAL TUNNEL SYNDROME ([redacted] 20[redacted] - [redacted] 20[redacted])

METHYL SALICYLATE for CARPAL TUNNEL SYNDROME ([redacted] 20[redacted] - [redacted] 20[redacted])

GABAPENTIN for CARPAL TUNNEL SYNDROME AND PRONATOR TERES SYNDROME and CARPAL TUNNEL SYNDROME AND PRONATOR TERES SYNDROME ([redacted] 20[redacted] - [redacted] 20[redacted])

PARACETAMOL for CARPAL TUNNEL SYNDROME AND PRONATOR TERES SYNDROME and CARPAL TUNNEL SYNDROME AND PRONATOR TERES SYNDROME ([redacted] 20[redacted] - [redacted] 20[redacted])

TRAMADOL for CARPAL TUNNEL SYNDROME AND PRONATOR TERES SYNDROME and CARPAL TUNNEL SYNDROME AND PRONATOR TERES SYNDROME ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1)　Carpal tunnel syndrome (10007697)　(Carpal tunnel syndrome (10007697))　[v.23.1]　[10007697]

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 WORSENING SYMPTOMS OF CARPAL TUNNEL SYNDROME

- Investigator: Enteropathic arthritis secondary to UC

- AbbVie: RISK FACTORS INCLUDE FEMALE GENDER, PRE-EXISTING DIABETES MELLITUS AND ENTEROPATHIC ARTHRITIS.

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

Reason for Narrative

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

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

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
LEFT SIDED UC	20[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): STEATOSIS HEPATIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: 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	10 PACK	3	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 57		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4 g	QD	Y-M: 20[redacted]
MESALAZINE	30 g	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted] / -314
MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted] / -284
BECLOMETASONE;MESALAZINE	1 OTHER: KLYSMA	QD	Y-M: 20[redacted] / -253
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -212
INFLIXIMAB	400 mg	OTHER: FOLLOWING SCHEDULE	Y-M: 20[redacted] / -182
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -20
MESALAZINE	4000 mg	BID	Y: 20[redacted]
MESALAZINE	4800 mg	QD	Y: 20[redacted]
PREDNISONE	5 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
MESALAZINE	4 g	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 352
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -20	ONGOING
COLECALCIFEROL	50000 IU	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted] / 62	ONGOING
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 67
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
PARACETAMOL	100 mL	PRN	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
SODIUM CHLORIDE	42 OTHER: ML/HOUR	OTHER: CONTINUE	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 67
ALFENTANIL	0.25 mg	PRN	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
CEFTRIAXONE	2000 mg	PRN	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 64
MIDAZOLAM	3 mg	PRN	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
NADROPARIN	2850 IU	QD	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 68
PHOSPHORIC ACID;SODIUM PHOSPHATE	1 OTHER: KLYSMA	PRN	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
CEFTRIAXONE	1000 mg	PRN	Y-M: 20[redacted] / 64	Y-M: 20[redacted] / 66

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

Event Description	GASTROENTERITIS
Preferred term	胃腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 118 / 62
Age at AE Onset	5[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 62): NPTST149-LEUCOCYTEN: 14.4 [4 - 11] 10^9/L; [redacted]20[redacted] (RX DAY 63): NPTST085-CRP: 33 [0 - 10] MG/L; [redacted]20[redacted] (RX DAY 65): NPTST085-CRP: 11 [0 - 10] MG/L; NPTST150-LEUCOCYTES: 6.4 [4 - 11] 10^9/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 62): CHEST X-RAY: NO ABNORMALITIES; [redacted]20[redacted] (RX DAY 63): SIGMOIDOSCOPY: ULCERATIVE COLITIS ACTIVITY FROM 45 CM AB ANO, INCREASING DISTALLY. MAYO SCORE 2-3. SLIGHTLY IMPROVED COMPARED TO ENDOSCOPY ON [redacted]-[redacted]-20[redacted].

AE Stopped Initial Rx Day / Rx Day	122 / 66
Duration of AE	5 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

Generated: [redacted]20[redacted]:06:46

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。本被験者はオランダの 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，胃腸炎の事象を発現した。関連する病歴は，潰瘍性大腸炎及び脂肪性肝炎であった。

Event 1 の臨床経過：

投与118日後＊　　，被験者は胃腸炎を発現した。投与122日後＊　，胃腸炎は消失した。

投与118日後＊　　の朝から，被験者は発熱及び全身倦怠感を訴えた。被験者は，朝に多量の直腸出血を伴う頻回な排便（5 回）があり，悪心を訴えた。体温は摂氏 39.4°C まで上昇し，全身の不調を感じた。被験者は救急科を受診した。身体検査では，左下腹部の軽度の痛みを除いて，異常は認められなかった。被験者は入院し，抗生物質及び輸液の静脈内投与を開始した。入院中，被験者は抗生物質の投与を継続した。臨床経過では改善が認められ，投与122日後＊　　，被験者は退院した。

投与された薬剤は，paracetamol，メトクロプラミド，塩化ナトリウム，メトロニダゾール，nadroparine 及びセフトリアキソンであった。

The patient's past medications include:

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

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

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

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

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

6-MP for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BECLOMETASONE W/MESALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for ABT-494 (Open Label)

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1)　Gastroenteritis (10017888)　(Gastroenteritis (10017888))　[v.20.0]　[10017888]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of GASTROENTERITIS

- Investigator: Not applicable.

- AbbVie: Event likely due to disease flare and/or acute infectious etiology.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD CULTURE:** Not reported

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

[redacted] **20[redacted] CHEST X-RAY:** No abnormalities.

[redacted] **20[redacted] LAB TEST:** Mild leukocytosis (12.97 10^9/1). No further abnormalities.

[redacted] **20[redacted] SIGMOIDOSCOPY:** Revealed ulcerative colitis activity from 45 cm "ab ano" increasing distally; Mayo score was 2-3

[redacted] **20[redacted] URINE CULTURE:** Not reported

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
血中クレアチンホスホキナーゼ増加				X
COVID-19 肺炎	X			X
医療機器関連敗血症	X			X

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

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
LEFT SIDED UC	20[redacted]
LIVER DISEASE (EXCLUDING HEPATITIS): PRIMARY SCLEROSING CHOLANGITIS	20[redacted]
OTHER: AXIAL ARTHROPATHY	NOT REPORTED
OTHER: BARRET OESOPHAGUS	20[redacted]
OTHER: ERCP WITH STONEEXTRACTION	20[redacted]
OTHER: URINARY TRACT INFECTION	20[redacted]

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

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	UNKNOWN			
CIGARETTES	FORMER	1 PACK	32	20[redacted]
CIGARS	UNKNOWN			
PIPES	UNKNOWN			

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

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	25 mg	QD	Y-M: [redacted]
AZATHIOPRINE	50 mg	QD	Y-M: [redacted]
AZATHIOPRINE	50 mg	QD	Y-M: [redacted] / -314
INFLIXIMAB	5 mg/kg	OTHER: FOLLOWING SCHEDULE	Y-M: [redacted] / -273
ESOMEPRAZOLE	20 mg	QD	Y-M: [redacted] / -231
VEDOLIZUMAB	300 mg	OTHER: FOLLOWING SCHEDULE	Y-M: [redacted] / -217
CYANOCOBALAMIN	1 mg	OTHER: SCEDULE FROM GENERAL PRACTITIONER	Y-M: [redacted] / -104
MESALAZINE	4 g	QD	Y-M: [redacted] / -115
BUDESONIDE	2 mg	QD	Y-M: [redacted] / -126
CIPROFLOXACIN	500 mg	BID	Y-M: [redacted] / -126
URSODEOXYCHOLIC ACID	600 mg	QD	Y-M: [redacted] / -97
CALCIUM;CALCIUM PHOSPHATE;ERGOCALCIFEROL	500/440 OTHER: 500MG/440 IU	BID	Y-M: [redacted] / -98
PREDNISOLONE	10 mg	QD	Y-M: [redacted] / -70
CALCIUM	500 mg	NOT REPORTED	Y: [redacted]
COLECALCIFEROL	800 IU	NOT REPORTED	Y: [redacted]
MESALAZINE	4 g	QD	Y: [redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y: [redacted]
BECLOMETASONE	NOT REPORTED	NOT REPORTED	Y: [redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	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	
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -231	ONGOING
CYANOCOBALAMIN	1 mg	OTHER: SCEDULE FROM GENERAL PRACTITIONER	Y-M: 20[redacted] / -104	ONGOING
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -115	ONGOING
URSODEOXYCHOLIC ACID	600 mg	QD	Y-M: 20[redacted] / -97	ONGOING
ASCORBIC ACID	1000 mg	QD	Y-M: 20[redacted] / 142	Not reported
VITAMINS NOS	1 OTHER: B1 50 MG, B2 50 MG, B3 50 MG, B5 50 MG, B6 6 MG, B8 50 MCG, B11 400 MCG, B12 50 MCG, CHOLIN	QD	Y-M: 20[redacted] / 142	Not reported
BISACODYL	10 mg	QD	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 339
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 339	Y-M: 20[redacted] / 340
ALUMINIUM POTASSIUM SULFATE;LIDOCAINE;PROPYLPARABEN	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / 570	Not reported
COLECALCIFEROL;MAGNESIUM CITRATE;PYRIDOXINE;VIBURNUM OPULUS	2 OTHER: TABLETS	PRN	Y-M: 20[redacted] / 635	Not reported
BISACODYL	10 mg	QD	Y-M: 20[redacted] / 665	Y-M: 20[redacted] / 665
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 665	Y-M: 20[redacted] / 666
ALFENTANIL	0.5 mg	QD	Y-M: 20[redacted] / 666	Y-M: 20[redacted] / 666
MIDAZOLAM	2.5 mg	QD	Y-M: 20[redacted] / 666	Y-M: 20[redacted] / 666
DEXAMETHASONE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 868	Y-M: 20[redacted] / 883
CLONIDINE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 875	Y-M: 20[redacted] / 904
HALOPERIDOL	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 875	Y-M: 20[redacted] / 904
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE	1 OTHER: SACHET	PRN	Y-M: 20[redacted] / 875	Y-M: 20[redacted] / 935
METOPROLOL	25 mg	TID	Y-M: 20[redacted] / 875	Y-M: 20[redacted] / 901

MIRTAZAPINE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 875	Y-M: 20[redacted] / 904
NADROPARIN	2850 IU	BID	Y-M: 20[redacted] / 875	Y-M: 20[redacted] / 935
ZOPICLONE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 875	Y-M: 20[redacted] / 904
AMOXICILLIN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 880	Y-M: 20[redacted] / 886
CIPROFLOXACIN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 881	Y-M: 20[redacted] / 890
CLINDAMYCIN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 904
FLUCLOXACILLIN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 890	Y-M: 20[redacted] / 890
AMLODIPINE	10 mg	QD	Y-M: 20[redacted] / 902	Y-M: 20[redacted] / 990
METOPROLOL	200 mg	QD	Y-M: 20[redacted] / 902	Y-M: 20[redacted] / 990
ETORICOXIB	30 mg	PRN	Y-M: 20[redacted] / 970	Y-M: 20[redacted] / 1045
BECLOMETASONE;MESALAZINE	1 OTHER: KLYSMA	QD	Y-M: 20[redacted] / 997	ONGOING
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 997	ONGOING

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

Event Description	ELEVATED CK (665)
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] / 396 / 340
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
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 PNEUMONIA INFECTION
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted] / 917 / 861
Age at AE Onset	[redacted]

Laboratory Testing

[redacted] (RX DAY 900): NPTST059-CALPROTECTIN: 420 [0 - 50] MG/KG/DAY; [redacted] (RX DAY 901): Alanine Aminotransferase: 84 [0 - 45] U/L; Alkaline Phosphatase: 200 [0 - 115] U/L; Leukocytes: 12.3 [4 - 11] 10^9/L; NPTST085-CRP: 27 [0 - 10] MG/L; NPTST114-GAMMA-GLUTAMYLTRANSFERASE: 419 [0 - 55] U/L

Microbiology

[redacted] (RX DAY 878): BLOOD NPTST046-BLOOD CULTURE: Positive-STREPTOCOCCUS THERMOPHILUS; [redacted] (RX DAY 879): SPUTUM NPTST233-SPUTUM CULTURE: Positive-ENTEROBACTER CLOACAE; [redacted] (RX DAY 892): OTHER PCR NPTST082-COVID-19 PCR: Positive-COVID-19 POSITIVE; [redacted] (RX DAY 895): WOUND NPTST264-WOUND CULTURE: Negative; [redacted] (RX DAY 897): OTHER PCR NPTST082-COVID-19 PCR: Negative

SAE Supplemental Procedure

[redacted] (RX DAY 868): ECG: NORMAL ECG; [redacted] (RX DAY 871): CT CHEST: NO SIGN OF PULMONARY EMBOLISM. BILATERAL MULTIFOCAL GROUND-GLASS OPACITIES, CO-RADS 5.; [redacted] (RX DAY 890): INCISION AND DRAINAGE OF THE ABSCESS: THE ABSCESS HAS HEALED

AE Stopped Initial Rx Day / Rx Day	969 / 913
Duration of AE	53 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID-19
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

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

Event Description	CATHETER RELATED SEPSIS
Preferred term	医療機器関連敗血症
AE Onset Date / Initial Rx Day / Rx Day	[redacted] / 934 / 878
Age at AE Onset	[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted] (RX DAY 878): BLOOD NPTST086-CULTURE: Positive-STREPTOCOCCUS THERMOPHILAE

SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	942 / 886
Duration of AE	9 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]:06:46
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。本被験者はオランダの 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，COVID-19 肺炎の感染症及びカテーテル関連敗血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 32 年間），潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 2 及び 3 の臨床経過：

投与917日後＊　，被験者は COVID-19 肺炎の感染症を発現した。投与934日後＊　，被験者はカテーテル関連敗血症を発現した。投与942日後＊　　，カテーテル関連敗血症は消失した。投与969日後＊ ，COVID-19 肺炎の感染症は消失した。

入院前，被験者は呼吸困難，咳嗽及び発熱を経験していた。投与921日後＊　　，被験者は COVID-19 の検査で陽性であった。被験者は抗生物質の投与を開始した。

投与924日後＊　　，被験者は呼吸不全のため入院した。被験者は呼吸困難の症状を呈しており，酸素飽和度が 93%–94%，呼吸数が 26 回/分，両肺底部の轟音があり，体温が摂氏 38.6°C であった。投与929日後＊ ，被験者は集中治療室に移され，人工呼吸器が装着された。　投与946日後＊　　，被験者は膿瘍の切開及び排膿を受け，最終的に治癒した。被験者は，カテーテル関連敗血症，切開及び排膿を必要とする膿瘍を伴う静脈炎，洞性頻脈並びに譫妄があり，集中治

療室での治療は複雑化した。投与969日後＊　，被験者は退院した。

投与された薬剤は，メトプロロール，nadroparine，movicolon，アムロジピン，ゾピクロン，ミルタザピン，クロニジン，クリンダマイシン，シプロフロキサシン，amoxicilline，haldol，flucloxacilline 及びデキサメタゾンであった。

The patient's past medications include:

PREDNISOLON for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　COVID-19 pneumonia (10084380)　(COVID-19 pneumonia (10084380))　[v.23.1]　[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

2)　Catheter sepsis (10053212)　(Device related sepsis (10069802))　[v.23.1]　[10053212]

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 COVID-19 PNEUMONIA INFECTION- Investigator: Covid-19.

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

Event of CATHETER RELATED SEPSIS

- Investigator: COVID-19 INFECTION

- AbbVie: Event is more likely a complication arising from hospitalization for the concurrent COVID-19 pneumonia infection.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALAT:** 84 U/L (normal 0 to 45)

[redacted] **20[redacted] ALP:** 200 U/L (normal 0 to 15)

[redacted] **20[redacted] ALP:** 114 U/L (normal 0 to 15)

[redacted] **20[redacted] ASAT:** 23 U/L

[redacted] **20[redacted] BLOOD CULTURE:** STREPTOCOCCUS THERMOPHILUS

[redacted] **20[redacted] BMI:** 26.8 kg/m2

[redacted] **20[redacted] CALPRO:** 420 mg/kg (normal 0 to 50)

[redacted] **20[redacted] CHEST CT:** No sign of pulmonary embolism. Bilateral multifocal ground glass opacities, CO-RADS 5.

[redacted] **20[redacted] CHEST X-RAY:** Bilateral infiltrates right > left

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

[redacted] **20[redacted] COVID-19 PCR TEST:** Negative

[redacted] **20[redacted] CRP:** 27 MG/L (normal 0 to 10)

[redacted] **20[redacted] CRP:** 7 MG/L (normal 1 to 10)

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

[redacted] **20[redacted] GGT:** 419 U/L (normal 0 to 55)

[redacted] **20[redacted] GGT:** 157 U/L (normal 0 to 55)

[redacted] **20[redacted] LACTATE DEHYDROGENASE:** 250 U/L

[redacted] **20[redacted] LACTATE DEHYDROGENASE:** 231 U/L

[redacted] **20[redacted] NASOPHARYNGEAL SWAB - COVID:** COVID POSITIVE

[redacted] **20[redacted] SPUTUM CULTURE:** ENTEROBACTER CLOACAE

[redacted] **20[redacted] WBC:** 12.3 X10**9/L (normal 4 to 11)

[redacted] **20[redacted] WBC:** 8.9 X10**9/L (normal 4 to 11)

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

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
健忘	X	X		
潰瘍性大腸炎	X			
下痢	X			
疲労	X			
頭痛	X	X		
倦怠感	X			
悪心	X	X		
発作様現象	X	X		
嘔吐	X			

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

Medical History	Onset Year
DEPRESSION: DEPRESSION AND PANIC	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: COLITIS ULCEROSA	20[redacted]
INFLAMMATORY BOWEL DISEASE: HOSPITAL ADMISSION FOR UC	20[redacted]
MIGRAINE HEADACHE	20[redacted]
OTHER: AUTO-IMMUNE BULLOUS SKIN DISEASE	20[redacted]
OTHER: BASAL CELL CARCINOMA ON FOREHEAD. CURRENT TREATMENT: FLUOROURACIL CREAM 3-4 WEEKS.	20[redacted]
OTHER: BRIEF LOSS OF CONSCIOUSNESS	20[redacted]
OTHER: HERPES ZOSTER INFECTION	20[redacted]
OTHER: INFECTION OF WOUND	20[redacted]
OTHER: LOW VITAMIN B12	20[redacted]
OTHER: SUICIDE ATTEMPT	20[redacted]
SEIZURE DISORDER/CONVULSIONS: PSYCHOGENE NON - EPILEPTIC SEIZURES	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	20[redacted]
SURGERY: EXISION OF BASAL CELL CARCINOMA ON CHEST	20[redacted]
SURGERY: EXISION OF BASAL CELL CARCINOMA ON LEFT FACE (PRE-AURICULAR)	20[redacted]
SURGERY: EXISION OF BASAL CELL CARCINOMA ON RIGHT ABDOMEN	20[redacted]
SURGERY: EXISION OF BASAL CELL CARCINOMA ON RIGHT SCAPULA	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 54	[redacted]20[redacted] / 99	46

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETHINYLESTRADIOL;LEVONORGESTREL	30 mg	QD	Y-M: 20[redacted]-[redacted]
CALCIUM CARBONATE	1000 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISOLONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]-[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]-[redacted]
HYDROXOCOBALAMIN	500 uL	OTHER: FIRST MONTH 2X, THEREAFTER ONCE EVERY 2 MONTHS	Y-M: 20[redacted]-[redacted]

FOLIC ACID	0.5 mg	QD	Y-M: 20[redacted] / -183
BUDESONIDE	9 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -127
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -130
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / -77
PROPRANOLOL	10 mg	QD	Y-M: 20[redacted] / -42
OXAZEPAM	10 mg	PRN	Y-M: 20[redacted] / -14
TEMAZEPAM	UNK mg	PRN	Y-M: 20[redacted] / -14
INFLIXIMAB	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY TWO WEEKS	Y: 20[redacted]
PARACETAMOL	500 mg	PRN	Y: 20[redacted] / -257
QUETIAPINE	25 mg	QD	Y: 20[redacted] / -257

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
ETHINYLESTRADIOL;LEVONORGESTREL	30 mg	QD	Y-M: 20[redacted]	ONGOING
CALCIUM CARBONATE	1000 mg	QD	Y-M: 20[redacted]	ONGOING
HYDROXOCOBALAMIN	500 uL	OTHER: FIRST MONTH 2X, THEREAFTER ONCE EVERY 2 MONTHS	Y-M: 20[redacted]	ONGOING
FOLIC ACID	0.5 mg	QD	Y-M: 20[redacted] / -183	ONGOING
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / -77	ONGOING
PROPRANOLOL	10 mg	QD	Y-M: 20[redacted] / -42	Y-M: 20[redacted] / 47
OXAZEPAM	10 mg	PRN	Y-M: 20[redacted] / -14	ONGOING
TEMAZEPAM	UNK mg	PRN	Y-M: 20[redacted] / -14	ONGOING
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 12	ONGOING
METOCLOPRAMIDE	10 mg	TID	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 15
SODIUM CHLORIDE	1 OTHER: L/24H	OTHER: ONCE	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 15
CONTRAST MEDIA	UNK OTHER: UNK	OTHER: UNK	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
NADROPARIN	2850 IU	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 18
ONDANSETRON	8 mg	PRN	Y-M: 20[redacted] / 15	ONGOING
QUETIAPINE	50 mg	QD	Y-M: 20[redacted] / 42	ONGOING
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46
PARACETAMOL	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46

SODIUM CHLORIDE	1,5 L	OTHER: ONCE	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46
TRAMADOL	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 46	Y-M: 20[redacted] / 46
PARACETAMOL	500 mg	PRN	Y: 20[redacted] / -257	ONGOING
QUETIAPINE	25 mg	QD	Y: 20[redacted] / -257	Y-M: 20[redacted] / 40

Event #1: Serious Adverse Event

Event Description	GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE
Preferred term	下痢，疲労，倦怠感，嘔吐
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 67 / 14
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 14): Platelets: 446 [150 - 400] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 14): STOOL NPTST086-CULTURE: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 15): MRI: MRI RESULTS CONFIRM WEEK 0 COLONOSCOPY RESULTS. SCARRING OF THE COLON.

AE Stopped Initial Rx Day / Rx Day	68 / 15
Duration of AE	2 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 #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA
Preferred term	健忘，頭痛，悪心，発作様現象
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 99 / 46
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 46): Erythrocytes: 466 [0 - 18] /uL; Glucose: 7.9 [3.1 - 6.4] MMOL/L; HDL Cholesterol: 2.56 [1.16 - 1.68] MMOL/L; Leukocytes: 0.019 [0 - 0.01] 10^9/L; NPTST110-FREE T4: 25.8 [12 - 22] PMOL/L; NPTST113-GAMMA GT: 54 [0 - 38] U/L; NPTST235-SQUAMOUS CELL EPITHELIUM: 42 [0 - 4] /UL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 46): CT CEREBRUM: NO ABNORMALITIES; ECG: NO SIGNIFICANT ABNORMALITIES

AE Stopped Initial Rx Day / Rx Day	100 / 47 (1 DAY AFTER LAST TREATMENT)
Duration of AE	2 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PNES
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Serious Adverse Event

Event Description	ONGOING UC, NO IMPROVEMENT FROM TREATMENT
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 109 / 56 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 62): NPTST085-CRP: 136.6 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 63): NPTST085-CRP: 54.1 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 67): NPTST085-CRP: 103.7 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 60): X-RAY: NO DEVIATIONS WERE FOUND; [redacted]20[redacted] (RX DAY 61): SUBTOTAL COLECTOMY: SURGERY SUCCESFUL, PATIENT RECOVERING

AE Stopped Initial Rx Day / Rx Day	123 / 70 (24 DAYS AFTER LAST TREATMENT)
Duration of AE	15 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ONGOING UC
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

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。本被験者はオランダの 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，全身不快感（倦怠感），下痢，嘔吐及び疲労の事象を発現した。関連する病歴は，潰瘍性大腸炎であった。

Event 1 の臨床経過：

投与67日後＊　，被験者は全身不快感（倦怠感），下痢，嘔吐及び疲労を発現した。投与68日後＊　，全身不快感（倦怠感），下痢，嘔吐及び疲労は消失した。

投与67日後＊　，被験者は入院し，倦怠感，疲労，下痢，悪心及び嘔吐があった。被験者は自分の身の回りのことができなかった。血圧及び脈拍は正常範囲内であり，摂氏 38°C の発熱があった。被験者は，中心ラインを挿入され，1.5 L の生理食塩水及び制吐薬の投与を受けた。投与68日後＊　，MRI 検査が実施され，瘢痕を伴う汎大腸炎が認められたが，重度の活動性炎症の徴候は認められなかった。投与68日後＊　の終わりに，被験者は退院した。

投与された薬剤は，生理食塩水，temazepam，fraxiparine，メトクロプラミド，オンダンセトロン及びオキサゼパムであった。

The patient's past medications include:

HUMIRA for DRUG USED FOR UNKNOWN INDICATION

Causality for ABT-494 (Open Label)

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1)　Malaise (10025482)　(Malaise (10025482))　[v.20.1]　[10025482]

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

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

Dechallenge: Not Applicable

2)　Diarrhea (10012727)　(Diarrhoea (10012735))　[v.20.1]　[10012727]

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

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

Dechallenge: Not Applicable

3) Vomiting (10047700) (Vomiting (10047700)) [v.20.1] [10047700]

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

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

Dechallenge: Not Applicable

4) Fatigue (10016256) (Fatigue (10016256)) [v.20.1] [10016256]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of GENERAL DISCOMFORT (MALAISE), DIARRHOEA, VOMITING, FATIGUE

- Investigator: Not applicable

- AbbVie: Event likely represents worsening UC and Disease Flare.

Relevant Laboratory & Other Diagnostic Tests

Unknown date BLOOD PRESSURE: normal

Unknown date BODY TEMPERATURE: 38 Degrees C

[redacted] 20[redacted] **MRI:** showed pancolitis with scarring, but no signs of severe active inflammation

[redacted] 20[redacted] **PLATELET COUNT:** 446 X10**9/L (normal 150 to 400)

Unknown date PULSE: normal

[redacted] 20[redacted] **STOOL CULTURE:** negative
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオランダの 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，発作様エピソード，健忘，頭痛及び悪心の事象を発現した。関連する病歴は，潰瘍性大腸炎，基底細胞癌，心因性非てんかん発作，断眠からの発作，うつ病，短時間の意識消失及び片頭痛であった。

Event 2 の臨床経過：

投与99日後＊　　，被験者は発作様エピソード，健忘，頭痛及び悪心を発現した。投与100日後＊　，発作様エピソード，健忘，頭痛及び悪心は消失した。

投与99日後＊　　，被験者は，父親とともに自家用車に向かって歩いていた。被験者は，少しの荒々しい動作の後，倒れた。約 3 分間意識を失い，その後意識を取り戻した。発作後，被験者は混乱し，何が起こったのか思い出せなかった。被験者は救急治療室を受診し，医師の診察を受けた。医師が部屋を出た際，別の発作を起こし，発作は約 1.5 分間持続した。症状には，荒々しい動作の後の体の硬直，及び口から出たピンク色の泡が含まれた。被験者は意識を取り戻し，その後少し混乱した。被験者は精査のために入院した。悪心の他に異常は認められなかった。投与100日後＊　　，被験者は退院した。

治験責任医師によると，断眠が危険因子であった。

投与された薬剤は，トラマドールであった。

The patient's past medications include:

METOCLOPRAMIDE for NAUSEA ([redacted] 20[redacted] - [redacted] 20[redacted])

FRAXIPARINE for NAUSEA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Seizure like phenomena (10071048) (Seizure like phenomena (10071048)) [v.23.1] [10071048]

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) Amnesia (10001949) (Amnesia (10001949)) [v.23.1] [10001949]

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

3) Headache (10019211) (Headache (10019211)) [v.23.1] [10019211]

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

4) Nausea (10028813) (Nausea (10028813)) [v.23.1] [10028813]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of SEIZURE-LIKE EPISODE, AMNESIA, HEADACHE, NAUSEA

- Investigator: PNES

- AbbVie: Risk factors include concurrent sleep deprivation and seizure-like episode in a patient with pre-existing seizures from sleep deprivation, psychogenic non-epileptic seizures, loss of consciousness and migraine headache.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE (AT TIME OF ADMISSION):** 130/80 mmHg

[redacted] **20[redacted] FREE T4:** Results: 25.8 PMOL/L Lower normal range: >=12.0 Upper normal range: <=22.0

[redacted] **20[redacted] GAMMA GT:** 54 U/L (normal 0 to 38)

[redacted] **20[redacted] GLUCOSE:** 7.9 MMOL/L (normal 3.1 to 6.4)

[redacted] **20[redacted] HDL CHOLESTEROL:** 2.56 MMOL/L (normal 1.16 to 1.68)

[redacted] **20[redacted] HEART RATE (AT TIME OF ADMISSION):** 98 bpm

[redacted] **20[redacted] PHYSICAL EXAM:** Not reported

[redacted] **20[redacted] PHYSICAL EXAM:**

[redacted] **20[redacted] RED BLOOD CELLS (URINE):** Results: 466/uL Lower normal range: >=0 Upper normal range: <=18

[redacted] **20[redacted] RESPIRATIONS (AT TIME OF ADMISSION):** 17 /min

[redacted] **20[redacted] SPO2 (AT TIME OF ADMISSION):** 99 %

[redacted] **20[redacted] SQUAMOUS CELL EPITHELIUM (URINE):** Results: 42/uL Lower normal range: >=0 Upper normal range: 4

[redacted] **20[redacted] TEMPERATURE (AT TIME OF ADMISSION):** 37.7 Degrees C

[redacted] **20[redacted] WHITE BLOOD CELLS (URINE):** Results: 19/uL Lower normal range: >=0 Upper normal range: 10
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオランダの 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，継続中の潰瘍性大腸炎，及び治療による改善なしの事象を発現した。関連する病歴は，潰瘍性大腸炎及び潰瘍性大腸炎による入院であった。

Event 3 の臨床経過：
投与109日後＊　　，被験者は継続中の潰瘍性大腸炎，及び治療による改善なしを発現した。投与123日後＊　　，継続中の潰瘍性大腸炎，及び治療による改善なしは消失した。

投与109日後＊　　，被験者は今後の手術のために入院した。本事象に関連する徴候及び症状には，治療にもかかわらず継続中の潰瘍性大腸炎の症状が含まれた。投与114日後＊　　，回腸瘻造設を伴う結腸亜全摘術及びハルトマン手術又は回腸直腸吻合術に成功した。被験者は回復し，入院中に合併症はなかった。投与123日後＊　　，被験者は退院した。

Causality for UPADACITINIB (Open Label)

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1)　Ulcerative colitis (10045365)　(Colitis ulcerative (10009900))　[v.23.1]　[10045365]

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 ONGOING UC, NO IMPROVEMENT FROM TREATMENT

- Investigator: Ongoing UC.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 136.6 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 54.1 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 103.7 MG/L (normal 0 to 5)

[redacted] **20[redacted] X-RAY:** No deviations were found

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
結腸腺癌	X	X		X
基底細胞癌	X			X
血中クレアチンホスホキナーゼ増加				X
深部静脈血栓症	X			X

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

Medical History	Onset Year
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: DERMATOMYCOSE	20[redacted]
OTHER: FATIGUE	20[redacted]
OTHER: LEUCOPENIA	20[redacted]
OTHER: LUNG EMBOLISM	20[redacted]
OTHER: RENAL FUNCTION LAB ABNORMALITIES	20[redacted]
OTHER: THROMBOPENIA	20[redacted]
PERIPHERAL VASCULAR DISEASE-VENOUS: PAIN LEFT CALF EVERY YEAR SINCE 20[redacted]	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY DUE TO APPENDICITIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 57	[redacted] / 110	54
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 110	[redacted] / 1170	1061

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
TIOGUANINE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
BECLOMETASONE;MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
TIOGUANINE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
ADALIMUMAB	40 mg	OTHER: ONCE WEEKLY	Y-M: [redacted]
BECLOMETASONE;MESALAZINE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
BUDESONIDE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: [redacted]
TIOGUANINE	20 mg	QD	Y-M: [redacted]
MIRIKIZUMAB	600 mg	OTHER: EVERY MONTH	Y-M: [redacted] / -336
MICONAZOLE	1 OTHER: APPLICATION	BID	Y-M: [redacted] / -49
PHOSPHORIC ACID;SODIUM PHOSPHATE	10 mL	TID	Y-M: [redacted] / -49
MESALAZINE	2 g	QD	Y: [redacted]
MESALAZINE	NOT REPORTED	NOT REPORTED	Y: [redacted]
CALCIUM CARBONATE;COLECALCIFEROL	500/400 OTHER: MG/IU	QD	Y: [redacted]
PANTOPRAZOLE	40 mg	PRN	Y: [redacted]
PREDNISONE	15 mg	QD	Y: [redacted]
MERCAPTOPURINE	NOT REPORTED	NOT REPORTED	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	
MICONAZOLE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -49	ONGOING
MESALAZINE	1 g	QD	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 753
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 540	Y-M: 20[redacted] / 584
BISACODYL	10 mg	QD	Y-M: 20[redacted] / 667	Y-M: 20[redacted] / 667
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / 668	Y-M: 20[redacted] / 669
FENTANYL	100 ug	QD	Y-M: 20[redacted] / 669	Y-M: 20[redacted] / 669
MIDAZOLAM	2.5 mg	QD	Y-M: 20[redacted] / 669	Y-M: 20[redacted] / 669
NADROPARIN	15200 IU	QD	Y-M: 20[redacted] / 723	Y-M: 20[redacted] / 724
RIVAROXABAN	15 mg	BID	Y-M: 20[redacted] / 724	Y-M: 20[redacted] / 745
RIVAROXABAN	20 mg	QD	Y-M: 20[redacted] / 746	ONGOING
BISACODYL	10 mg	QD	Y-M: 20[redacted] / 1052	Y-M: 20[redacted] / 1052
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 L	QD	Y-M: 20[redacted] / 1053	Y-M: 20[redacted] / 1053
MIDAZOLAM	2.5 mg	QD	Y-M: 20[redacted] / 1054	Y-M: 20[redacted] / 1054
MESALAZINE	2 g	QD	Y: 20[redacted]	Y-M: 20[redacted] / 235
CALCIUM CARBONATE;COLECALCIFEROL	500/400 OTHER: MG/IU	QD	Y: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg	PRN	Y: 20[redacted]	ONGOING

Event #1: 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] / 362 / 253
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
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 - Possible Malignancies, Event of Interest - Malignancy, Event of Interest - Non-melanoma Skin Cancer (NMSC)

Event Description	BASAL CELL CARCINOMA ON TOP OF HEAD.
Preferred term	基底細胞癌
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 832 / 723
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	893 / 784
Duration of AE	62 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: Serious Adverse Event, Event of Interest - Adjudicated Cardiovascular events, Event of Interest - Adjudicated Venous Thromboembolic Event

Event Description	DEEP VEIN THROMBOSIS OF THE LOWER RIGHT LIMB
Preferred term	深部静脈血栓症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 832 / 723
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 724): NPTST089-D-DIMER: 3647 [NOT REPORTED - 500] ug/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 724): VASCULAR ENDOSCOPY: THROBOSIS RIGHT CALF

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #4: Serious Adverse Event, Event of Interest - Possible Malignancies, Event of Interest - Malignancy, Event of Interest - Non-melanoma Skin Cancer (NMSC)

Event Description	BASAL CELL CARCINOMA ON TOP OF HEAD
Preferred term	基底細胞癌
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 984 / 875
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 1017): REMOVAL BASAL CELL CARCINOMA WITH SKIN TRANSPLANT: WOUND IS HEALING.

AE Stopped Initial Rx Day / Rx Day	1127 / 1018
Duration of AE	144 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, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #5: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC

Event Description	ADENOMACARCINOMA SIGMOID COLON
Preferred term	結腸腺癌
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1163 / 1054
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
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	ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:06:46
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。本被験者はオランダの 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，右下肢の深部静脈血栓症の事象を発現した。関連する病歴は，疲労，炎症性腸疾患，潰瘍性大腸炎，肺塞栓症，血小板減少症，非喫煙者，現飲酒者（1 日 2 杯未満），血栓症の家族歴（母親）及び 20[redacted] 年以降毎年の右ふくらはぎ痛であった。

Event 3 の臨床経過：

投与832日後＊　，被験者は右下肢の深部静脈血栓症を発現した。

被験者は，脚の圧痛，痛み，腫れ及び皮膚の紅斑があった。D ダイマーの上昇が認められ，超音波検査で血栓症が確認された。投与833日後＊ ，被験者は血管内視鏡検査を受けた。投与833日後＊　，被験者は退院した。

カルテによると，被験者は過去 2 週間半，上腿に疲労感があり，後に疲労感は右脚の膝窩及びふくらはぎに移動した。

投与された薬剤は，リバーロキサバン及び nadroparine であった。

The patient's past medications include:

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

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

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

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

BECLOMETHASON/MESALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - 20[redacted])

BECLOMETHASON/MESALAZINE ENEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - 20[redacted])

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

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

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

MIRIKIZUMAB 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], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Deep vein thrombosis leg (10065052) (Deep vein thrombosis (10051055)) [v.22.1] [10065052]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of DEEP VEIN THROMBOSIS OF THE LOWER RIGHT LIMB

- Investigator: Not applicable.

- AbbVie: Event is more likely related to pre-existing history of lung embolism. Additional risk factors include pre-existing ulcerative colitis and history of thrombosis in his mother.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALP:** 52 U/L (normal <11)

[redacted] **20[redacted] D-DIMER:** 3647 micrograms/liter (normal <500)

[redacted] **20[redacted] HEMATOCRIT:** 0.40 % (normal 0.41 to 0.53)

[redacted] **20[redacted] HEMOGLOBIN:** 8.7 MMOL/L (normal 8.4 to 10.8)

[redacted] **20[redacted] SEDIMENTATION RATE:** 2 MM/HR (normal 1 to 20)

[redacted] **20[redacted] THROMBOCYTE:** 183 X10**9/L (normal 150 to 400)

20[redacted] ULTRASOUND: Confirmed thrombosis.

[redacted] **20[redacted] VASULAR ENDOSCOPY:** thrombosis right calf

[redacted] **20[redacted] VENOUS DOPPLER:** Proximal DVT with thrombus in the distal VPS, v. poplitea, v.gastroanemia, prox/mid. VTP

[redacted] **20[redacted] WEIGHT:** 9[redacted] KG
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオランダの 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，頭頂部の基底細胞癌の事象を発現した。関連する病歴は，潰瘍性大腸炎及び皮膚真菌症であった。

Event 4 の臨床経過：

投与の約33ヵ月後＊，被験者は頭頂部の基底細胞癌を発現した。投与1127日後＊，頭頂部の基底細胞癌は消失した。

本事象発現前の 投与の約28ヵ月後＊，被験者は基底細胞癌（非重篤）を発現した。病変を切除したが，最初，医療過誤のため病変は完全には切除されず，傷は回復しなかった。

投与1126日後＊　，被験者は，頭頂部への皮膚移植のため入院した。基底細胞癌の外科的治療の傷が回復しなかったため，右大腿から採取した皮膚片の移植手術を受けた。 投与1127日後＊，被験者は退院し，傷はきれいに回復した。

The patient's past medications include:

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

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

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

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

BECLOMETHASON/MESALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - 20[redacted])

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

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

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

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

PREDNISON for UC ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Basal cell carcinoma (10004146) (Basal cell carcinoma (10004146)) [v.23.0] [10004146]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of BASAL CELL CARCINOMA ON TOP OF HEAD

- Investigator: Not applicable

- AbbVie: Basal cell carcinoma is the most common cancer occurring worldwide, with incidence rate in European countries of 129.3 in men per 100,000 person-years, European standard. Caucasian race is an additional risk factor.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はオランダの 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，S 状結腸腺癌の事象を発現した。関連する病歴は，炎症性腸疾患，非喫煙者，現飲酒者（1 日 2 杯未満）及び潰瘍性大腸炎であった。

Event 5 の臨床経過：

投与1163日後＊ ，被験者は S 状結腸腺癌を発現した。

投与1210日後＊ ，被験者は S 状結腸腺癌の治療処置のため入院した。投与1212日後＊ ，被験者は回腸嚢肛門吻合術を伴う直腸結腸切除術を受けた。合併症はなく，手術は成功した。投与1223日後＊ ，被験者は退院した。

治験薬の投与は完全に中止された。

The patient's past medications include:

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

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

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

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

BECLOMETHASON/MESALAZINE ENEMA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - 20[redacted])

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

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

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

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

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

Causality for UPADACITINIB (Open Label)

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1) Adenocarcinoma of sigmoid colon (10075432) (Adenocarcinoma of colon (10001167)) [v.23.1] [10075432]

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 ADENOMACARCINOMA SIGMOID COLON

- Investigator: Ulcerative Colitis.

- AbbVie: risk factors include pre-existing ulcerative colitis and subject's age.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** No inflammation seen (normal mucosa).

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** No inflammation seen (normal mucosa).

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Basal cell carcinoma ([redacted]20[redacted]): Basal Cell Carcinoma was removed.
Blood creatine phosphokinase increased: Symptom of muscle pain, related to vigorous physical activity.

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
毛巣嚢胞	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: FERRIPRIVE ANEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
NEPHROLITHIASIS	20[redacted]
OTHER: ACNE IN FACE	20[redacted]
OTHER: CMV INFECTION	20[redacted]
OTHER: FOLIC ACID DEFICIENCY	20[redacted]
OTHER: PYROSIS	20[redacted]
OTHER: VITAMIN D DEFICIENCY	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 60		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	125 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	60 mg	QD	Y-M: 20[redacted]-[redacted]
IRON	100 mg	NOT REPORTED	Y-M: 20[redacted]-[redacted]
PREDNISONE	20 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted]-[redacted]
MESALAZINE	3 g	BID	Y-M: 20[redacted]-[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	350 mg	OTHER: PER PROTOCOL	Y-M: 20[redacted]-[redacted]
IRON	900 mg	NOT REPORTED	Y-M: 20[redacted]-[redacted]
IRON	900 mg	NOT REPORTED	Y-M: 20[redacted]-[redacted]
MESALAZINE	4	NOT REPORTED	Y-M: 20[redacted]-[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]-[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]-[redacted]
BECLOMETASONE;MESALAZINE	100 g	QD	Y-M: 20[redacted]-[redacted]
IRON	1000 mg	NOT REPORTED	Y-M: 20[redacted]-[redacted]
IRON	1500 mg	NOT REPORTED	Y-M: 20[redacted]-[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: 1X/8 WKS	Y-M: 20[redacted]-[redacted]
IRON	1000 mg	NOT REPORTED	Y-M: 20[redacted]-[redacted]
METHOTREXATE	25 mg	1 time per week	Y-M: 20[redacted]-[redacted]
FOLIC ACID	1 mg	QD	Y-M: 20[redacted]-[redacted] / -103
VITAMIN D NOS	25.000 IU	OTHER: 1X/WEEK	Y-M: 20[redacted]-[redacted] / -103
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -83

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
SERTRALINE	50 mg	QD	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 1059
IRON	1000 mg	QD	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 156
IRON	1000 mg	QD	Y-M: 20[redacted] / 270	Y-M: 20[redacted] / 270
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 906	Y-M: 20[redacted] / 910
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 934	ONGOING
MORPHINE	2.5 mg	OTHER: AS NEEDED	Y-M: 20[redacted] / 935	Y-M: 20[redacted] / 935
MACROGOL	13.8 g	OTHER: AS NEEDED	Y-M: 20[redacted] / 1153	Not reported
CALCIUM CARBONATE	500 mg	QD	Y-M: 20[redacted] / 1160	Not reported
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 1173	Not reported

Event #1: Event of Interest - Anemia

Event Description	ANAEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 153 / 94
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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

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

Event Description	SINUS PILONIDALIS ABSCESS
Preferred term	毛巣嚢胞
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 993 / 934
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 935): DRAINAGE ABCESS SINUS PILONIDALIS: SUCCESFULLY DRAINED	
AE Stopped Initial Rx Day / Rx Day	995 / 936
Duration of AE	3 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HOSPITALIZATION DUE TO SURGICAL INTERVENTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

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。本被験者はオランダの 2[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，毛巣洞の膿瘍の事象を発現した。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 2 の臨床経過：

投与993日後＊　，被験者は毛巣洞の膿瘍を発現した。投与995日後＊　，毛巣洞の膿瘍は消失した。

本事象発現前の投与から約32ヵ月目＊の上旬に，被験者は肛門周囲膿瘍（非重篤）の排膿を経験していた。

投与994日後＊　，被験者は毛巣洞の排膿のために入院した。処置は成功した。投与995日後＊，被験者は退院した。

投与された薬剤は，paracetamol 及びモルヒネであった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

FERRIC CARBOXYMALTOSE for ANEMIA ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted])

ISOMALTOSE, FERRIC COMPLEX for ANEMIA ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

BECLOMETASONE;MESALAZINE for ULCERATIVE COLITIS ([redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　Pilonidal abscess (10035041)　(Pilonidal cyst (10035043))　[v.24.0]　[10035041]

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 SINUS PILONIDALIS ABSCESS

- Investigator: HOSPITALIZATION DUE TO SURGICAL INTERVENTION

- AbbVie: risk factors include age(early twenties) , male gender and obesity (BMI 31.7).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY WEIGHT:** 9[redacted] kg

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

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
OTHER: GRAVES	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 59	[redacted]20[redacted] / 169	111

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2.4 g	BID	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
HYDROCORTISONE	100 mg	TID	Y-M: 20[redacted]
IRON	1.5 g	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	2 g	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: 8 WEEKS	Y-M: 20[redacted]
METRONIDAZOLE	400 mg	BID	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: 4 WEEKS	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -337
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -139

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -337	ONGOING

Event #1: Serious Adverse Event

Event Description	REFLEX SYNCOPE
Preferred term	失神
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 172 / 114 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 114): Albumin: 47 [36 - 48] G/L; Calcium: 2.55 [2.15 - 2.51] MMOL/L; Hemoglobin: 146 [134 - 170] G/L; NPTST152-LEUKOCYTES: 12.8 [3.5 - 8.8] 10^9/L; NPTST246-TROPONIN: 7 [0 - 15] NG/L; Sodium: 135 [137 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 53): ECG: 54 BPM, PR INT 178 MS, QRS: 91, QT/QTC: 418/404; [redacted]20[redacted] (RX DAY 114): BLOODPRESSURE: 158/93; PULSE: 58; RF: 16/MIN; SPO2: 98%; TELEMETRY: NORMAL; TEMPERATURE: 36.2 C

AE Stopped Initial Rx Day / Rx Day	173 / 115 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	2 DAYS
Severity	MILD

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECT HAS A SERIOUS UC AND WERE VERY DEHYDRATED AND THAT WAS THE REASON FOR THE PASIENT FAINTED.SUBJECT WAS IN HOSPITAL FOR OBSERVATION ONE DAY, AND HE GOT FLUID THERE.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]#[redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はノルウェーの 2[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，反射性失神の事象を発現した。関連する病歴は，グレーブス病，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172日後＊ ，被験者は反射性失神を発現した。投与173日後＊ ，反射性失神は消失した。

投与172日後＊ ，被験者は治験責任医師の診察を受けた。被験者は時折，胸部の下に痛みがあると訴えた。治験責任医師は，この痛みは重篤な汎大腸炎から来るものと述べた。

同日，被験者が診察から帰宅した後，自宅で約 10–15 秒間続く失神を発現した。被験者の母親が救急車を呼び，被験者は救急治療室に運ばれた。

被験者は重症の潰瘍性大腸炎があり，1 日 20 回程度の排便があるため，脱水症状であると指摘された。

医療記録より：投与172日後＊ ，被験者は入院した。被験者は午後 3 時頃，台所に立っているときに気が遠くなり，座り込んだ。被験者は視力喪失（失神したときによくあるように視界が黒くなった）に気づき，その状態は座った状態でも続いており，横になろうとした。被験者は数歩進んだところで気を失い，前頭部を打ち，腹部に 2 箇所の切り傷を負った。被験者は失神からのことを何も覚えていなかった。失神時に一緒にいた母親は，被験者は 10–15 秒ほど気を失っていたと述べた。失神前，被験者の心拍数は増加していなかった。被験者が目覚めた時，母親は救急治療室に電話していた。被験者は体を起こそうとしたが，新たな視力喪失があり，横

にならざるを得なかった。その後，被験者は気分が良くなり，トイレに行き，ゆっくりと歩いた。被験者は辛うじてトイレに辿り着いたが，排便はなかった。その後，被験者は徐々に気分が良くなった。

失神の後，被験者は以前よりも強い腹痛を経験した。被験者は，胸部の左側に断続的な痛みがあったと述べ，その後，両肺の基底部及び心窩部から来ていると思われる鋭い痛みを経験した。どちらの痛みも，体を動かすと始まり，体の動きを止めると多少改善した。痛みは背部に広がり，腕や頚部/喉にはなかった。診察時，被験者は，漏斗胸があり，四肢は温かく華奢であり，両側の後脛骨動脈の脈拍は良好であった。被験者は，治験薬の投与開始前からこれらの種類の痛みを経験していたが，治験薬を服用すると悪化すると表現した。治験薬の投与を中止していた前週は，痛みが軽減されていた。結論として，反射性失神であり，心臓に起因する疑いはないと診断された。投与173日後＊　，被験者は退院した。

Causality for ABT-494 (Open Label)

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1)　Syncope (10042772)　(Syncope (10042772))　[v.21.0]　[10042772]

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 REFLEX SYNCOPE

- Investigator: SUBJECT HAS A SERIOUS UC AND WERE VERY DEHYDRATED AND THAT WAS THE REASON FOR THE PASIENT FAINTED.SUBJECT WAS IN HOSPITAL FOR OBSERVATION ONE DAY, AND HE GOT FLUID THERE.

- AbbVie: Development of the event is not consistent with study drug's mechanism of action. Additional risk factors include subject's age and pre-existing UC.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** . 158/93

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

[redacted] **20[redacted] CHOLESTEROL:** 3.7 mmol/l

[redacted] **20[redacted] ECG:** Sinus, frequency 54/min. No significant ST changes. Narrow QRS complexes. Upright T waves. Good R-progression on frontal wall

[redacted] **20[redacted] HDL:** 1.1 MMOL/L (normal 0.8 to 2.1)

[redacted] **20[redacted] HEMOGLOBIN:** 14.6 G/DL (normal 13.4 to 17.0)

[redacted] **20[redacted] PULSE:** 58 No units

[redacted] **20[redacted] RESPIRATION:** 16 /min

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

[redacted] **20[redacted] TRIGLYCERIDES:** 0.69 MMOL/L (normal 0.45 to 2.60)

[redacted] **20[redacted] TROPONIN T:** 7 ng/l (normal 0 to 15)

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

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: ANXIETY ATTACK WITH PALPITATIONS	20[redacted]
OTHER: ATOPIC DERMATITIS	NOT REPORTED
OTHER: MIGRAINE	20[redacted]
OTHER: RIGHT SIDE DERMOID CYST	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 315	259

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 315

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	QD	Y-M: 20[redacted]
LACTULOSE	20 mL	PRN	Y-M: 20[redacted]
MESALAZINE	1 g	BID	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
MESALAZINE	3 g	QD	Y-M: 20[redacted]
AZATHIOPRINE	25 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	20 mg	TID	Y-M: 20[redacted]
PREDNISONE	25 mg	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
MESALAZINE	1.5 g	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / -275
ETHINYLESTRADIOL;LEVONORGESTREL	1 ug	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
LACTULOSE	20 mL	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	1.5 g	QD	Y-M: 20[redacted]	ONGOING
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / -275	ONGOING
MECILLINAM	400 mg	TID	Y-M: 20[redacted] / 470	Y-M: 20[redacted] / 472
SULFAMETHOXAZOLE;TRIMETHOPRIM	2 OTHER: TABLET	BID	Y-M: 20[redacted] / 472	Y-M: 20[redacted] / 475
CLARITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 476	ONGOING
IPRATROPIUM	0.25 OTHER: MG/ML	PRN	Y-M: 20[redacted] / 477	ONGOING
SALBUTAMOL	1 OTHER: MG/ML	PRN	Y-M: 20[redacted] / 477	ONGOING
ETHINYLESTRADIOL;LEVONORGESTREL	1 ug	QD	Y: 20[redacted]	ONGOING

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

Event Description	COVID 19
Preferred term	COVID-19
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 781 / 467
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 476): Alanine Aminotransferase: 66 [10 - 45] U/L; Aspartate Aminotransferase: 74 [15 - 35] U/L; NPTST085-CRP: 60 [0 - 5] MG/L; NPTST222-SARS-COV-2: POSITIV [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 477): NPTST107-FERRITIN: 1127 [10 - 170] UG/L; NPTST126-HAPTOGLOBIN: 2.9 [0.4 - 1.9] G/L; [redacted]20[redacted] (RX DAY 486): NPTST085-CRP: 2 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 476): SPUTUM NPTST222-SARS-COV-2: Positive-NO RELEVANT FINDINGS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 476): X-RAY LUNGS: DENSITIES BIBASALLY APPROPRIATE WITH INFECTION

AE Stopped Initial Rx Day / Rx Day	835 / 521
Duration of AE	55 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COV 19
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

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。本被験者はノルウェーの 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，COVID-19 の事象を発現した。関連する病歴は，潰瘍性大腸炎，アトピー性皮膚炎，現飲酒者（1 日 2 杯未満），非喫煙者及び喘息であった。

Event 1 の臨床経過：

投与781日後＊，被験者は COVID-19 を発現した。投与の約28ヵ月後＊，COVID-19 は消失した。

投与780日後＊　，被験者は，発熱，咳嗽及び喘鳴を伴う呼吸器症状，頭痛，疲労，並びに若干の下痢を経験した。投与784日後＊　　，被験者は selexid を開始したが効果がなかったため，bactrim を開始した。1 日後に発疹（非重篤）が発現したため，投与789日後＊　　に bactrim を中止した。治験薬の投与は中止された。症状が常に悪化していたため，投与790日後＊　　に被験者は入院した。被験者は，全身状態の悪化，呼吸困難及び疲労感があった。また，高熱，乾性咳嗽，肺の痛み，頭部及び頚部の痛みがあった。当初は尿路感染症が疑われたが，抗生物質の投与で変化がなく，症状が悪化したため，COVID-19 と診断された。血液ガスは I 型呼吸不全を示していた。被験者は，右側に減弱した肺音が確認され，X 線検査では両肺底部で感染の妥当性を示す密度が認められた。klacid が開始された。酸素飽和度は，1 L の酸素を投与して 93%であった。酸素を 2 L に増やしたところ，酸素飽和度は 95%に上昇した。被験者は，安静時には呼吸努力をしていなかったが，起床時には呼吸状態が悪化した。被験者はアトロベント及び ventoline による噴霧器での治療を受け，良好な効果を得た。投与800日後＊，被験者は退院した。

投与された薬剤は，klacid，selexid，bactrim，アトロベント及び ventoline であった。

The patient's past medications include:

MESALAZIN for ULCERATIVE COLITIS ([redacted])

MESALAZIN ENEMA for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

SOLU-MEDROL for ULCERATIVE COLITIS ([redacted])

AZATIOPRIN for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　COVID-19 (10084268)　(COVID-19 (10084268))　[v.23.1]　[10084268]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of COVID 19

- Investigator: COVID 19

- AbbVie: Event is more likely related to a pandemic outbreak that has spread worldwide. Additional risk factor includes pre-existing asthma.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 66 U/L (normal 10 to 45)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 74 U/L (normal 15 to 35)

[redacted] **20[redacted] BLOOD GAS:** respiratory failure type 1, po2 8.2.

[redacted] **20[redacted] CRP:** 60 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 2 MG/L (normal 0 to 5)

[redacted] **20[redacted] LUNG X-RAY:** Densities bibasally appropriate with infection

[redacted] **20[redacted] SARS-COV-2:** Nasal: Positive

[redacted] **20[redacted] SARS-COV-2:** Sputum: Positive

[redacted] **20[redacted] SPO2:** 93 %

[redacted] **20[redacted] SPO2:** 95 %

[redacted] **20[redacted] U-STIX:** Slightly positive

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 30 mg	3[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: EARDRUM RUPTUR	20[redacted]
OTHER: GILBERTS SYNDROME	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 54	[redacted]20[redacted] / 418	365
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 419		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]
BLINDED THERAPY	1 OTHER: TBL	NOT REPORTED	Y-M: 20[redacted]
FISH OIL	1 OTHER: CAPSEL	QD	Y: 20[redacted]
VITAMIN D NOS	20 ug	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
MESALAZINE	4 g	QD	Y-M: 20[redacted]	ONGOING
BUPIVACAINE	75 mg	OTHER: ONCE	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
DALTEPARIN	5000 IU	QD	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
DEXAMETHASONE	8 mg	OTHER: ONCE	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
FENTANYL	350 ug	PRN	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
GLYCOPYRRONIUM;NEOSTIGMINE	1 OTHER: ML	OTHER: ONCE	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
METRONIDAZOLE	1.5 g	OTHER: ONCE	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
PARACETAMOL	1000 mg	BID	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
PROPOFOL	1598 mg	OTHER: ONCE	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
REMIFENTANIL	3.59 mg	OTHER: ONCE	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
ROCURONIUM	140 mg	PRN	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
THIOPENTAL	600 mg	OTHER: ONCE	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 520
TRAMADOL	50 mg	TID	Y-M: 20[redacted] / 520	Y-M: 20[redacted] / 532
DALTEPARIN	5000 IU	OTHER: ONCE	Y-M: 20[redacted] / 521	Y-M: 20[redacted] / 521
FISH OIL	1 OTHER: CAPSEL	QD	Y: 20[redacted]	ONGOING
VITAMIN D NOS	20 ug	QD	Y: 20[redacted]	ONGOING

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

Event Description	ACUTE APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 936 / 518

Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 519): Bilirubin: 74 [0 - 25] UMOL/L; NPTST085-CRP: 19 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 520): Bilirubin: 90 [0 - 25] UMOL/L; NPTST085-CRP: 29 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 521): Bilirubin: 130 [0 - 25] UMOL/L; NPTST085-CRP: 100 [0 - 5] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 520): APPENDECTOMY: GOOD

AE Stopped Initial Rx Day / Rx Day	939 / 521
Duration of AE	4 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN AT THE MOMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はノルウェーの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性虫垂炎の事象を発現した。関連する病歴は，広範囲な潰瘍性大腸炎（全大腸炎型），ジルベール症候群，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936日後＊　，被験者は急性虫垂炎を発現した。投与939日後＊　，急性虫垂炎は消失した。

投与936日後＊　，被験者は右下腹部の腹痛を発現し，その痛みには発現と消失の波があった。

投与937日後＊　，被験者は右下腹部の中等度/重度の持続性の痛みのために入院した。被験者は腹部 CT 検査を受け，虫垂炎が確認された。投与938日後＊　　，被験者は虫垂切除術を受け，

順調に経過した。投与939日後＊，被験者は退院した。

投与された薬剤は，ダルテパリン，フラジール，フラグミン，トラマドール及びレミフェンタニルであった。

The patient's past medications include:

SULFAZALAZIN for IBD-U ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

MONGERSEN for IBD ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Acute appendicitis (10000677) (Appendicitis (10003011)) [v.23.1] [10000677]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE APPENDICITIS

- Investigator: UNKNOWN AT THE MOMENT

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BILIRUBIN:** 74 umol/L (normal 0 to 25)

[redacted] **20[redacted] BILIRUBIN:** 130 umol/L (normal 0 to 25)

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 19 MG/L (normal 0 to 5)

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 100 MG/L (normal 0 to 5)

[redacted] **20[redacted] CT ABDOMEN:** Appendicitis

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	1[redacted]	MALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
ULCERATIVE COLITIES	20[redacted]
YERSINIA INFECTION	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 419	363
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 420		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4 g	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	600 mg	PRN	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
METHOTREXATE	25 mg	1 time per week	Y-M: 20[redacted]
AMPICILLIN	2 g	QID	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
GENTAMICIN	360 mg	QD	Y-M: 20[redacted]
MESALAZINE	2.4 g	QD	Y-M: 20[redacted]
METHOTREXATE	10 mg	1 time per week	Y-M: 20[redacted]
METHYLPREDNISOLONE	10 mg	BID	Y-M: 20[redacted]
METRONIDAZOLE	450 mg	TID	Y-M: 20[redacted]
SULFAMETHOXAZOLE;TRIMETHOPRIM	2 OTHER: TABLET	BID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
MESALAZINE	4 g	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
MESALAZINE	1 g	QD	Y-M: 20[redacted] / 61	ONGOING
MORPHINE	UNK mg	PRN	Y-M: 20[redacted] / 234	Y-M: 20[redacted] / 235

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

Event Description	PERIANAL ABSCESS
Preferred term	肛門膿瘍
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 624 / 205
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure	
NOT REPORTED	
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	CAUSE OF EVENT IS PATEINT ULCERATIVE COLITIES, AND THERE ARE NO KNOWN RISK FACTORS
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]:06:46
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。本被験者はノルウェーの 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肛門周囲膿瘍の事象を発現した。関連する病歴は，潰瘍性大腸炎，エルシニア感染，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与の約33ヵ月後＊，被験者は肛門周囲膿瘍を発現した。

投与653日後＊　，被験者は発熱，膿瘍部周辺の局所的な痛み，及び腫脹のために入院した。被験者は全般的に良好な状態であった。投与654日後＊　，被験者は肛門周囲膿瘍の切開手術を受けた。同日，被験者は良好な状態で退院した。

投与された薬剤は，トラマドール及びモルヒネであった。

The patient's past medications include:

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

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

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

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

SOLU-MEDROL for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

Causality for UPADACITINIB (Blinded)

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1) Perianal abscess (10034447) (Anal abscess (10048946)) [v.24.0] [10034447]

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 PERIANAL ABSCESS

- Investigator: CAUSE OF EVENT IS PATEINT ULCERATIVE COLITIES, AND THERE ARE NO KNOWN RISK FACTORS.

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

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
トランスアミナーゼ上昇				X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
HAY FEVER	20[redacted]
HEADACHE	20[redacted]
LEFT SIDED UC	20[redacted]
MENSTRUAL PAIN	19[redacted]
NEPHROLITHIASIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: SIGMOIDOSCOPY	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53

M14-234 SS2 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 54	[redacted]20[redacted] / 109	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 110	[redacted]20[redacted] / 473	364
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 474		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2 g	BID	Y-M: 20[redacted]
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
MESALAZINE	2 g	QD	Y-M: 20[redacted]
MESALAZINE	8 OTHER: TABLET	QD	Y-M: 20[redacted] / -335
ALFACALCIDOL	0.25 ug	QD	Y-M: 20[redacted] / -280

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
MESALAZINE	8 OTHER: TABLET	QD	Y-M: 20[redacted] / -335	Not reported
ALFACALCIDOL	0.25 ug	QD	Y-M: 20[redacted] / -280	Not reported
VITAMIN D NOS	2 g	QD	Y-M: 20[redacted] / 2	Not reported
DEXAMETHASONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
ENOXAPARIN	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
METAMIZOLE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
PARACETAMOL	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 113
BUDESONIDE	400 OTHER: MCG	BID	Y-M: 20[redacted] / 113	Not reported
DEXAMETHASONE	8 mg	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 116

Event #1: 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] / 572 / 99
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 110): Basophils: 0 [0 - 0.2] 10^9/L; Blood Urea Nitrogen: 3.319821 [2.820063 - 8.317401]

MMOL/L; Creatine Kinase MB: 0.34 [0.1 - 2.88] UG/L; Creatinine: 58.346152 [44.20163 - 79.562934] UMOL/L; Eosinophils: 0.01 [0 - 0.5] 10^9/L; Erythrocytes: 4.16 [3.9 - 5.1] 10^12/L; Glucose: 5.273165 [3.88549 - 5.495193] MMOL/L; Hematocrit: 0.371 [0.34 - 0.43] FRACTION OF 1; Hemoglobin: 125 [123 - 153] G/L; Leukocytes: 4.91 [4 - 10] 10^9/L; Lymphocytes: 0.54 [0.9 - 5] 10^9/L; Monocytes: 0.3 [0.2 - 1.2] 10^9/L; NPTST032-APTT: 30.3 [26 - 40] SEC; NPTST033-APTT RATIO: 1.04 [0.75 - 1.25] UNIT NOT REPORTED; NPTST085-CRP: 73.0 [0 - 5] MG/L; NPTST092-EGFR CKD-EPI: >60.0 [60 - NOT REPORTED] mL/min/1.73m2; NPTST137-IMMATURE GRANULOCYTES: 0.03 [0 - 0.09] 10^3/UL; NPTST139-INR: 1.07 [0.75 - 1.3] UNIT NOT REPORTED; NPTST157-MCH: 30.0 [28 - 33] PG; NPTST158-MCHC: 33.7 [33 - 36] G/DL; NPTST159-MCV: 89.2 [80 - 96] FL; NPTST165-MPV: 9.1 [8 - 12] FL; NPTST177-P-LCR: 17.8 [13 - 47] %; NPTST180-PCT: 0.27 [NOT REPORTED - NOT REPORTED] %; NPTST181-PDW: 9.7 [9 - 16] FL; NPTST194-PROTHROMBIN INDEX: 94.2 [75 - 110] %; NPTST196-PROTHROMBIN TIME: 13.7 [11.2 - 17.2] SEC; NPTST207-RDW-CV: 12.0 [11.5 - 14.5] %; NPTST208-RDW-SD: 39.9 [37 - 50] FL; NPTST251-TROPONIN T HS: 0.004 [0 - 0.014] NG/ML; NPTST256-UREA: 20 [17 - 50] MG/DL; Neutrophils: 4.06 [1.9 - 8] 10^9/L; Platelets: 292 [130 - 400] 10^9/L; Potassium: 4.01 [3.7 - 5.4] MMOL/L; Sodium: 140 [133 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 112): Alanine Aminotransferase: 104 [5 - 31] U/L; Aspartate Aminotransferase: 78 [5 - 31] U/L; Basophils: 0 [0 - 0.2] 10^9/L; Blood Urea Nitrogen: 3.998064 [2.820063 - 8.317401] MMOL/L; Creatinine: 50.389858 [44.20163 - 79.562934] UMOL/L; Eosinophils: 0 [0 - 0.5] 10^9/L; Erythrocytes: 3.73 [3.9 - 5.1] 10^12/L; Glucose: 8.32605 [3.88549 - 5.495193] MMOL/L; Hematocrit: 0.324 [0.34 - 0.43] FRACTION OF 1; Hemoglobin: 114 [123 - 153] G/L; Leukocytes: 4.45 [4 - 10] 10^9/L; Lymphocytes: 0.55 [0.9 - 5] 10^9/L; Monocytes: 0.19 [0.2 - 1.2] 10^9/L; NPTST085-CRP: 46.2 [0 - 5] MG/L; NPTST092-EGFR CKD-EPI: >60.0 [60 - NOT REPORTED] ML/MIN/1.73M^2; NPTST137-IMMATURE GRANULOCYTES: 0.02 [0 - 0.09] 10^3/UL; NPTST157-MCH: 30.6 [28 - 33] PG; NPTST158-MCHC: 35.2 [33 - 36] G/DL; NPTST159-MCV: 86.9 [80 - 96] FL; NPTST165-MPV: 9.8 [8 - 12] FL; NPTST177-P-LCR: 23.1 [13 - 47] %; NPTST180-PCT: 0.32 [NOT REPORTED - NOT REPORTED] %; NPTST181-PDW: 11.0 [9 - 16] FL; NPTST207-RDW-CV: 11.6 [11.5 - 14.5] %; NPTST208-RDW-SD: 38.0 [37 - 50] FL; NPTST254-TSH: 0.167 [0.27 - 4.2] UIU/ML; NPTST256-UREA: 24 [17 - 50] MG/DL; Neutrophils: 3.71 [1.9 - 8] 10^9/L; Platelets: 329 [130 - 400] 10^9/L; Potassium: 4.66 [3.7 - 5.4] MMOL/L; Sodium: 139 [133 - 145] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 110): OTHER UNKNOWN NPTST220-SARS COV 2 RNA REAL TIME PCR: Positive-SARS-COV-2; [redacted]20[redacted] (RX DAY 112): URINE NPTST260-URINE CULTURE: Negative; [redacted]20[redacted] (RX DAY 113): OTHER UNKNOWN NPTST223-SARS-COV-2 ANTIGEN TEST: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 110): COMPUTED TOMOGRAPHY OF THE CHEST WITHOUT CONTRAST: GROUND-GLASS OPACITIES, SCATTERED, PERIPHERALLY LOCATED, WITHOUT SIGNS OF ENLARGED MEDIASTINAL LYMPH NODES, NO FEATURES OF FLUID IN THE PLEURAL CAVITIES, MAY CORRESPOND TO INFLAMMATORY CHANGES IN THE COURSE OF COVID WITH AN INTENSITY OF ABOUT 15-18/40 POINTS ON THE CT SS SCALE

AE Stopped Initial Rx Day / Rx Day	586 / 113
Duration of AE	15 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	SARS-COV-2 INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Hepatic Disorder

Event Description	ELEVATED TRANSAMINASES
Preferred term	トランスアミナーゼ上昇
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 585 / 112
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	606 / 133
Duration of AE	22 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]:06:46
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。本被験者はポーランドの 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 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572日後＊　　，被験者は COVID-19 の感染症を発現した。投与586日後＊，COVID-19 の感染症は消失した。

投与572日後＊　　，被験者は重度のインフルエンザ様症状及び持続的な咳嗽を経験し始めた。投与583日後＊　，被験者は入院した。同日，被験者はCOVID-19の検査で陽性となり，胸部CT検査ですりガラス状陰影が認められた。被験者はステロイド薬及び非ステロイド性抗炎症薬での治療を受けた。被験者は呼吸不全の徴候を経験せず，被験者の全身状態は徐々に改善した。投与586日後＊，被験者はCOVID-19の検査で陰性となり，退院した。

投与された薬剤は，pyralgina，paracetamol，dexaven，クレキサン，デキサメタゾン及びパルミコートタービュヘイラーであった。

The patient's past medications include:

ASAMAX for ULCERATIVE COLITIS ([redacted])

ENCORTON for ULCERATIVE COLITIS ([redacted])

METYPRED for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　COVID-19 (10084268)　(COVID-19 (10084268))　[v.23.1]　[10084268]

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 COVID-19 INFECTION

- Investigator: SARS-COV-2 infection.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALT:** 104 U/L (normal 5 to 31)

[redacted] **20[redacted] AST:** 78 U/L (normal 5 to 31)

[redacted] **20[redacted] BMI:** 27 kg/m2

[redacted] **20[redacted] BUN:** 9.3 mg/dL (normal 7.9 to 23.3)

[redacted] **20[redacted] CHEST CT:** GROUND-GLASS OPACITIES, SCATTERED, PERIPHERALLY LOCATED, WITHOUT SIGNS OF ENLARGED MEDIASTINAL LYMPH NODES, NO FEATURES OF FLUID IN THE PLEURAL CAVITIES, MAY CORRESPOND TO INFLAMMATORY CHANGES IN THE COURSE OF COVID WITH AN INTENSITY OF ABOUT 15-18/40 POINTS ON THE CT SS SCALE

[redacted] **20[redacted] CKMB:** 0.34 NG/ML (normal 0.10 to 2.88)

[redacted] **20[redacted] CREATININE:** 0.66 mg/dL (normal 0.50 to 0.90)

[redacted] **20[redacted] CRP:** 73.0 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] CRP:** 46.2 MG/L (normal 0.0 to 5.0)

[redacted] **20[redacted] GLUCOSE:** 95 mg/dL (normal 70 to 99)

[redacted] **20[redacted] HEMATOCRIT:** 37.1 % (normal 34.0 to 43.0)

[redacted] **20[redacted] HEMOGLOBIN:** 12.5 G/DL (normal 12.3 to 15.3)

[redacted] **20[redacted] NASOPHARYNGEAL SWAB SARS-COV-2:** Positive

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

[redacted] **20[redacted] PLT:** 292 X10**3/MCL (normal 130 to 400)

[redacted] **20[redacted] POTASSIUM:** 4.0 MMOL/L (normal 3.7 to 5.4)

[redacted] **20[redacted] SODIUM:** 140 MMOL/L (normal 133 to 145)

[redacted] **20[redacted] TROPONIN T:** 0.004 NG/ML (normal 0.000 to 0.014)

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

[redacted] **20[redacted] WBC:** 4.91 X10**3/MCL (normal 4.00 to 10.00)

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY ANEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 54	54
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 55		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	5 mg/kg	OTHER: 8/8 WEEKS	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: 8/8 WEEKS	Y-M: 20[redacted]
BUDESONIDE	2 mg	QD	Y-M: 20[redacted] / -296
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -296
MESALAZINE	3 mg	QD	Y-M: 20[redacted] / -143
DESOGESTREL	75 ug	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
MESALAZINE	3 mg	QD	Y-M: 20[redacted] / -143	ONGOING
ETHINYLESTRADIOL;GESTODENE	0.105 mg	QD	Y-M: 20[redacted] / 599	Y-M: 20[redacted] / 1083
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 OTHER: SACHETS	QD	Y-M: 20[redacted] / 1011	Y-M: 20[redacted] / 1012
PROPOFOL	170 mg	QD	Y-M: 20[redacted] / 1012	Y-M: 20[redacted] / 1012
ETHINYLESTRADIOL;ETONOGESTREL	0,120 + 0,015 mg	OTHER: ONGOING	Y-M: 20[redacted] / 1091	ONGOING
RIVAROXABAN	10 mg	QD	Y-M: 20[redacted] / 1120	Y-M: 20[redacted] / 1130

Event #1: Serious Adverse Event

Event Description	LOWER LIMBS VARICOSE VEINS
Preferred term	静脈瘤
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1080 / 1026
Age at AE Onset	2[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day 1174 / 1120

Duration of AE	95 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	LOWER LIMBS INSUFFICIENCY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はポルトガルの 2[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，下肢静脈瘤の事象を発現した。関連する病歴は，潰瘍性大腸炎，鉄欠乏性貧血，非喫煙者，非飲酒者及び母方の静脈瘤の家族歴であった。家族歴は，母方の静脈瘤であった。

Event 1 の臨床経過：

投与1080日後＊　，被験者は下肢静脈瘤を発現した。投与1174日後＊，下肢静脈瘤は消失した。

被験者は，夏場の下肢の痛み及び静脈瘤の存在を訴えていた。

投与1173日後＊ ，被験者は入院した。被験者は左大伏在静脈の結紮術及びストリッピング手術を受けた。投与1174日後＊，被験者は退院した。

投与された薬剤は，イグザレルトであった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Open Label)

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1) Varicose veins of lower extremities (10047013) (Varicose vein (10046996)) [v.24.0] [10047013]

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 LOWER LIMBS VARICOSE VEINS

- Investigator: Lower limbs insufficiency

- AbbVie: Risk factors include maternal history of varicose veins and female gender. Additionally, lower limb varicose veins are common in the general population with reported prevalence ranging between 10% and 30% worldwide.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY WEIGHT:** 5[redacted] KG

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

Reason for Narrative

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

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

Medical History	Onset Year
CYTOMEGALOVIRUS INFECTION	20[redacted]
DUODENAL ULCER	20[redacted]
EPSTEIN-BARRA VIRUS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HEAD INJURY	19[redacted]
HEPATITIS A	19[redacted]
LABIAL HERPES	20[redacted]
LEFT SIDED UC	20[redacted]
MYOPIA	19[redacted]
PROTRUSION OF THE LUMBAR SPINE	20[redacted]
TOXIC HEPATITIS	20[redacted]
ULCERATIVE COLITIS, CHRONIC RECURRENT COURSE, TOTAL LESION	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	0.3 PACK	15	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 58	58
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 59	[redacted] / 142	84
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 143		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	4 mg	QD	Y: 20[redacted]
SULFASALAZINE	1.5 g	BID	Y: 20[redacted]
MESALAZINE	2 g	BID	Y: 20[redacted]
MESALAZINE	3 g	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
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	111.896 g	BID	Y-M: 20[redacted] / 209	Y-M: 20[redacted] / 209
GADOPENTETIC ACID	16.6 mL	QD	Y-M: 20[redacted] / 209	Y-M: 20[redacted] / 209
PROPOFOL	UNKNOWN mg	QD	Y-M: 20[redacted] / 210	Y-M: 20[redacted] / 210
MESALAZINE	3 g	QD	Y: 20[redacted]	Not reported

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted] / 351 / 209
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted] (RX DAY 209): MR-PICTURE OF THE SMALL PELVIS WITH CONTRAST ENHANCEMENT: THE MRI PICTURE MAY CORRESPOND TO MILD INFLAMMATORY CHANGES IN THE RECTUM AND PARTIALLY VISUALIZED PARTS OF THE SIGMOID COLON. QUANTITATIVE AND MILDLY EXPRESSED QUALITATIVE

INCREASE IN PARORECTAL, SAC RAL AND GLUTEAL LYMPH NODES. THE MRI PICTURE MAY CORRESPOND TO INFLAMMATORY CHANGES (PROBABLY CHRONIC) OF THE PROSTATE GLAND. THE ABOVE CHANGES IN THE PERIPHERAL ZONE CORRESPOND TO 2 POINTS ON THE SCA LE PI-RADSV 2.; [redacted]20[redacted] (RX DAY 210): COLONOSCOPY WITH EXAMINATION OF THE TERMINAL ILEUM: UC MODERATE FORM (MODERATE DEGREE OF INFLAMMATION ACTIVITY); FIBROESOPHAGEAL GASTRODUODENOSCOPY: SUPERFICIAL GASTRITIS. SUPERFICIAL DUODENITIS.

AE Stopped Initial Rx Day / Rx Day	353 / 211
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	LACK OF EFFECTIVENESS OF THE STUDY DRUG
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はロシア連邦の 3[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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 0.3 箱を 15 年間），十二指腸潰瘍，潰瘍性大腸炎（慢性的な再燃の経過，全病変部），胃食道逆流性疾患及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与351日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。

本事象発現前，被験者は肛門科医の診察を受け，生検を伴う内視鏡検査を受けた。被験者は結腸内視鏡検査も受け，潰瘍性大腸炎の悪化が確認された。

投与351日後＊　，被験者は更なる検査及び管理のために入院した。被験者は肛門管の痛み及び不快感を経験し，粘液及び血塊を伴う便が 1 日 3–4 回認められた。被験者は外科の診察も受けた。投与353日後＊　，被験者は，居住地で治療を続けることを勧められ，退院した。

投与された薬剤は，prednisone，cortiment 及びメサラジンであった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.1] [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 EXACERBATION OF ULCERATIVE COLITIS

- Investigator: LACK OF EFFECTIVENESS OF THE STUDY DRUG

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

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] COLONOSCOPY WITH EXAMINATION OF THE TERMINAL ILEUM:** UC moderate form (moderate degree of inflammation activity)

[redacted] **20[redacted] FIBROESOPHAGEAL GASTRODUODENOSCOPY**: Superficial gastritis. Superficial duodenitis.

[redacted] **20[redacted] MR-PICTURE OF THE SMALL PELVIS WITH CONTRAST ENHANCEMENT:** The mri picture may correspond to mild inflammatory changes in the rectum and partially visualized parts of the sigmoid colon. Quantitative and mildly expressed qualitative increase in parorectal, sacral and gluteal lymph

nodes. The mri picture may correspond to inflammatory changes (probably chronic) of the prostate gland. Theabove changes in the peripheral zone correspond to 2 points on the scale pi-radsv 2.

[redacted] **20[redacted] WEIGHT:** 8[redacted] KG

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
甲状腺腺腫	X			

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

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
RECTAL PSEUDOPOLYPOSIS	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-675 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 111	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 112	[redacted]20[redacted] / 202	91
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 203		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	TID	Y-M: 20[redacted]
MESALAZINE	2.5 g	QD	Y-M: 20[redacted]
MESALAZINE	1.2 g	BID	Y-M: 20[redacted]
MESALAZINE	3 g	QD	Y: 20[redacted]
MESALAZINE	2 g	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
MESALAZINE	1.2 g	BID	Y-M: 20[redacted]	Not reported

Event #1: Serious Adverse Event

Event Description	FOLLICULAR ADENOMA OF THE LEFT LOBE OF THE THYROID GLAND
Preferred term	甲状腺腺腫
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 306 / 104
Age at AE Onset	3[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 105): HISTOLOGICAL EXAMINATION OF THE THYROID GLAND: FOLLICULAR ADENOMA (4.0 CM) OF THE LEFT LOBE OF THE THYROID GLAND; LEFT HEMITERIOIDECTOMY: THE POSTOPERATIVE PERIOD WAS UNREMARKABLE. WITH CONTROL LARYNGOSCOPY, THE VOCAL CORDS ARE MOBILE, SYMMETRICAL, AND CLOSE COMPLETELY. THE POSTOPERATIVE WOUND HEALS BY PRIMARY INTENTION.; [redacted]20[redacted] (RX DAY 106): VIDEO LARYNGOSCOPY: FROM THE SIDE OF THE NASOPHARYNX AND OROPHARYNX WITHOUT INFLAMMATORY AND ORGANIC PATHOLOGY. CHERPANONADLARYNGEAL FOLDS AND PIRIFORM SINUSES WITHOUT VISIBLE PATHOLOGICAL CHANGES. LARYNX - THE MUCOUS ME MBRANE IS HYPEREMIC, SMOOTH. THE GLOTTIS IS TRIANGULAR, SYMMETRICAL. THE VOCAL CORDS ARE MOBILE, COMPLETELY CLOSED DURING PHONATION

AE Stopped Initial Rx Day / Rx Day	308 / 106
Duration of AE	3 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DIFFUSE NODULAR GOITER

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

Generated: [redacted]20[redacted]:06:46
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。本被験者はロシア連邦の 3[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，甲状腺左葉の濾胞性腺腫の事象を発現した。関連する病歴は，潰瘍性大腸炎，直腸の偽性ポリポーシス，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：
投与306日後＊　，被験者は甲状腺左葉の濾胞性腺腫を発現した。投与308日後＊　，甲状腺左葉の濾胞性腺腫は消失した。

投与の約8ヵ月後＊から約10ヵ月後＊に，被験者はびまん性及び結節性の甲状腺腫（非重篤）を経験した。

投与306日後＊　，被験者は入院した。投与307日後＊　　，被験者は右側甲状腺切除術及び甲状腺の組織学的検査を受けた。投与308日後＊　，被験者はビデオカメラでの喉頭鏡検査を受け，同日，被験者は退院し，外来診療に切り替えられた。

The patient's past medications include:

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

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

Causality for UPADACITINIB (Open Label)

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1) Thyroid adenoma (10043688) (Thyroid adenoma (10043688)) [v.23.1] [10043688]

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

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

Dechallenge: Yes

Alternative Etiology for UPADACITINIB (Open Label)

Event of FOLLICULAR ADENOMA OF THE LEFT LOBE OF THE THYROID GLAND

- Investigator: Diffuse nodular goiter

- AbbVie: Follicular adenoma is a common neoplasm of the thyroid gland with incident rate of 3-4.3%. Most cases arise sporadically but known risk factors include iodine deficiency and genetic alterations.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] HISTOLOGY EXAMINATION OF THE THYROID GLAND:** FOLLICULAR ADENOMA (4.0 CM) OF THE LEFT LOBE OF THE THYROID GLAND

[redacted] **20[redacted] VIDEO LARYNGOSCOPY:** FROM THE SIDE OF THE NASOPHARYNX AND OROPHARYNX WITHOUT INFLAMMATORY AND ORGANIC PATHOLOGY. CHERPANONADLARYNGEAL FOLDS AND PIRIFORM SINUSES WITHOUT VISIBLE PATHOLOGICAL CHANGES. LARYNX - THE MUCOUS MEMBRANE IS HYPEREMIC, SMOOTH. THE GLOTTIS IS TRIANGULAR, SYMMETRICAL. THE VOCAL CORDS ARE MOBILE, COMPLETELY CLOSED DURING PHONATION.

[redacted] **20[redacted] WEIGHT:** 6[redacted] KG

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
子宮頚部扁平上皮癌	X	X		X

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: FRACTURE OF RIGHT MALLEOLAR JOINT	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	0.5 PACK	2	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 420	363
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 420	[redacted]20[redacted] / 616	197

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	QID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	TID	Y-M: 20[redacted]
PREDNISONE	20 mg	BID	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
DROTAVERINE	40 mg	OTHER: AS NEEDED	Y-M: 20[redacted] / -278

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
MESALAZINE	1 g	QID	Y-M: 20[redacted]	Not reported
DROTAVERINE	40 mg	OTHER: AS NEEDED	Y-M: 20[redacted] / -278	ONGOING
METAMIZOLE	500 mg	TID	Y-M: 20[redacted] / 177	ONGOING

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

Event Description SQUAMOUS CELL CARCINOMA OF CERVIX OF UTERI

Preferred term 子宮頚部扁平上皮癌

AE Onset Date / Initial Rx Day / Rx Day [redacted]20[redacted] / 603 / 184

Age at AE Onset 4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 184): NPTST132-HISTOLOGY: CARCINOMA [NOT REPORTED - NOT REPORTED] HISTOLOGY

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 184): GYNECOLOGICAL EXAMINATION WITH HISTOLOGY: WELL-DIFFERENTIATED NON-KERATISING SQUAMOUS CARCINOMA OF CERVIX; [redacted]20[redacted] (RX DAY 241): GYNAECOLOGIC ULTRASOUND: CARCINOMA OF THE CERVIX UTERI SQUAMOCELLULAR, STAGE TIIB, REFERRED FOR NEOADJUVANT RADIOTHERAPY; [redacted]20[redacted] (RX DAY 491): PET CT (FDG): POST NEOADJUVANT THERAPY OF CA CERVICIS UTERIS WITH NO FDG-AVID VIABLE TISSUE IN THE PELVIC REGION ON THE PET CT SCAN. MYOMA UTERI.; [redacted]20[redacted] (RX DAY 515): GYNAECOLOGIC EXAMINATION + US: CA CERVICIS IIA, POST CHEMOTHERAPY, RADIOTHERAPY, BRACHYTHERAPY. CERVIX WITH NO DEFINITE LESION. SURGICAL THERAPY IS NOT INDICATED DUE TO GOOD RESPONSE TO ONCOLOGICAL THERAPY.

AE Stopped Initial Rx Day / Rx Day ONGOING

Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PROGRESSION FROM POSSIBLE DYSPLASIA
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:06:46

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。本被験者はスロバキア共和国の 4[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，子宮頚部の扁平上皮癌の事象を発現した。関連する病歴は，元喫煙者（1 日 0.5 箱を 2 年間），潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与603日後＊，被験者は子宮頚部の扁平上皮癌を発現した。

投与591日後＊ ，被験者は月経と関係のない膣出血を経験し始めた。投与603日後＊，被験者は子宮頸癌の疑いで婦人科医の診察を受けた。投与615日後＊，組織検査の結果，子宮頚部の癌が指摘された。被験者は外科療法を受けることとなった。

投与659日後＊ ，被験者は入院し，検査が完了した。投与660日後＊，被験者は退院した。

ヒトパピローマウイルス感染の有無は確認できなかった。治験薬の投与は完全に中止された。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Squamous cell carcinoma of the cervix (10041848) (Squamous cell carcinoma of the cervix (10041848)) [v.23.0] [10041848]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of SQUAMOUS CELL CARCINOMA OF CERVIX OF UTERI

- Investigator: Progression from possible dysplasia

- AbbVie: Events etiology more likely related to HPV infection; Human papillomavirus (HPV) is central to the development of cervical neoplasia and can be detected in 99.7 percent of cervical cancers.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] GYNAECOLOGIC EXAMINATION/ULTRASOUND:** Ca cervicis IIA, post chemotherapy, radiotherapy, brachytherapy. Cervix with no definite lesion. Surgical therapy is not indicated due to good response to oncological therapy.

[redacted] **20[redacted] GYNAECOLOGIC ULTRASOUND:** Carcinoma of the cervix uteri squamocellular stage TIIB, referred for neoadjuvant radiotherapy.

[redacted] **20[redacted] HISTOLOGY:** Specimen: cervical tissue - well-differentiated non-keratising squamous carcinoma of cervix

[redacted] **20[redacted] MRI:** Stage II A1

20[redacted] PAP SMEAR: negative

[redacted] **20[redacted] PET CT (FDG):** Post neoadjuvant therapy of Ca cervicis uteris with no FDG-avid viable tissue in the pelvic region on the PET CT scan. Myoma uteri.

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

Reason for Narrative

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

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

Medical History	Onset Year
BILATERAL CATARACT	20[redacted]
CATARACTS SECONDARY TO PREDNISONE	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTRITIS	20[redacted]
GENERALIZED JOINT TENDERNESS ARTHRITIS	20[redacted]
HEADACHES	20[redacted]
INTERMITTENT ANEMIA	20[redacted]
IRITIS	20[redacted]
NASAL ULCERS	20[redacted]
OSTEOPEMINA	20[redacted]
PALPITATIONS IDIOPATHIC	20[redacted]
ULCERATIVE COLITIS	20[redacted]
UVEITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: BILATERAL CATARACT REMOVAL	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	3	
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 56	[redacted] / 420	365
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 421		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	15 mg	QD	Y-M: [redacted]
PARACETAMOL	1 g	QD	Y-M: [redacted]
FOLIC ACID	5 mg	OTHER: DAILY	Y: [redacted]
MESALAZINE	1.6 g	OTHER: DAILY	Y: [redacted]
PREDNISONE	5 mg	OTHER: DAILY	Y: [redacted]
SULFASALAZINE	10 mg	OTHER: EVERY SECOND DAY	Y: [redacted]
CALCIUM CARBONATE;GLYCINE	2 mg	OTHER: DAILY	Y: [redacted]
LANSOPRAZOLE	30 mg	OTHER: DAILY	Y: [redacted]
ERGOCALCIFEROL	50 000 OTHER: IU	OTHER: WEEKLY	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
PARACETAMOL	1 g	QD	Y-M: [redacted]	Not reported
CAFFEINE;CODEINE;MEPROBAMATE;PARACETAMOL	2 OTHER: TABLETS	PRN	Y-M: [redacted] / 97	Not reported
AMOXICILLIN	1 g	TID	Y-M: [redacted] / 98	Y-M: [redacted] / 103
AMOXICILLIN;CLAVULANIC ACID	1 G 4 HOURLY g	OTHER: 4 HOURLY	Y-M: [redacted] / 98	Y-M: [redacted] / 98
AMOXICILLIN;CLAVULANIC ACID	625 mg	TID	Y-M: [redacted] / 98	Y-M: [redacted] / 101
FOLIC ACID	5 mg	OTHER: DAILY	Y: [redacted]	Not reported

CALCIUM CARBONATE;GLYCINE	2 mg	OTHER: DAILY	Y: 20[redacted]	Not reported
LANSOPRAZOLE	30 mg	OTHER: DAILY	Y: 20[redacted]	Not reported
ERGOCALCIFEROL	50 000 OTHER: IU	OTHER: WEEKLY	Y: 20[redacted]	Not reported

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

Event Description	CELLULITIS 5TH FINGER RIGHT HAND
Preferred term	蜂巣炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 517 / 97
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	551 / 131
Duration of AE	35 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:06:46
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。本被験者は南アフリカの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右手第 5 指の蜂巣炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，全身の関節圧痛及び関節炎，現喫煙者（1 日 1 箱を 3 年間）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517日後＊　，被験者は右手第 5 指の蜂巣炎を発現した。投与551日後＊　，右手第 5 指の蜂巣炎は消失した。

本事象発現前の投与の約16ヵ月後＊，被験者は右手第5指の爪真菌症（非重篤）を経験した。その後，投与から約17ヵ月目＊の初旬に爪を除去した。投与517日後＊，被験者は感染の悪化による蜂巣炎と診断された。指全体が赤く腫れており，膿が出ていた。被験者は抗生物質での治療を完了し，傷の管理を継続した。被験者は週 1 回の通院を継続し，著しい改善が認められた。

投与された薬剤は，アモキシシリン，stilpane 及びオーグメンチンであった。

The patient's past medications include:

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1)　Cellulitis of finger (10007910)　(Cellulitis (10007882))　[v.23.0]　[10007910]

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 CELLULITIS 5TH FINGER RIGHT HAND

- Investigator: Not applicable

- AbbVie: Event more likely related to a complication from the nail removal procedure for concurrent onychomycosis approximately 2 weeks prior to event onset.

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
喘息	X			
ウイルス性肺炎	X			X

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

Medical History	Onset Year
ASTHMA: INTERMITTENT	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: INTERMITTENT LOWER BACK PAIN POST MOTORCAR ACCIDENT	20[redacted]
OTHER: INTERMITTENT SINUS CONGESTION FOR PAST 3 YEARS	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	15	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	7.5 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 315	259

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 316

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ETHAMBUTOL;ISONIAZID;PYRAZINAMIDE;RIFAMPICIN	4 OTHER: TABLET	QD	Y-M: 20[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]
METHOTREXATE	25 mg	OTHER: WEEKLY	Y-M: 20[redacted]
PREDNISONE	15 mg	QD	Y-M: 20[redacted]
FLUTICASONE	1 OTHER: SPRAY	QD	Y-M: 20[redacted] / -28

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]	ONGOING
METHOTREXATE	25 mg	OTHER: WEEKLY	Y-M: 20[redacted]	ONGOING
FLUTICASONE	1 OTHER: SPRAY	QD	Y-M: 20[redacted] / -28	ONGOING
BUDESONIDE	1 OTHER: NEBULE	BID	Y-M: 20[redacted] / 111	ONGOING
FEXOFENADINE	180 mg	QD	Y-M: 20[redacted] / 111	ONGOING
IPRATROPIUM;SALBUTAMOL	1 OTHER: NEBULE	QID	Y-M: 20[redacted] / 111	ONGOING
METHYLPREDNISOLONE	40 mg	BID	Y-M: 20[redacted] / 111	ONGOING
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 371	Y-M: 20[redacted] / 378
IPRATROPIUM;SALBUTAMOL	2.5/800 mg	QID	Y-M: 20[redacted] / 371	Y-M: 20[redacted] / 378
SALBUTAMOL	2 mg	PRN	Y-M: 20[redacted] / 371	Y-M: 20[redacted] / 372
ERTAPENEM	1 g	QD	Y-M: 20[redacted] / 372	Y-M: 20[redacted] / 377
AZITHROMYCIN	25 mg	OTHER: THREE TIMES PER WEEK	Y-M: 20[redacted] / 377	Y-M: 20[redacted] / 398
BUDESONIDE	25 mg	TID	Y-M: 20[redacted] / 377	Y-M: 20[redacted] / 384
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 377	Y-M: 20[redacted] / 382

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF ASTHMA
Preferred term	喘息
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 426 / 111

Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 111): Hemoglobin: 152 [130 - 170] G/L; NPTST085-CRP: 1 [0 - 5] MG/L; NPTST103-ESTIMATED GFR: 89 [0 - 90] ML/MIN; NPTST135-IGE: 97.3 [0 - 22] IU/ML; NPTST182-PHADIATOP: 0.19 [0 - 0.35] IU/ML; NPTST248-TROPONIN I (STRATUS): <10 [0 - 10] MG/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 114): BRONCHIAL LAVAGE: NO PUS CELLS BACTERIA ABSENT YEAST CELLS ABSENT ACID BACILLI BACTERIAL FLORA ABSENT NORMAL ORAL BACTERIA FLORA

AE Stopped Initial Rx Day / Rx Day	435 / 120
Duration of AE	10 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PRE -EXISTING CONDITION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

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

Event Description	PNEUMONIA (VIRAL)
Preferred term	ウイルス性肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 686 / 371
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 371): Bicarbonate: 30 [21 - 31] MMOL/L; Chloride: 98 [101 - 109] MMOL/L; Creatinine: 82 [59 - 104] UMOL/L; Erythrocytes: 4.91 [4.5 - 5.9] 10^12/L; Hemoglobin: 143 [125 - 173] G/L; Leukocytes: 44 [40 - 50] 10^9/L; NPTST058-C-REACTIVE PROTEIN: 132 [NOT REPORTED - 5] mg/L; NPTST157-MCH: 29 [28 - 35] PG; NPTST159-MCV: 90 [81 - 95] FL; Potassium: 4.8 [3.5 - 5.1] MMOL/L; Sodium: 136 [136 - 146] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	692 / 377
Duration of AE	7 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	MEDICAL HISTORY
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]:06:46
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。本被験者は南アフリカの 3[redacted] 歳の男性であり，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，喘息の悪化の事象を発現した。関連する病歴は，喘息及び断続的な副鼻腔うっ血，元喫煙者（1 日 1 箱を 15 年間）及び現飲酒者（1 日 2–4 杯）であった。

Event 1 の臨床経過：

投与426日後＊　　，被験者は喘息の悪化を発現した。投与435日後＊ ，喘息の悪化は消失した。

本事象発現前の投与206日後＊，被験者は喘息の悪化（非重篤）を発現していた。

被験者は 投与427日後＊，喘息の悪化があり，入院した。被験者は，息切れ及び持続的な咳の発作に伴う失神を訴えた。胸部 CT 検査（日付不明）が実施され，投与429日後＊ に気管支鏡検査及び気管支洗浄を受けた。投与436日後＊　，被験者は退院した。

投与された薬剤は，パルミコート，fexo，ソル・メドロール，prednisone 及び duolin nebulizer 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], [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) Exacerbation of asthma (10015575) (Asthma (10003553)) [v.23.0] [10015575]

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 EXACERBATION OF ASTHMA

- Investigator: PRE -EXISTING CONDITION

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BRONCHIAL LAVAGE:** No Pus cells Bacteria absent Yeast cells absent Acid bacilli bacterial flora absent normal oral bacteria flora

20[redacted] CHEST CT: Results not reported

Unknown date CHEST X-RAY: Results not provided

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

[redacted] **20[redacted] IGE:** 97.3 IU/mL (normal 0 to 22)
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者は南アフリカの 3[redacted] 歳の男性であり，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，肺炎（ウイルス性）の事象を発現した。関連する病歴は，喘息，潰瘍性大腸炎，副鼻腔うっ血，元喫煙者（1 日 1 箱を 15 年間）及び現飲酒者

（1 日 2–4 杯）であった。

Event 2 の臨床経過：

投与686日後＊　，被験者は肺炎（ウイルス性）を発現した。投与692日後＊，肺炎（ウイルス性）は消失した。

入院の約 1 週間前，被験者は喘息の悪化（非重篤）を経験していた。被験者は急性呼吸不全及び急性の息切れも発現したが，治療に反応しなかった。投与686日後＊　，被験者は肺炎で入院した。投与692日後＊　，被験者は退院した。

投与された薬剤は，ventolin，duolin，クレキサン及び entapenem であった。

The patient's past medications include:

PREDNISONE for UC ([redacted])

BINDOCLAV for BRONCHITIS ([redacted])

PHOLTEX for BRONCHITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Pneumonia viral (10035737) (Pneumonia viral (10035737)) [v.22.0] [10035737]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of PNEUMONIA (VIRAL)

- Investigator: Medical History

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BRONCHIAL LAVAGE:** NO PUS CELLS BACTERIA ABSENT YEAST CELLS ABSENT ACID BACILLI BACTERIAL FLORA ABSENT NORMAL ORAL BACTERIA FLORA

[redacted] **20[redacted] CRP:** 1 MG/L (normal 0 to 5)

[redacted] **20[redacted] EGFR:** 89 ML/Min (normal 0 to 90)

[redacted] **20[redacted] HEMATOCRIT:** 44 % (normal 40 to 50)

[redacted] **20[redacted] HEMOGLOBIN:** 15.2 G/DL (normal 13.0 to 17.0)

[redacted] **20[redacted] HEMOGLOBIN:** 14.3 G/DL (normal 12.5 to 17.3)

[redacted] **20[redacted] IGE:** 97.3 IU/mL (normal 0 to 22.0)

[redacted] **20[redacted] MCH:** 29 PG (normal 28 to 35)

[redacted] **20[redacted] MCV:** 90 FL (normal 81 to 95)

[redacted] **20[redacted] PHADIATOP:** 0.19 IU/mL (normal 0.00 to 0.35)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.91 X10**12/L (normal 4.5 to 5.9)

[redacted] **20[redacted] TROPONIN 1:** <10 mg/L

[redacted] **20[redacted] X-RAY:** No abnormalities seen.

[redacted] **20[redacted] X-RAY:** Left lower lobe vague opacification with partial effacemt of the left hemidiaphragm countour suggestive of subsegmental consolidation.

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

Reason for Narrative

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

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

Medical History	Onset Year
COGNITIVE OR PSYCHIATRIC DISORDER: POST TRAUMATIC STRESS DISORDER	20[redacted]
DEPRESSION: DUE TO TRAUMATIC EVENT	20[redacted]
DRUG ABUSE: INTERMITTENT COCAINE USE STOPPED 1 YEAR AGO	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ACNE	20[redacted]
OTHER: INTERMITTENT SINUS CONGESTION	19[redacted]
OTHER: JOINT PAIN ANKLES AND KNEES	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	CURRENT	0.05 PACK	15	
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 365	308
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 367		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	25 mg	1 time per week	Y-M: 20[redacted]
BUDESONIDE	1 OTHER: ENEMA	BID	Y-M: 20[redacted]
METHOTREXATE	25 mg	OTHER: WEEKLY	Y-M: 20[redacted]
PROBIOTICS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted]
FOLIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -276
PARACETAMOL;TRAMADOL	2 OTHER: TABLETS	PRN	Y-M: 20[redacted] / -128
TETRACYCLINE	300 mg	QD	Y-M: 20[redacted] / -36
DROSPIRENONE;ETHINYLESTRADIOL	1 OTHER: TABLET	QD	Y: 20[redacted]
PANTOPRAZOLE	20 mg	PRN	Y: 20[redacted] / -347

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FOLIC ACID	5 mg	OTHER: ONCE WEEKLY	Y-M: 20[redacted] / 170	ONGOING
METHOTREXATE	25 mg	OTHER: ONCE WEEKLY	Y-M: 20[redacted] / 170	Y-M: 20[redacted] / 343
AMOXICILLIN;CLAVULANIC ACID	500 mg	BID	Y-M: 20[redacted] / 292	Y-M: 20[redacted] / 322
BUDESONIDE	200 mg	TID	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 350
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 344
PIPERACILLIN	4 g	QID	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 350
SALBUTAMOL	200 mg	PRN	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 350
HYDROCORTISONE	200 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / 344	Y-M: 20[redacted] / 344
POVIDONE-IODINE	1 OTHER: SPRAY	TID	Y-M: 20[redacted] / 346	Y-M: 20[redacted] / 350
XYLOMETAZOLINE	1 OTHER: PUFF	TID	Y-M: 20[redacted] / 346	Y-M: 20[redacted] / 350
DROSPIRENONE;ETHINYLESTRADIOL	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING
PANTOPRAZOLE	20 mg	PRN	Y: 20[redacted] / -347	Y-M: 20[redacted] / 559

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 707 / 341
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 343): Leukocytes: 11.4 [4 - 10.5] 10^9/L; NPTST085-CRP: 150.8 [0 - 5] MG/L; NPTST086-CULTURE: NORMAL [NOT REPORTED - NOT REPORTED] NOT APPLICABLE

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 343): CHEST X-RAY: SHADOWING IN BOTH MIDZONES

AE Stopped Initial Rx Day / Rx Day	716 / 350
Duration of AE	10 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INFLUENZA
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はオランダの 3[redacted] 歳の女性であり，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，肺炎の事象を発現した。関連する病歴は，断続的な副鼻腔うっ血，断続的な副鼻腔炎，潰瘍性大腸炎，現喫煙者（1 日 0.5 箱を 15 年間）及び現飲酒者（1 日 2–4 杯）であった。

この被験者は，先行の M14-234 試験では，被験者番号 [redacted] であり，20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで盲検化された治験薬を投与された。

Event 1 の臨床経過：

投与707日後＊，被験者は肺炎を発現した。投与716日後＊，肺炎は消失した。

投与701日後＊ ，被験者はインフルエンザ（非重篤）を発現し，投与709日後＊ ，発熱及び息切れのため入院した。被験者は肺炎と診断された。被験者は，7 日間の抗生物質の投与を完了した。被験者の症状は改善したが，頭痛及び振戦は続いていた。被験者は神経科を紹介された。投与716日後＊ ，被験者は退院した。

投与された薬剤は，ventolin，レボフロキサシン，ピペラシリン及びパルミコートであった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Open Label)

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

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Open Label)

Event of PNEUMONIA

- Investigator: Influenza

- AbbVie: Event more likely a complication of influenza infection, a common viral infection in the general population. Additional risk factors include current smoker (0.5 ppd) and alcohol (2-4 drinks per day).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** SHADOWING IN BOTH MIDZONES

[redacted] **20[redacted] CRP:** 150.8 MG/L (normal 0 to 5)

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

[redacted] **20[redacted] WBC:** 11.4 X10**9/L (normal 4 to 10.5)

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

Reason for Narrative

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

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

Medical History	Onset Year
BILATERAL SHOULDER TENDONITIS	20[redacted]
FATIGUE	20[redacted]
GASTRIC REFLUX	20[redacted]
INTERMITTENT MIGRAINE	20[redacted]
LEFT SIDED UC	20[redacted]
LOWER BACK PAIN	20[redacted]
TUBAL LIGATION	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	CURRENT	0.25 PACK	10	
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 64	64

M14-675 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 65	[redacted]20[redacted] / 112	48
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 113	[redacted]20[redacted] / 366	254
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 367		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHOTREXATE	25 mg	1 time per week	Y-M: 20[redacted]
INFLIXIMAB	0 OTHER	OTHER: 0	Y-M: 20[redacted]
MESALAZINE	1 OTHER: ENEMA	OTHER: ENEMA	Y-M: 20[redacted]
MESALAZINE	1 OTHER: SUPPOSITRY	OTHER: SUPPOSITRY	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
ETROLIZUMAB	105 mg	OTHER: 4 WEEKLY	Y-M: 20[redacted]
LESSERTIA FRUTESCENS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
TIOGUANINE	0.5 OTHER: TABLET	QD	Y-M: 20[redacted]
GARCINIA MANGOSTANA	30 mL	BID	Y-M: 20[redacted]
BUDESONIDE;SODIUM CHLORIDE	1 OTHER: ENEMA	QD	Y-M: 20[redacted]
CETIRIZINE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -359
FLUTICASONE	1 OTHER: SPRAY	QD	Y-M: 20[redacted] / -359
ASCORBIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -282
ASCORBIC ACID	5 mL	QD	Y-M: 20[redacted] / -282
IRON IN OTHER COMBINATIONS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -293
HOMEOPATHIC PREPARATION	1/4 OTHER: TEASPOON	BID	Y-M: 20[redacted] / -261
METFORMIN	500 mg	BID	Y-M: 20[redacted] / -203
PREGABALIN	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -119
HYOSCINE	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / -65
METFORMIN;VILDAGLIPTIN	1 OTHER: CAPSULE	BID	Y-M: 20[redacted] / -51
MEBEVERINE	1 OTHER: TABLET	QD	Y: 20[redacted]
METHYLSULFONYLMETHANE	2 OTHER: CAPSULE	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
LESSERTIA FRUTESCENS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]	Not reported
GARCINIA MANGOSTANA	30 mL	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 45
CETIRIZINE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -359	Not reported
FLUTICASONE	1 OTHER: SPRAY	QD	Y-M: 20[redacted] / -359	Not reported
ASCORBIC ACID	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -282	Not reported
ASCORBIC ACID	5 mL	QD	Y-M: 20[redacted] / -282	Not reported
IRON IN OTHER COMBINATIONS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -293	Not reported
HOMEOPATHIC PREPARATION	1/4 OTHER: TEASPOON	BID	Y-M: 20[redacted] / -261	Not reported
METFORMIN	500 mg	BID	Y-M: 20[redacted] / -203	Not reported
PREGABALIN	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -119	Not reported
HYOSCINE	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / -65	Not reported
METFORMIN;VILDAGLIPTIN	1 OTHER: CAPSULE	BID	Y-M: 20[redacted] / -51	Not reported
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	1000 mL	QID	Y-M: 20[redacted] / 12	ONGOING
METHYLPREDNISOLONE	100 mg	TID	Y-M: 20[redacted] / 12	ONGOING
GLIMEPIRIDE	4 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 41
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 15	Not reported
STERCULIA URENS	5 mL	PRN	Y-M: 20[redacted] / 57	ONGOING
BETAMETHASONE	5.7 mg	OTHER: STAT	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 62
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 70
BUDESONIDE	1 OTHER: NEBULE	QD	Y-M: 20[redacted] / 68	ONGOING
CHLORAMPHENICOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 107	Y-M: 20[redacted] / 111
ERYTHROMYCIN	250 mg	BID	Y-M: 20[redacted] / 107	Y-M: 20[redacted] / 111
BETAMETHASONE	2 mL	OTHER: STAT	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 162
LIDOCAINE	20 mg	OTHER: STAT	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 162
PARACETAMOL;TRAMADOL	37.5/325 mg	PRN	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 163
MEBEVERINE	1 OTHER: TABLET	QD	Y: 20[redacted]	Not reported
METHYLSULFONYLMETHANE	2 OTHER: CAPSULE	QD	Y: 20[redacted]	Not reported

Event #1: Serious Adverse Event

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] / 378 / 12
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 12): Alanine Aminotransferase: 11 [0 - 35] U/L; Albumin: 38 [20 - 35] G/L; Alkaline Phosphatase: 2 [35 - 105] U/L; Aspartate Aminotransferase: 11 [0 - 32] U/L; Basophils: 0.02 [0 - 0.02] 10^9/L; Bilirubin: 3 [0 - 21] UMOL/L; Chloride: 106 [98 - 107] MMOL/L; Creatinine: 79 [49 - 90] UMOL/L; Eosinophils: 0 [0 - 0.45] 10^9/L; Erythrocytes: 4.37 [3.8 - 4.8] 10^12/L; Hematocrit: 0.371 [0.36 - 0.46] FRACTION OF 1; Leukocytes: 6.35 [3.92 - 9.88] 10^9/L; Lymphocytes: 1.05 [1 - 4] 10^9/L; Monocytes: 0.14 [0.18 - 1] 10^9/L; NPTST027-ANION GAP: 16 [8 - 20] MMOL/L; NPTST078-CO2: 24 [22 - 29] MMOL/L; NPTST085-CRP: 8 [0 - 5] MG/L; NPTST103-ESTIMATED GFR: 83 [60 - 90] ML/MIN/1.73M2; NPTST222-SARS-COV-2: NEGATIVE [0 - 0] UNIT NOT REPORTED; NPTST256-UREA: 4.4 [0 - 8.4] MMOL/L; Neutrophils: 5.11 [2 - 7.5] 10^9/L; Platelets: 305 [150 - 450] 10^9/L; Potassium: 4.5 [3.5 - 5.1] MMOL/L; Sodium: 141 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DISEASE UNDER STUDY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

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。本被験者は南アフリカの 3[redacted] 歳の女性であり，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，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，現喫煙者（1 日 0.25 箱を 10 年間）及び非飲酒者であった。

Event 1 の臨床経過：

投与378日後＊ ，被験者は潰瘍性大腸炎の悪化を発現した。

本事象発現前の 投与336日後＊ ，被験者は排便回数の増加及び直腸出血を経験していた。投与353日後＊ ，内視鏡検査が実施された。

投与378日後＊ ，被験者は静脈内投与による副腎皮質ステロイドでの治療のため入院した。投与381日後＊ ，被験者は退院した。

投与された薬剤は，prednisone，ringer lactat（塩化カルシウム，塩化カリウム，乳酸ナトリウム），及びソル・メドロールであった。

The patient's past medications include:

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

ETROLIZUMAB for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

LANVIS for ULCERATIVE COLITIS ([redacted])

ENTOCORT ENEMAS for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.1] [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 WORSENING OF ULCERATIVE COLITIS

- Investigator: Disease under study.

- AbbVie: Event more likely related to pre-existing Ulcerative Colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 38 G/L (normal 20 to 35)

[redacted] **20[redacted] CRP:** 8 MIN (normal 0 to 5)

[redacted] **20[redacted] ENDOSCOPY:** Local read = 3

[redacted] **20[redacted] MONOCYTES ABS:** 0.14 X10**9/L (normal 0.18 to 1.0)

[redacted] **20[redacted] SARS-COV-2:** 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
肝機能検査値上昇				X

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

Medical History	Onset Year
ANAEMIA	20[redacted]
ARTHRALGIA	20[redacted]
ECZEMA	20[redacted]
FUNGAL TOENAIL INFECTION	20[redacted]
LEFT SIDED UC	19[redacted]
VARICOSE VEINS	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: FLEXIBLE SIGMOIDOSCOPY	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 57	[redacted] / 427	371
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 428		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	QD	Y-M: [redacted]
MESALAZINE	2 g	BID	Y-M: [redacted]
CHLORPHENAMINE	4 mg	PRN	Y-M: [redacted]
CALCIUM CARBONATE;GLYCINE	2.5 g	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
MESALAZINE	2 g	BID	Y-M: [redacted]	Not reported
OENOTHERA BIENNIS	1 OTHER: CAPSULE	QD	Y-M: [redacted] / 1	Not reported
OMEGA-3 FATTY ACIDS	1 OTHER: CAPSULE	QD	Y-M: [redacted] / 1	Not reported
GRISEOFULVIN	500 mg	BID	Y-M: [redacted] / 81	Y-M: [redacted] / 164
MELOXICAM	15 mg	QD	Y-M: [redacted] / 81	Y-M: [redacted] / 164
PARACETAMOL	1 g	TID	Y-M: [redacted] / 158	Y-M: [redacted] / 177
ASCORBIC ACID	1000 mg	QD	Y-M: [redacted] / 161	Y-M: [redacted] / 177
VITAMIN D NOS	1000 IU	QD	Y-M: [redacted] / 161	Y-M: [redacted] / 177
ZINC	20 mg	QD	Y-M: [redacted] / 161	Y-M: [redacted] / 177
AZITHROMYCIN	500 mg	QD	Y-M: [redacted] / 171	Y-M: [redacted] / 173
SALBUTAMOL	200 ug	PRN	Y-M: [redacted] / 171	Y-M: [redacted] / 177
DEXAMETHASONE	8 mg	QD	Y-M: [redacted] / 177	Y-M: [redacted] / 186
PARACETAMOL	1 g	TID	Y-M: [redacted] / 177	Y-M: [redacted] / 182
AZITHROMYCIN	500 mg	QD	Y-M: [redacted] / 178	Y-M: [redacted] / 180
CEFTRIAXONE	1 g	QD	Y-M: [redacted] / 178	Y-M: [redacted] / 184
ENOXAPARIN	80 mg	BID	Y-M: [redacted] / 178	Y-M: [redacted] / 191
PREDNISONE	40 mg	QD	Y-M: [redacted] / 187	Y-M: [redacted] / 191
BUDESONIDE	200 ug	BID	Y-M: [redacted] / 191	Y-M: [redacted] / 247

SALBUTAMOL	100 ug	PRN	Y-M: 20[redacted] / 191	Y-M: 20[redacted] / 247
FOSFOMYCIN	3 g	QD	Y-M: 20[redacted] / 206	Y-M: 20[redacted] / 206
CALCIUM CARBONATE;GLYCINE	2.5 g	QD	Y: 20[redacted]	Not reported

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] / 604 / 177
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 178): Albumin: 29 [35 - 52] G/L; Hematocrit: 0.329 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 112 [125 - 173] G/L; Leukocytes: 9.58 [4 - 11] 10^9/L; NPTST089-D-DIMER: >5.00 [0 - 0.25] MG/L; Potassium: 5.3 [3.5 - 5.1] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 177): CHEST XRAY: EXTENSIVE BILATERAL PULMONARY OPACIFICATION, IN KEEPING WITH A SEVERE COVID-19 PNEUMONITIS/ INFECTION. THERE IS DENSE RIGHT LOWER LOBE CONSOLIDATION.

AE Stopped Initial Rx Day / Rx Day	618 / 191
Duration of AE	15 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, LIFE THREATENING

Event #2: Event of Interest - Hepatic Disorder

Event Description	RAISED LFT'S
Preferred term	肝機能検査値上昇
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 633 / 206
Age at AE Onset	5[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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

Generated: [redacted]20[redacted]:06:46
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。本被験者は南アフリカの 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，COVID-19 肺炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，貧血，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与604日後＊ ，被験者は COVID-19 肺炎を発現した。投与618日後＊ ，COVID-19 肺炎は消失した。

投与585日後＊ ，被験者は非重篤な COVID-19 感染の事象を発現した。治験責任医師によると，被験者は発熱，咳嗽，疲労及び咽頭痛もあった。

入院前，被験者の咳嗽は徐々に悪化し，酷い息切れを感じ，低酸素症（自宅での酸素飽和度は，室内気で 70%–80%）を発現した。

投与604日後＊ ，被験者は更なる管理のため，入院した。胸部 X 線検査では，重度の COVID-19 肺炎/感染と一致する両側肺の不透明化が認められた。被験者は，酸素，ステロイド及

び抗生物質で治療された。被験者は着実に回復した。投与618日後＊　，被験者は退院した。

治験責任医師は，炎症性腸疾患が本事象の危険因子であると判断した。

投与された薬剤は，デキサメタゾン，アジスロマイシン，prednisone，paracetamol，エノキサパリン，酸素及びセフトリアキソンであった。

The patient's past medications include:

ASACOL SUPPOSITORIES 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.23.1]　[10084380]

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 COVID 19 PNEUMONIA

- Investigator: Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 29 G/L (normal 35 to 52)

[redacted] **20[redacted] BMI:** 34.8 Kg/m2

[redacted] 20[redacted] **CHEST X-RAY:** Extensive bilateral pulmonary opacification, in keeping with a severe COVID-19 Pneumonitis/ infection. There is dense right lower lobe consolidation.

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

[redacted] 20[redacted] **D-DIMER:** >5.00 mg/L

[redacted] 20[redacted] **HCT:** 0.329 l/l (normal 0.40 to 0.50)

[redacted] 20[redacted] **HGB:** 11.2 G/DL (normal 12.5 to 17.3)

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

[redacted] 20[redacted] **O2 SAT:** 70 to 80 percent

[redacted] 20[redacted] **POTASSIUM:** 5.3 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **WEIGHT:** 8[redacted].[redacted] KG

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 9.58 X10**9/L (normal 4.0 to 11.0)

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Liver function test increased: Asymptomatic.

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			

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
FINGER SURGERY	20[redacted]
FRACTURED SMALL FINGER LEFT HAND	20[redacted]
GASTRO ESOPHAGEAL REFLUX DISEASE	20[redacted]
INSOMNIA	20[redacted]
INTERMITTENT HEADACHES	19[redacted]
INTERMITTENT HEARTBURN	20[redacted]
LATENT TB	20[redacted]
UMBILICAL HERNIA REPAIR	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: GASTROSCOPY	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	1	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 419	362
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 421		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	500 mg	TID	Y-M: 20[redacted]-[redacted]
PREDNISONE	10 mg	QD	Y-M: 20[redacted]-[redacted]
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted]-[redacted]
ISONIAZID	300 mg	QD	Y-M: 20[redacted]-[redacted]
BACLOFEN	0.5 OTHER: TABLET	BID	Y-M: 20[redacted]-[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
LAMOTRIGINE	50 mg	QD	Y-M: 20[redacted]-[redacted] / 134	Y-M: 20[redacted]-[redacted] / 240
QUETIAPINE	75 mg	QID	Y-M: 20[redacted]-[redacted] / 134	Y-M: 20[redacted]-[redacted] / 148
SERTRALINE	25M mg	QID	Y-M: 20[redacted]-[redacted] / 134	Y-M: 20[redacted]-[redacted] / 148
LAMOTRIGINE	150 mg	QD	Y-M: 20[redacted]-[redacted] / 210	Y-M: 20[redacted]-[redacted] / 299
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	TID	Y-M: 20[redacted]-[redacted] / 342	Y-M: 20[redacted]-[redacted] / 343
MIDAZOLAM	1 mg	QD	Y-M: 20[redacted]-[redacted] / 343	Y-M: 20[redacted]-[redacted] / 343
PROPOFOL	3 mL	QD	Y-M: 20[redacted]-[redacted] / 343	Y-M: 20[redacted]-[redacted] / 343

Event #1: Serious Adverse Event

Event Description	FIRST EPISODE OF ANXIETY
Preferred term	不安
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 554 / 134
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

NOT REPORTED

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	THIS WAS THE FIRST ADMISSION FOR LOW MOOD. PATIENT APPARENTLY SUFFERED MULTIPLE HEAD INJURIES PREVIOUSLY, AND HAD ANGER MANAGEMENT ISSUES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	FIRST EPISODE OF DEPRESSION
Preferred term	うつ病
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 554 / 134
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

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	THIS WAS THE FIRST ADMISSION FOR LOW MOOD. PATIENT APPARENTLY SUFFERED MULTIPLE HEAD INJURIES PREVIOUSLY, AND HAD ANGER MANAGEMENT ISSUES
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者は南アフリカの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，うつ病の最初のエピソード及び不安の最初のエピソードの事象を発現した。関連する病歴は，間欠性の頭痛，不眠症，元喫煙者（1 日 1 箱を 1 年間），潰瘍性大腸炎，現飲酒者（1 日 2 杯未満）及び複数の頭部外傷であった。

Event 1 及び 2 の臨床経過：

投与554日後＊　，被験者はうつ病の最初のエピソード及び不安の最初のエピソードを発現した。

投与554日後＊　，被験者は抑うつ気分，過去の衝動制御障害及びたびたび憤激を伴う「ブラックアウト」で入院した。被験者は，早期に薬物療法に反応した。認知行動療法，作業療法及びアンガーマネジメントのレジメンを開始した。投与568日後＊　，被験者は退院した。

治験責任医師は，複数の頭部外傷及び脳震盪，並びに複数の環境ストレス要因が関連する危険因子であると報告した。

投与された薬剤は，セルトラリン，serinem 及びクエチアピンであった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Blinded)

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1)　Depression (10012378)　(Depression (10012378))　[v.23.1]　[10012378]

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

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

Dechallenge: Not Applicable

2) Anxiety (10002855) (Anxiety (10002855)) [v.23.1] [10002855]

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 FIRST EPISODE OF DEPRESSION

- Investigator: This was the first admission for low mood. Patient apparently suffered multiple head injuries previously, and had anger management issues.

- AbbVie: Risk factors include pre-existing impulse control issues, multiple prior head injuries and concussions, and multiple environmental stressors (per PI)

Event of FIRST EPISODE OF ANXIETY

- Investigator: This was the first admission for low mood. Patient apparently suffered multiple head injuries previously, and had anger management issues.

- AbbVie: Risk factors include pre-existing impulse control issues, multiple prior head injuries and concussions, and multiple environmental stressors (per PI)

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODYWEIGHT:** 8[redacted] KG

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

Reason for Narrative

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

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

Medical History	Onset Year
ARTHRALGIAS	NOT REPORTED
EXTENSIVE UC/PANCOLITIS	20[redacted]
HEADACHE	NOT REPORTED
HIGH BLOOD PRESSURE	19[redacted]
MENOPAUSE	20[redacted]
NODULE IN VOCAL CORD	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: VOCAL CORD NODULE REMOVAL BY LAGINGOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	0.2 PACK	26	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56

M14-234 SS2 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 113	57
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted]20[redacted] / 114	[redacted]20[redacted] / 471	358
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted]20[redacted] / 472		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	NOT REPORTED	OTHER: WEEK 6	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	80 mg	OTHER: EVERY WEEK	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]
PREDNISONE	50 mg	QD	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
MESALAZINE	3600 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
HYDROCHLOROTHIAZIDE;TELMISARTAN	40 mg	QD	Y-M: 20[redacted]
BECLOMETASONE	10 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	QD	Y-M: 20[redacted]
MESALAZINE	3 g	QD	Y-M: 20[redacted]
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / -186
MESALAZINE	1200 mg	QD	Y: 19[redacted]
MESALAZINE	2.4 g	QD	Y: 19[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZATHIOPRINE	NOT REPORTED	QD	Not reported	Not reported
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]	Not reported
HYDROCHLOROTHIAZIDE;TELMISARTAN	40 mg	QD	Y-M: 20[redacted]	Not reported
MESALAZINE	3 g	QD	Y-M: 20[redacted]	Not reported

PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / -186	Not reported
ASCORBIC ACID;CODEINE;PARACETAMOL	650/10/500 mg	QID	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 112
PARACETAMOL	1 g	TID	Y-M: 20[redacted] / 112	Not reported
MESALAZINE	3 g	QD	Y-M: 20[redacted] / 113	Not reported
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 117
BARICITINIB	4 mg	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 123
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 125
DEXAMETHASONE	6 mg	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 136
ENOXAPARIN	40 IU	BID	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 120
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 116	Y-M: 20[redacted] / 147
CODEINE	UNK mg	TID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 137
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 150
DEXAMETHASONE	3 mg	QD	Y-M: 20[redacted] / 136	Y-M: 20[redacted] / 139
DEXAMETHASONE	2 mg	QD	Y-M: 20[redacted] / 140	Y-M: 20[redacted] / 143
DEXAMETHASONE	1 mg	QD	Y-M: 20[redacted] / 144	Y-M: 20[redacted] / 147

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

Event Description	PNEUMONIA BY COVID-19 INFECTION
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 579 / 108
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 116): X-RAY: PNEUMONIA	
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	COVID-19 INFECTION (WORSENING OF SYMPTOMS)
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はスペインの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，COVID-19 による肺炎の事象を発現した。関連する病歴は，元喫煙者（1 日 0.2 箱），高血圧，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580日後＊，被験者は COVID-19 による肺炎を発現した。

投与580日後＊　　，被験者は COVID-19 の症状に適合する筋肉痛を経験し始めた。投与583日後＊，被験者は COVID-19 検査で陽性となった。投与587日後＊　　，被験者は入院した。徴候及び症状には，発熱，酷い筋肉痛及び息切れが含まれた。身体検査が実施され，生化学検査，血液学的検査及び凝固検査の検体が採取された（検査結果は保留）。投与608日後＊　　，被験者は退院した。

投与された薬剤は，dexametasona，オメプラゾール，algidol，paracetamol，enoxapraina，azitromicina，バリシチニブ及び ceftriaxona であった。

The patient's past medications include:

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

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

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

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

MEZAVANT for ULCERATIVE COLITIS (Stopped [redacted] 20[redacted], Started [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

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

DACORTIN for ULCERATIVE COLITIS (Stopped [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.23.1] [10084380]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMONIA BY COVID-19

- Investigator: COVID-19 INFECTION (WORSENING OF SYMPTOMS)

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

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] NASOPHARYNGEAL SWAB:** Positive for COVID-19

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			

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

Medical History	Onset Year
ARTHRALGIAS	NOT REPORTED
HEADACHE	NOT REPORTED
LEFT SIDED UC	20[redacted]
SEASONAL ALLERGY	NOT REPORTED
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: APHERESIS	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	18	20[redacted]
CIGARS	UNKNOWN			
PIPES	UNKNOWN			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 116	60

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 116	[redacted]20[redacted] / 333	218

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]
MESALAZINE	2400 mg	QD	Y-M: 20[redacted]
METRONIDAZOLE	250 mg	BID	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted] / -231
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -62
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -31
EBASTINE	10 mg	PRN	Y: 19[redacted]
METAMIZOLE	1150 mg	PRN	Y: 19[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ADALIMUMAB	NOT REPORTED	OTHER: EVERY 2 WEEKS	Not reported	Not reported
GOLIMUMAB	50 mg	OTHER: EVERY 4 WEEKS	Not reported	Not reported
INFLIXIMAB	NOT REPORTED	OTHER: UNKNOWN	Not reported	Not reported
MERCAPTOPURINE	NOT REPORTED	QD	Not reported	Not reported
METHOTREXATE	NOT REPORTED	QD	Not reported	Not reported
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / -62	ONGOING
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -31	ONGOING
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 124	ONGOING
DIAZEPAM	2.5 mg	PRN	Y-M: 20[redacted] / 152	ONGOING
AMOXICILLIN	750 mg	TID	Y-M: 20[redacted] / 166	Y-M: 20[redacted] / 173
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / 202	ONGOING
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / 213	ONGOING
DIAZEPAM	5 mg	QD	Y-M: 20[redacted] / 213	ONGOING
METOCLOPRAMIDE	10 mg	PRN	Y-M: 20[redacted] / 213	ONGOING
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 213	ONGOING

PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 213	ONGOING
EBASTINE	10 mg	PRN	Y: 19[redacted]	ONGOING
METAMIZOLE	1150 mg	PRN	Y: 19[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	WORSENING OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 317 / 202
Age at AE Onset	4[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 214): NPTST058-C-REACTIVE PROTEIN: 26.4 [0 - 5] MG/L	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
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	ULCERATIVE COLITIS WORSENING
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はスペインの 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，潰瘍性大腸炎の悪化の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 18 年間），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317日後＊，被験者は潰瘍性大腸炎の悪化を発現した。

投与328日後＊　，被験者は直腸出血及び発熱があり，入院した。投与330日後＊　，被験者は退院した。

投与された薬剤は，ジアゼパム，paracetamol，メトロニダゾール，シプロフロキサシン，clipper 及び metoclopramida であった。

The patient's past medications include:

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

INTESTIFALK for ULCERATIVE COLITIS ([redacted])

MESALAZINE for ULCERATIVE COLITIS ([redacted])

METRONIDAZOLE for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

MEZAVANT for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS

GOLIMUMAB for ULCERATIVE COLITIS

INFLIXIMAB for ULCERATIVE COLITIS

MERCAPTOPURINA for ULCERATIVE COLITIS

METHOTREXATE for ULCERATIVE COLITIS

Causality for UPADACITINIB (Open Label)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.23.1]　[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 WORSENING OF UC

- Investigator: ulcerative colitis worsening.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY WEIGHT:** 8[redacted] KG

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
膀胱タンポナーデ	X			
潰瘍性大腸炎	X			
大腸菌性敗血症	X			X
鉄欠乏性貧血				X
処置後出血	X			
前立腺炎	X			X

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

Medical History	Onset Year
BENIGN PROSTATIC HYPERPLASIA	20[redacted]
DEPRESSION: MIDDLE GRAD	19[redacted]
DIABETES MELLITUS: TYP 2	20[redacted]
EYE DISEASE/DISORDER: CATARACTAPOSTERIOR BOTH EYES , OPERATION [redacted] /20[redacted]	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: GRADE 2	19[redacted]
HYPERLIPIDEMIA	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: CRONICAL CERVICOTHORACAL PAIN SYNDROM	19[redacted]
OTHER: MICRO HAEMATURIE	20[redacted]
OTHER: MICRO HEMATURIA	20[redacted]
OTHER: OVERWEIGHT	20[redacted]
OTHER: RECCURENT UROGENITAL INFECTIONS	20[redacted]
OTHER: VITAMIN B12 DEFICIENCY	20[redacted]
SLEEP APNEA: CPAP NEEDED	20[redacted]
TUBERCULOSIS: LATENT [redacted]/20[redacted] QUANTIFERON TEST POSITIV, NO SIGNS IN X RAY ,TREATED WITH ISONIAZID [redacted]/20[redacted]-[redacted]/20[redacted]	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	40	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 63	63
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 64		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	2 g	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	2000 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	500 mg	OTHER: 6 WEEKS	Y-M: 20[redacted]-[redacted]
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted]-[redacted]
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	1000 mg	OTHER: 6 WEEKS	Y-M: 20[redacted]-[redacted]
LISINOPRIL	2.5 mg	QD	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: 4 WEEKS	Y-M: 20[redacted]-[redacted]
CICLOSPORIN	200 mg	QD	Y-M: 20[redacted]-[redacted]
METHYLPREDNISOLONE	50 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]-[redacted]
SULFAMETHOXAZOLE;TRIMETHOPRIM	800 mg	OTHER: 3 TIMES A WEEK	Y-M: 20[redacted]-[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4500 mg	TID	Y-M: 20[redacted]-[redacted]
HYDROCORTISONE	10 mg	BID	Y-M: 20[redacted]-[redacted] / -23
PREDNISONE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -7
ESOMEPRAZOLE	20 mg	QD	Y: 19[redacted]

PARACETAMOL	2000 mg	PRN	Y: 19[redacted]
MIANSERIN	30 mg	QD	Y: 19[redacted]
SERTRALINE	175 mg	TID	Y: 19[redacted]
INSULIN LISPRO	AS NEEDED IU	OTHER: PER PLAN	Y: 20[redacted]
LOPERAMIDE	2 mg	PRN	Y: 20[redacted]
ALFUZOSIN	10 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 / Stop Year-Month / RX Day	
ACETYLSALICYLIC ACID	100 mg	QD	Y-M: 20[redacted]	ONGOING
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted]	ONGOING
LISINOPRIL	2.5 mg	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	4500 mg	TID	Y-M: 20[redacted]	ONGOING
HYDROCORTISONE	10 mg	BID	Y-M: 20[redacted] / -23	Y-M: 20[redacted] / 379
ACICLOVIR	30 mg	OTHER: EVERY 5 HOURS	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 202
BUDESONIDE	2 mg	QD	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 202
CALCIUM CARBONATE;COLECALCIFEROL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 202
MESALAZINE	1 g	QD	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 202
MESALAZINE	1000 mg	BID	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 202
MESALAZINE	2 g	QD	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 202
PREDNISONE	60 mg	OTHER: ONCE	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 192
SEA WATER	1 OTHER: SPREAT	QID	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 202
STERCULIA URENS	1 OTHER: TABLESPOON	QD	Y-M: 20[redacted] / 192	ONGOING
VITAMIN B NOS	1 OTHER: DRAGEE	QD	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 202
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 232
ACICLOVIR	30 mg	OTHER: EVERY 5 HOURS	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 225
CALCIUM CARBONATE;COLECALCIFEROL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 225
CEFTRIAXONE	1000 mg	BID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 208
INSULIN ASPART	0-8 IU	PRN	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 225
METAMIZOLE	500 mg	QID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 225

NICOTINAMIDE;PANTOTHENIC ACID;PYRIDOXINE;RIBOFLAVIN; THIAMINE	1 OTHER: DRAGEE	QD	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 225
NORFLOXACIN	400 mg	BID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 204
PARACETAMOL	1 g	BID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 225
SEA WATER	1 OTHER: SPREAT	QID	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 225
AMOXICILLIN	400 mg	BID	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 209
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 210	Y-M: 20[redacted] / 247
HYDROCORTISONE	10 mg	BID	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 683
HYDROCORTISONE	20 mg	QD	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 683
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 490	Y-M: 20[redacted] / 525
DUTASTERIDE;TAMSULOSIN	0,5/04 mg	QD	Y-M: 20[redacted] / 660	Y-M: 20[redacted] / 720
MIRABEGRON	50 mg	QD	Y-M: 20[redacted] / 660	ONGOING
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted] / 779	Y-M: 20[redacted] / 803
IRON	2X500 mg	QD	Y-M: 20[redacted] / 794	Y-M: 20[redacted] / 794
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / 804	Y-M: 20[redacted] / 838
ESOMEPRAZOLE	20 mg	QD	Y: 19[redacted]	ONGOING
PARACETAMOL	2000 mg	PRN	Y: 19[redacted]	ONGOING
MIANSERIN	30 mg	QD	Y: 19[redacted]	ONGOING
SERTRALINE	175 mg	TID	Y: 19[redacted]	ONGOING
INSULIN LISPRO	AS NEEDED IU	OTHER: PER PLAN	Y: 20[redacted]	ONGOING
LOPERAMIDE	2 mg	PRN	Y: 20[redacted]	ONGOING
ALFUZOSIN	10 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 659

Event #1: Serious Adverse Event

Event Description	FLARE OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 255 / 192
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 192): NPTST085-CRP: 5.8 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (RX DAY 194): NPTST076-CLOSTRIDIUM DIFICILE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST086-CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 192): ABDOMINAL CT: WALLTHICKENING DITAL SIGMOID; [redacted]20[redacted] (RX DAY 201):

RECTOSIGMOIDOSCOPY: INFLAMATION DISTAL COLON DESCENDENS TIL RECTUM

AE Stopped Initial Rx Day / Rx Day	265 / 202
Duration of AE	11 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	UROSEPSIS WITH E.COLI
Preferred term	大腸菌性敗血症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 267 / 204
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 204): NPTST142-LACTAT: 2.2 [0.5 - 1.6] MMOL/L; [redacted]20[redacted] (RX DAY 205): NPTST085-CRP: 252 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (RX DAY 207): NPTST085-CRP: 109.4 [NOT REPORTED - 5] mg/L; [redacted]20[redacted] (RX DAY 208): NPTST085-CRP: 57.3 [NOT REPORTED - 5] mg/L; NPTST198-PSA: 73.30 [NOT REPORTED - 4] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 204): BLOOD NPTST046-BLOOD CULTURE: Negative; URINE NPTST260-URINE CULTURE: Positive-E COLI

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 204): SONOGRAPHY GENITO-URONARY SYSTEM: 29ML REST URIN , NO CONGESTION, NO PYELONEPHRITIS; [redacted]20[redacted] (RX DAY 209): MRI BOWLAND ILEO SACRAL JOINT: NO PATHOLOGIC OUTCOME; SONOGRAPHY GENITO URONARY SYSTEM: REST URIN 85ML ,NO CONGESTION, PROSTATAHYPERPLASY,NO PYOLONEPHRITIS

AE Stopped Initial Rx Day / Rx Day	288 / 225
Duration of AE	22 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	BENIGN PROSTATE HYPERPLASIA AND HOSPITAL STAY DUE TO SAE A FEW DAYS AGO
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	ACUTE PROSTATITIS
Preferred term	前立腺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 553 / 490
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 490): BLOOD NPTST046-BLOOD CULTURE: Negative; URINE NPTST258-URIN CLULTURE: Positive-GRAMNEGATIV BACTERIA 1000BACTERIAS PER ML

SAE Supplemental Procedure

NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	557 / 494
Duration of AE	5 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 #4: Serious Adverse Event

Event Description	POST OP BLEEDING
Preferred term	処置後出血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 802 / 739
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 739): Erythrocytes: 7447 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Hemoglobin: 117 [134 - 170] G/L; Leukocytes: 374 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Leukocytes: 7.9 [4.5 - 11] 10^9/L; NPTST085-CRP: 1.2 [NOT REPORTED - 5] mg/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 739): INSERTION OF A BLADDER LAVAGE CATHETER: NO BLEEDING AGAIN, CLEAN URIN BEFORE REMOVAL; UROGENITAL ULTRASOUND: VESICAL BLOOD COAGULATION, MULTIPLE KIDNEY CYSTES LEFTSIDE, OTHERWISE WITHOUT OTHER PATHOLOGICAL FINDINGS, , NO URINARY RETENTION

AE Stopped Initial Rx Day / Rx Day	806 / 743
Duration of AE	5 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PREVIOUS PLANED TUR PROSTATA OPERATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #5: Serious Adverse Event

Event Description	VESICAL BLADDER TAMPONADE AFTER TUR OPERATION
Preferred term	膀胱タンポナーデ
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 817 / 754
Age at AE Onset	5[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 754): BLADDER IRRIGATION AND BIPOLARE COAGULATION OD PROSTATA LOGE: NO BLEEDING VISUAL AFTER COAGULATION; INSERTION OF A BLADDER LAVAGE CATHETER: LAVAGE CATHETER REMOVED AFTER 2 DAYS

AE Stopped Initial Rx Day / Rx Day	824 / 761
Duration of AE	8 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COMPLICATION AFTER AN ELECTIVE PROSTATA TUR OPERATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #6: Event of Interest - Anemia

Event Description	IRON DEFICIENCY ANEMIA
Preferred term	鉄欠乏性貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 834 / 771
Age at AE Onset	5[redacted]

Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	908 / 845
Duration of AE	75 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

Generated: [redacted]20[redacted]:06:46
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。本被験者はスイスの 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ ABT-494）の治験でウパダシチニブが投与され，潰瘍性大腸炎の再燃及び大腸菌による尿路性敗血症の事象を発現した。関連する病歴は，グレード 2 の胃食道逆流性疾患，中等度のうつ病，CPAP を必要とする睡眠時無呼吸，2 型糖尿病，過体重，潰瘍性大腸炎，良性前立腺肥大症，ビタミンB12 欠乏，高脂血症，高血圧，泌尿生殖器系感染の再発，元喫煙者（1 日 1 箱を 40 年間）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：

Event 1 及び 2 の発現前である 投与53日後＊　，被験者は尿路性敗血症を発現し，入院した。

投与255日後＊　，被験者は潰瘍性大腸炎の再燃を発現した。投与265日後＊　，潰瘍性大腸炎の再燃は消失した。投与267日後＊　　，大腸菌による尿路性敗血症を発現した。投与288日後＊　，大腸菌による尿路性敗血症は消失した。

投与255日後＊　，被験者は潰瘍性大腸炎の再燃のため入院した。下痢及び腸の痛みがあった。投与265日後＊　，被験者は退院した。

投与267日後＊　，被験者は大腸菌による尿路性敗血症のため入院した。腸の痛み及び排尿障害があった。投与288日後＊，被験者は退院した。

投与された薬剤は，metamizol natrium，dafalgan，becocym，becozym forte，salofalk，çalcimagon D3 citron，fluimare，アモキシシリン，セフトリアキソン，ノルフロキサシン，プレドニゾン及びシプロフロキサシンであった。

The patient's past medications include:

BUDENOFALK for ULCERATIVE COLITIS ([redacted])

SALOFALK for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

SANDIMMUN for ULCERATIVE COLITIS ([redacted])

SOLUMEDROL for ULCERATVE COLITIS ([redacted])

PREDNISON for UC ([redacted])

BACTRIM for ULCERATIVE COLITIS ([redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Open Label)

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1)　UC aggravated (10045283)　(Colitis ulcerative (10009900))　[v.21.1]　[10045283]

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

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

Dechallenge: Not Applicable

2) Escherichia sepsis (10015296) (Escherichia sepsis (10015296)) [v.21.1] [10015296]

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 FLARE OF UC

- Investigator: Not applicable

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

Event of UROSEPSIS WITH E.COLI

- Investigator: Benign prostate hyperplasia and hospital stay due to SAE a few days ago.

- AbbVie: Event more likely related to pre-existing history of recurrent urogenital infections, benign prostatic hyperplasia and diabetes mellitus. Recent hospitalization is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT:** WALL THICKENING DISTAL SIGMOID

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

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE:** NEGATIVE

[redacted] **20[redacted] CRP:** 5.6 MG/L (normal <5)

[redacted] **20[redacted] CRP:** 252 MG/L (normal <5)

[redacted] **20[redacted] CRP:** 109.4 MG/L (normal <5)

[redacted] **20[redacted] CRP:** 57.3 MG/L (normal <5)

[redacted] **20[redacted] LACTATE:** 2.2 MMOL/L (normal 0.5 to 1.6)

[redacted] **20[redacted] MRI BOWLAND ILEO SACRAL JOINT:** No pathologic outcome

[redacted] **20[redacted] PSA:** 73.3 MG/L (normal <5)

[redacted] **20[redacted] RECTOSIGMOIDOSCOPY:** INFLAMATION DISTAL COLON DESCENDENS TIL RECTUM

[redacted] **20[redacted] SONOGRAPHY GENITO-URINARY SYSTEM:** 29ml rest urine, no congestion, no pyelonephritis

[redacted] **20[redacted] SONOGRAPHY GENITO-URINARY SYSTEM:** 85ml rest urine, no congestion, prostatahyperplasia, no pyelonephritis

[redacted] **20[redacted] URINE CULTURE:** Positive E. coli
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はスイスの 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，急性前立腺炎の事象を発現した。関連する病歴は，うつ病，2 型糖尿病，潰瘍性大腸炎，良性前立腺肥大症，顕微鏡的血尿，ビタミン B12 欠乏，高血圧，泌尿生殖器系感染の再発，元喫煙者（1 日 1 箱を 40 年間）及び元飲酒者（1 日 2 杯未満）であった。

Event 3 の臨床経過：

投与553日後＊　，被験者は急性前立腺炎を発現した。投与557日後＊，急性前立腺炎は消失した。

投与553日後＊　，被験者は排尿時の灼熱感及び下腹部痛を訴え，入院した。投与557日後＊，被験者は退院した。

投与された薬剤は ciproxin であった。

Causality for ABT-494 (Open Label)

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1)　Acute prostatitis (10001021)　(Prostatitis (10036978))　[v.22.0]　[10001021]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Open Label)

Event of ACUTE PROSTATITIS

- Investigator: Not Applicable.

- AbbVie: Risk factors include pre-existing benign prostatic hyperplasia and recurrent urogenital infections.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] URINE CULTURE:** Positive. Gram negative bacteria. 1000 bacteria per ml

[redacted] **20[redacted] BLOOD CULTURE:** Negative
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-533

治験責任医師からの報告。本被験者はスイスの 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，処置後の出血及び経尿道的切除術後の膀胱タンポナーデの事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 40 年間），糖尿病，潰瘍性大腸炎，良性前立腺肥大症，顕微鏡的血尿，高脂血症，高血圧，泌尿生殖器系感染の再発及び元飲酒者（1 日 2 杯未満）であった。

Event 4 及び 5 の臨床経過：

投与802日後＊ ，被験者は処置後の出血を発現した。投与806日後＊ ，処置後の出血は消失した。投与817日後＊ ，被験者は経尿道的切除後の膀胱タンポナーデを発現した。投与824日後＊，経尿道的切除後の膀胱タンポナーデは消失した。

投与802日後＊ ，被験者は入院した。被験者は，待機的な前立腺の経尿道的切除後の膀胱タンポナーデを 投与783日後＊ に発現した。その後，被験者は排尿時の強い痛み及び数日間の血液凝固を経験した。膀胱洗浄カテーテルを挿入し，再度の出血はなく，カテーテル除去前には

清明な尿が認められた。投与806日後＊，被験者は退院した。

投与817日後＊　，被験者は前立腺の手術後に出血を発現した。再度入院し，膀胱洗浄，前立腺のバイポーラ電極を用いた凝固術及び膀胱洗浄カテーテルの挿入を受け，膀胱洗浄カテーテルは 2 日後に除去された。投与824日後＊ ，被験者は退院した。

The patient's past medications include:

BUDENOFALK FOAM for ULCERATIVE COLITIS and DUE TO FLARE OF UC ([redacted])

SALOFALK FOAM for ULCERATIVE COLITIS and FLARE OF UC ([redacted])

SALOFALK SUPP for ULCERATIVE COLITIS and FLARE TO UC ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

SANDIMMUN for ULCERATIVE COLITIS ([redacted])

SOLU MEDROL for ULCERATIVE COLITIS ([redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted])

BECOZYM FORTE for UC FLARE ([redacted])

SALOFALK ENEMA for FLARE OF UC ([redacted])

SPIRICORT for FLARE OF UC ([redacted])

BECOZYME for GIVEN IN THE HOSPITAL DUE TO FLARE OF UC ([redacted])

DAFALGAN for FLARE OF UC ([redacted])

METAMIZOL NATRIUM for FLARE OF UC ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Postoperative bleeding (10036277) (Post procedural haemorrhage (10051077)) [v.23.0] [10036277]

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

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

Dechallenge: Not Applicable

2) Bladder tamponade (10062656) (Bladder tamponade (10062656)) [v.23.0] [10062656]

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 POST OP BLEEDING

- Investigator: previous planed tur prostata operation

- AbbVie: Event more likely a complication of recent transurethral resection of the prostate procedure.

Event of VESICAL BLADDER TAMPONADE AFTER TUR OPERATION

- Investigator: Complication after an elective prostate TUR operation.

- AbbVie: Event more likely a complication of recent transurethral resection of the prostate procedure.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 1.2 MG/L (normal <5)

[redacted] **20[redacted] HEMOGLOBIN:** 117 G/L (normal 134 to 170)

[redacted] **20[redacted] URINE WBC:** 374 no units

[redacted] **20[redacted] UROGENITAL ULTRASOUND:** Vesical blood coagulation, multiple kidney cystes leftside, otherwise without other pathological findings, , no urinary retention

[redacted] **20[redacted] WBC:** 7.9 X10**3/MCL

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
鼠径ヘルニア	X			
リンパ球減少症				X

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

Medical History	Onset Year
APPENDECTOMY	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
IRON DEFICIENCY ANEMIA	20[redacted]
LACTOSE INTEROLERANCE	20[redacted]
MULTIPLE NAEVI	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55

M14-675 ABT-494 (OL)	45 mg	QD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 112	57
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 113	[redacted]20[redacted] / 154	42
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 155		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CURCUMA LONGA	3 g	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	4.5 g	QD	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
LECITHIN	1.6 g	NOT REPORTED	Y-M: 20[redacted]
RIFAXIMIN	550 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	400 mg	OTHER: 400	Y-M: 20[redacted]
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	800 mg	OTHER: 4 WEEKS	Y-M: 20[redacted]
MESALAZINE	4.8 mg	QD	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
COLECALCIFEROL	1 OTHER: BOTTLE	OTHER: ONCE A MONTH	Y-M: 20[redacted] / -98
SODIUM PHOSPHATE	3 OTHER: CAPSULES	TID	Y-M: 20[redacted] / -98
TRIMIPRAMINE	25 gtt	QD	Y-M: 20[redacted] / -56
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -36

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
COLECALCIFEROL	1 OTHER: BOTTLE	OTHER: ONCE A MONTH	Y-M: 20[redacted] / -98	Not reported

SODIUM PHOSPHATE	3 OTHER: CAPSULES	TID	Y-M: 20[redacted] / -98	Y-M: 20[redacted] / 295
TRIMIPRAMINE	25 gtt	QD	Y-M: 20[redacted] / -56	Not reported
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -36	Y-M: 20[redacted] / 53
PREDNISONE	17.5 mg	QD	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 60
PAPAVER SOMNIFERUM	4X15 gtt	QID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 212
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 67
PREDNISONE	12.5 mg	QD	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 74
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 75	Y-M: 20[redacted] / 82
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 94
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 95	Y-M: 20[redacted] / 120
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 200
PAPAVER SOMNIFERUM	15 gtt	TID	Y-M: 20[redacted] / 213	Y-M: 20[redacted] / 295
METAMIZOLE	4X40 gtt	PRN	Y-M: 20[redacted] / 262	Y-M: 20[redacted] / 264
CALCIUM CARBONATE;COLECALCIFEROL	500 mg	QD	Y-M: 20[redacted] / 295	ONGOING
PAPAVER SOMNIFERUM	10 gtt	TID	Y-M: 20[redacted] / 296	ONGOING
PROPOFOL	250 mg	PRN	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
SODIUM PHOSPHATE;SODIUM PHOSPHATE MONOBASIC (ANHYDROUS)	2 OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
OTHER VIRAL VACCINES	1 OTHER: DOSE	OTHER: ONCE	Y-M: 20[redacted] / 354	Y-M: 20[redacted] / 354

Event #1: Event of Interest - Lymphopenia

Event Description	LYMPHOZYTOPENIA
Preferred term	リンパ球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 193 / 39
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	210 / 56
Duration of AE	18 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 Description	INGUINAL HERNIA BOTH SIDES
Preferred term	鼠径ヘルニア
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 203 / 49
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
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	PREFERED HERNIOTOMY TO AVOID INCARCERATION
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]:06:46
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。本被験者はスイスの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験でウパダシチニブが投与され，両側鼠径ヘルニアの事象を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与203日後＊　，被験者は両側鼠径ヘルニアを発現した。

投与416日後＊　，被験者は両側腹膜外腔のメッシュ挿入のため，入院した。投与418日後＊，被験者は退院した。

The patient's past medications include:

KURKUMA for ULCERATIVE COLITIS ([redacted])

MEZALAZIN for ULCERATIVE COLITIS ([redacted])

PREDNISON for ULCERATIVE COLITIS ([redacted])

IMUREK for ULCERATIVE COLITIS ([redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted])

MEZALAZIN KLYSMA for ULCERATIVE COLITIS ([redacted])

LECITIN for ULCERATIVE COLITIS ([redacted])

XIFAXAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

BUDENOFALK RECTAL FOAM for ULCERATIVE COLITIS ([redacted])

MEZAVANT for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　Bilateral inguinal hernia (10067165)　(Inguinal hernia (10022016))　[v.23.1]　[10067165]

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 INGUINAL HERNIA BOTH SIDES

- Investigator: Preferred herniotomy to avoid incarceration

- AbbVie: Inguinal hernias are common in the general population with a lifetime risk of 27.5 percent in men.

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA: IRON ANEMIA	20[redacted]
DEPRESSION	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
NEPHROLITHIASIS: RIGHT	20[redacted]
OTHER: ANXIETY	20[redacted]
OTHER: ERYTHEMA NODOSUM	20[redacted]
OTHER: EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY RIGHT	20[redacted]
OTHER: SWOLLEN ANCLE LEFT	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 55

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
METHOTREXATE	15 mg	QD	Y-M: 20[redacted]
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY WEEKS	Y-M: 20[redacted]
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted]
AMOXICILLIN;CLAVULANIC ACID	500 mg	BID	Y-M: 20[redacted]
VANCOMYCIN	125 mg	QID	Y-M: 20[redacted]
GOLIMUMAB	100 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
METHOTREXATE	15 mg	1 time per week	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -270
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / -111
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -111
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -111
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -111
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -76
CIPROFLOXACIN	500 mg	BID	Y: 20[redacted]
MESALAZINE	6 g	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
CALCIUM CARBONATE;COLECALCIFEROL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 445	Y-M: 20[redacted] / 473
VITAMIN D NOS	20 gtt	QD	Y-M: 20[redacted] / 474	Y-M: 20[redacted] / 477
ESCITALOPRAM	2 gtt	QD	Y-M: 20[redacted] / 477	Y-M: 20[redacted] / 479

HUMULUS LUPULUS;VALERIANA OFFICINALIS	2 OTHER: DRG	PRN	Y-M: 20[redacted] / 477	Y-M: 20[redacted] / 481
VITAMIN D NOS	10 gtt	QD	Y-M: 20[redacted] / 478	Y-M: 20[redacted] / 550
ESCITALOPRAM	4 gtt	QD	Y-M: 20[redacted] / 480	Y-M: 20[redacted] / 481
ESCITALOPRAM	6 gtt	QD	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 483
ESCITALOPRAM	8 gtt	QD	Y-M: 20[redacted] / 484	Y-M: 20[redacted] / 485
ESCITALOPRAM	10 gtt	QD	Y-M: 20[redacted] / 486	Y-M: 20[redacted] / 490
ESCITALOPRAM	12 gtt	QD	Y-M: 20[redacted] / 491	Y-M: 20[redacted] / 493
ESCITALOPRAM	14 gtt	QD	Y-M: 20[redacted] / 494	Y-M: 20[redacted] / 558
ARIPIPRAZOLE	10 mg	QD	Y-M: 20[redacted] / 528	Y-M: 20[redacted] / 534
ESCITALOPRAM	20 mg	QD	Y-M: 20[redacted] / 559	Y-M: 20[redacted] / 596
ARIPIPRAZOLE	10 mg	QD	Y-M: 20[redacted] / 597	Y-M: 20[redacted] / 703
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	SACHET OTHER: SACHET	BID	Y-M: 20[redacted] / 672	Y-M: 20[redacted] / 672
FENTANYL	50 ug	QD	Y-M: 20[redacted] / 673	Y-M: 20[redacted] / 673
FLUOXETINE	40 mg	BID	Y-M: 20[redacted] / 673	Y-M: 20[redacted] / 825
PROPOFOL	180 mg	QD	Y-M: 20[redacted] / 673	Y-M: 20[redacted] / 673
CALCIUM CARBONATE;COLECALCIFEROL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 1030
COLECALCIFEROL	8 gtt	QD	Y-M: 20[redacted] / 938	Y-M: 20[redacted] / 1030
SULFAMETHOXAZOLE;TRIMETHOPRIM	800/160 mg	QD	Y-M: 20[redacted] / 944	Y-M: 20[redacted] / 948
SULFAMETHOXAZOLE;TRIMETHOPRIM	800/160 mg	QD	Y-M: 20[redacted] / 1061	Y-M: 20[redacted] / 1065
LEVONORGESTREL	1 OTHER: PIECE	QD	Y-M: 20[redacted] / 1120	ONGOING
INFLUENZA VACCINE	0.5 mL	OTHER: 1X	Y-M: 20[redacted] / 1184	Y-M: 20[redacted] / 1184
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	BID	Y-M: 20[redacted] / 1339	Y-M: 20[redacted] / 1339
FENTANYL	75 ug	OTHER: ONCE TIME	Y-M: 20[redacted] / 1340	Y-M: 20[redacted] / 1340
PROPOFOL	260 mg	OTHER: ONCE TIME	Y-M: 20[redacted] / 1340	Y-M: 20[redacted] / 1340

Event #1: Serious Adverse Event

Event Description	DEPRESSION
Preferred term	うつ病
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 528 / 474

Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
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	MEDICAL HISTORY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:06:46
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。本被験者はスイスの 2[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，うつ病の事象を発現した。関連する病歴は，潰瘍性大腸炎，結節性紅斑，不安，うつ病，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与528日後＊　　，被験者はうつ病を発現した。

投与528日後＊　　，被験者はうつ病と関連した徴候及び症状のため，入院した。被験者は，疲労，人生の虚無感，無価値感及び不眠症を経験した。投与554日後＊　，被験者は退院した。

投与された薬剤は，valverde，エビリファイ，cipralex 及びフルオキセチンであった。

The patient's past medications include:

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

METHOTREXATE for ULCERTIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

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

CALZIMAGON D3 FORTE for VITAMIN D DEFICIENCY ([redacted] 20[redacted] - [redacted] 20[redacted])

UREK for ULCERTIVE COLITIS

Causality for UPADACITINIB (Open Label)

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1) Depression (10012378) (Depression (10012378)) [v.23.1] [10012378]

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 DEPRESSION

- Investigator: MEDICAL HISTORY

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING DEPRESSION.

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		

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

Medical History	Onset Year
ANEMIA: IRON DEFICIENCY	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OSTEOPOROSIS	20[redacted]
OTHER: AXIAL HIATUSHERNIA	20[redacted]
OTHER: HEPATITIS C	20[redacted]
OTHER: LIVER CIRRHOSIS	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 52	52

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 53	[redacted]20[redacted] / 60	8

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2 g	BID	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
CALCIUM CARBONATE;COLECALCIFEROL	VIT. D3: 800UI CALCIUMCARBONA T2.5 G CALCIUM: 1G OTHER: DRUG	QD	Y-M: 20[redacted]
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted]
ZINC	20 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	800 mg	OTHER: 4 WEEKS	Y-M: 20[redacted]
MESALAZINE	2 g	QD	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / -212
COLECALCIFEROL	16 gtt	OTHER: QW	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
MESALAZINE	2 g	BID	Y-M: 20[redacted]	ONGOING
CALCIUM CARBONATE;COLECALCIFEROL	VIT. D3: 800UI CALCIUMCARBONA T2.5 G CALCIUM: 1G OTHER: DRUG	QD	Y-M: 20[redacted]	ONGOING
ZINC	20 mg	QD	Y-M: 20[redacted]	ONGOING
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;MALIC ACID;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	OTHER: 24H/D	Y-M: 20[redacted] / 8	ONGOING
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 8	ONGOING
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 8	ONGOING
SODIUM CHLORIDE	100 mL	OTHER: 24H/D	Y-M: 20[redacted] / 8	ONGOING
COLECALCIFEROL	16 gtt	OTHER: QW	Y: 20[redacted]	ONGOING

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

Event Description	PERSISTENT ULCERATIVE COLITIS ACTIVITY
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 60 / 8
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DEHYDRATION WEIGHT LOSS 20X BM/D
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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。本被験者はスイスの 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，持続的な潰瘍性大腸炎の活動の事象を発現した。関連する病歴は，鉄欠乏，潰瘍性大腸炎，C 型肝炎，肝硬変，軸性裂孔ヘルニア，胃食道逆流性疾患及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与60日後＊ ，被験者は持続的な潰瘍性大腸炎の活動を発現した。

投与60日後＊　，被験者は，下腹部の刺すような痛み，24 時間で 20 回の血性下痢，1 週間で 2 kg の体重減少，発熱を伴わない戦慄，悪心を伴わない食欲不振で入院した。触診の間に痛みは拡散した。被験者はステロイドの静脈内投与の導入療法及びその他の薬物療法に部分的に反応した（非血性便が 1 日 7–9 回）。被験者はベースラインの来院時にも同様の事象があった。投与71日後＊ ，被験者は退院した。

投与された薬剤は，ringerfundin，ステロイド，ブデゾニド，塩化カリウム，vitamin D3 wild oel, solu medrol，塩化ナトリウム 0.9%，budenofalk，パントプラゾール，salofalk 及びエンタイビオであった。

Causality for UPADACITINIB (Open Label)

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1)　Ulcerative colitis (10045365)　(Colitis ulcerative (10009900))　[v.23.1]　[10045365]

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 PERSISTENT ULCERATIVE COLITIS ACTIVITY

- Investigator: DEHYDRATION, WEIGHT LOSS, 20X BM/D

- AbbVie: Event more likely due to progression of pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 31.1 G/L (normal 34 to 48)

[redacted] **20[redacted] CHLORIDE:** 104 MMOL/L (normal 95 to 113)

[redacted] **20[redacted] CREATININE:** 90 umol/l (normal <115)

[redacted] **20[redacted] CREATININE:** 81 umol/l

[redacted] **20[redacted] CRP:** 31 mg/l (normal <8)

[redacted] **20[redacted] CRP:** 5 mg/l

Unknown date CRP: UNKNOWN

Unknown date ELECTROLYTES: UNKNOWN

[redacted] **20[redacted] GLUCOSE:** 5.5 MMOL/L (normal 3.9 to 5.6)

Unknown date HEMATOLOGY: unknown

Unknown date HEPATIC PARAMETERS: UNKNOWN

[redacted] **20[redacted] IRON:** 4.2 umol/l (normal 10 to 27)

[redacted] **20[redacted] PHYSICAL EXAM: CV:** normal finding Pulmonary: normal finding Abdomen: diffuse pain during palpation. Skin and others: normal finding

[redacted] **20[redacted] POTASSIUM:** 4.2 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] POTASSIUM:** 4.1 MMOL/L

Unknown date RENAL PARAMETER: UNKNOWN

[redacted] **20[redacted] SODIUM:** 132 MMOL/L (normal 136 to 144)

[redacted] **20[redacted] SODIUM:** 141 MMOL/L

[redacted] **20[redacted] TSH:** 1.08 mlu/l (normal 0.25 to 4)

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

Reason for Narrative

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

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

Medical History	Onset Year
ANEMIA, UNSPECIFIED	20[redacted]
AXIAL ARTHROPATHY (INCLUDING SACROILIITIS OR ANKYLOSING SPONDYLITIS)	20[redacted]
BENIGN NEOPLASM OF SKIN, SITE UNSPECIFIED	20[redacted]
CONTACT DERMATITIS	20[redacted]
DISEASE OF STOMACH AND DUODENUM, UNSPECIFIED	20[redacted]
DISORDERS OF FUNCTION OF STOMACH	20[redacted]
ECZEMA	20[redacted]
HEADACHE	20[redacted]
INSOMNIA, UNSPECIFIED	20[redacted]
LEFT SIDED UC	20[redacted]
LEFT-SIDED ULCERATIVE (CHRONIC) COLITIS	20[redacted]
MIXED SIMPLE AND MUCOPURULENT CHRONIC BRONCHITIS	20[redacted]
NONINFECTIVE GASTROENTERITIS AND COLITIS, UNSPECIFIED	20[redacted]
OTHER ACNE	20[redacted]
OTHER CHRONIC BRONCHITIS	20[redacted]
OTHER SPECIFIED DYSPEPSIA	20[redacted]
OTHER URTICARIA	20[redacted]
PAIN IN UNSPECIFIED JOINT	20[redacted]
REFLUX ESOPHAGITIS	20[redacted]
SEBORRHEIC DERMATITIS	20[redacted]
UNSPECIFIED CONTACT DERMATITIS, UNSPECIFIED CAUSE	20[redacted]
UNSPECIFIED CONTACT DERMATITIS, UNSPECIFIED CAUSE	20[redacted]
UNSPECIFIED FUNCTIONAL DISORDER OF INTESTINE	20[redacted]
UNSPECIFIED LOCAL INFECTION OF SKIN AND SUBCUTANEOUS TISSUE	20[redacted]

URTICARIA, UNSPECIFIED	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 315	258
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 316		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
MESALAZINE	500 mg	BID	Y-M: 20[redacted]
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]

PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
MESALAZINE	500 mg	BID	Y-M: 20[redacted]
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	OTHER: Q3D	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
MESALAZINE	2 g	OTHER: QOD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	25 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: Q2W	Y-M: 20[redacted]
MESALAZINE	500 mg	BID	Y-M: 20[redacted]
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
DIMETICONE	40 mg	BID	Y-M: 20[redacted] / -120
SERTACONAZOLE	2 %	OTHER: BIW	Y-M: 20[redacted] / -14

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]	Not reported
DIMETICONE	40 mg	BID	Y-M: 20[redacted] / -120	Not reported
ISOTRETINOIN	10 mg	OTHER: QN	Y-M: 20[redacted] / 289	Y-M: 20[redacted] / 317
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 340
TRIAMCINOLONE	10 mg	OTHER: STAT	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 312
TRANEXAMIC ACID	5 mL	OTHER: Q8H	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 324
TRANEXAMIC ACID	5 mL	OTHER: STAT	Y-M: 20[redacted] / 321	Y-M: 20[redacted] / 321
HYDROCORTISONE	100 mg	OTHER: Q8H	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 324

HYDROCORTISONE	100 mg	OTHER: STAT	Y-M: 20[redacted] / 322	Y-M: 20[redacted] / 322
HYDROCORTISONE	100 mg	OTHER: Q12H	Y-M: 20[redacted] / 324	Y-M: 20[redacted] / 325
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted] / 325	Not reported
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	16.2 g	OTHER: STAT	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 331
FENTANYL	0.1 mg	OTHER: STAT	Y-M: 20[redacted] / 331	Y-M: 20[redacted] / 331
MIDAZOLAM	5 mg	OTHER: STAT	Y-M: 20[redacted] / 331	Y-M: 20[redacted] / 331
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 394
TRIAMCINOLONE	10 mg	OTHER: STAT	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
PARACETAMOL;TRAMADOL	1 DF	TID	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 417
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / 410	Y-M: 20[redacted] / 417
BENZOCAINE;CHLORPHENAMINE	5 g	BID	Y-M: 20[redacted] / 417	ONGOING
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 417	Not reported
TRIAMCINOLONE	10 mg	OTHER: STAT	Y-M: 20[redacted] / 417	Y-M: 20[redacted] / 417

Event #1: Serious Adverse Event

Event Description	WORSENING OF LEFT SIDED ULCERATIVE COLITIS WITHOUT COMPLICATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 635 / 320
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 320): Erythrocytes: 4.48 [4.5 - 5.7] 10^12/L; Hemoglobin: 98 [137 - 170] G/L; Leukocytes: 7.7 [3.6 - 11.2] 10^9/L; Lymphocytes/Leukocytes: 11.8 [16 - 43.5] %; [redacted]20[redacted] (RX DAY 321): Hemoglobin: 88 [137 - 170] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 320): CHEST X-RAY: NO ACTIVE LUNG LESION NO PROMINENT PLEURAL EFFUSION; [redacted]20[redacted] (RX DAY 321): KUB: CALCIFIED DENSITY NOTED IN RIGHT PELVIS; MAYBE PHLEBOLITH OR LOWER URETERAL STONE NARROWING OF SACROILIAC JOINT.

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	WORSENING OF DISEASE
Discontinued Study Drug Due to the Event	NO

SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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] / 724 / 409
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	757 / 442
Duration of AE	34 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

Generated: [redacted]20[redacted]:06:46
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。本被験者は台湾の 3[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，合併症を伴わない潰瘍性大腸炎（左側）の悪化の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），貧血（詳細不明），慢性気管支炎，胃及び十二指腸の疾患（詳細不明），非感染性胃腸炎及び大腸炎（詳細不明），非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与635日後＊　，被験者は合併症を伴わない潰瘍性大腸炎（左側）の悪化を発現した。

本事象発現前（日付不明），被験者はフォローアップで消化管外来を受診し，1 ヵ月間血便があったことを報告した。腹部痛，嘔吐，下痢，吐血及び発熱はなかった。神経学的欠損は認められなかった。投与635日後＊　，被験者は入院した。潰瘍性大腸炎の再発のため高用量のステロイドを投与され，下痢による低カリウム血症のため塩化カリウムを投与された。消化管下部の出血に対して，輸血，トラネキサム酸投与及び急速輸液が行われた。入院中，バイタルサインは安定し，排便の頻度は減少した。投与640日後＊ ，被験者は退院した。

投与された薬剤は，ヒドロコルチゾン，トラネキサム酸及びプレドニゾロンであった。

The patient's past medications include:

MESALAZINE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

MESALAZINE ENEMA for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.1] [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 WORSENING OF LEFT SIDED ULCERATIVE COLITIS WITHOUT COMPLICATION

- Investigator: WORSENING OF DISEASE

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY WEIGHT:** 6[redacted].[redacted] KG

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

[redacted] **20[redacted] CHEST XRAY:** NO ACTIVE LUNG LESION. NO PROMINENT PLEURAL EFFUSION.

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

[redacted] **20[redacted] HEMOGLOBIN:** 9.8 G/DL (normal 13.7 to 17)

[redacted] **20[redacted] HEMOGLOBIN:** 8.8 G/DL (normal 13.7 to 17)

[redacted] **20[redacted] KUB:** CALCIFIED DENSITY NOTED IN RIGHT PELVIS; MAYBE PHLEBOLITH OR LOWER URETERAL STONE. NARROWING OF SACROILIAC JOINT.

[redacted] **20[redacted] LYMPHOCYTES %:** 11.8 % (normal 16 to 43.5)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.48 10^6/uL (normal 4.5 to 5.7)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 7.7 10^3/uL (normal 3.6 to 11.2)

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
精巣（純粋）セミノーマ	X	X		X

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

Medical History	Onset Year
BENIGN LEFT TESTICULAR LUMP	20[redacted]
CEREBROVASCULAR ACCIDENT	20[redacted]
CHRONIC BACK PAIN	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HEARTBURN	20[redacted]
INSOMNIA	19[redacted]
IRON DEFICIENCY	20[redacted]
LAZY LEFT EYE	20[redacted]
MILD LEFT SIDED LOWER EXTREMITY NUMBNESS	20[redacted]
NASAL CONGESTION	20[redacted]
PERIPHERAL ARTERY DISEASE	20[redacted]
RECURRENT LOWER EXTREMITY DEEP VENOUS THROMBOSIS	20[redacted]
RESTLESS LEG SYNDROME	20[redacted]
RIGHT PNEUMOTHORAX	20[redacted]
SPINAL FRACTURE	20[redacted]
SUBDURAL HEMATOMA	20[redacted]
VITAMIN D DEFICIENCY	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	20	20[redacted]
CIGARS	NEVER			

PIPES NEVER

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		QD	[redacted] / 1	[redacted] / 58	58
M14-234 SS2 ABT-494 (OL)	45 mg	QD	[redacted] / 59	[redacted] / 112	54
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 113	[redacted] / 154	42
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 155	[redacted] / 444	290

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 g	QD	Y-M: [redacted]
BUDESONIDE	9 mg	QD	Y-M: [redacted]
COLECALCIFEROL	1000 OTHER: UNITS	BID	Y-M: [redacted]
INFLIXIMAB	10 mg/kg	OTHER: EVERY 4 WEEKS	Y-M: [redacted]
IRON	300 mg	QD	Y-M: [redacted]
CALCIUM;COLECALCIFEROL	1 OTHER: TABLET	BID	Y-M: [redacted]
LOPERAMIDE	2 mg	PRN	Y-M: [redacted]
MESALAZINE	1000 mg	BID	Y-M: [redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: [redacted] / -281
OMEPRAZOLE	40 mg	QD	Y-M: [redacted] / -267
PREDNISONE	20 mg	QD	Y-M: [redacted] / -8
APIXABAN	5 mg	BID	Y: [redacted]
GLUTAMIC ACID	1000 mg	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
COLECALCIFEROL	1000 OTHER: UNITS	BID	Y-M: 20[redacted]	ONGOING
IRON	300 mg	QD	Y-M: 20[redacted]	ONGOING
CALCIUM;COLECALCIFEROL	1 OTHER: TABLET	BID	Y-M: 20[redacted]	ONGOING
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted]	ONGOING
OMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -267	ONGOING
CHONDROITIN;GLUCOSAMINE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 149	ONGOING
DIPHENHYDRAMINE	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 289	Y-M: 20[redacted] / 289
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted] / 290	Y-M: 20[redacted] / 294
OXYCODONE;PARACETAMOL	1 OTHER: TABLET	PRN	Y-M: 20[redacted] / 290	Y-M: 20[redacted] / 313
APIXABAN	5 mg	BID	Y: 20[redacted]	ONGOING
GLUTAMIC ACID	1000 mg	BID	Y: 20[redacted]	Y-M: 20[redacted] / 302

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

Event Description	LEFT TESTICULAR SEMINOMA
Preferred term	精巣（純粋）セミノーマ
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 444 / 290
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 290): LEFT ORCHIECTOMY: HISTOLOGIC TYPE: SEMINOMA. PATHOLOGIC STAGE: PT2 NX. LYMPHOVASCULAR INVASION PRESENT.	
AE Stopped Initial Rx Day / Rx Day	444 / 290
Duration of AE	1 DAY
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HISTORY OF BENIGN TESTICULAR LUMP
Discontinued Study Drug Due to the Event	YES
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:06:46
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，左側精巣セミノーマの事象を発現した。関連する病歴は，良性左側精巣腫瘤，下肢深部静脈血栓症の再発，末梢動脈疾患，軽度の左下肢しびれ感，硬膜下血腫，元喫煙者（1 日 1 箱を 20 年間），潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与444日後＊　　，被験者は左側精巣セミノーマを発現した。投与444日後＊　　，左側精巣セミノーマは消失した。

本事象発現前の投与343日後＊　，被験者は左側精巣腫瘤の悪化が発現した。陰嚢の超音波検査に基づき，悪性腫瘍が疑われた。

投与444日後＊　　，被験者は待機的な左側精巣摘出術を受け，左側精巣セミノーマが明らかとなった。病理学的ステージは pT2，NX であり，リンパ管又は静脈侵襲ありであった。更なる治療（放射線を含む）は不要であった。最終的な病理は上述の通りであった。組織型：セミノーマ，病理学的ステージ：pT2，NX，リンパ管又は静脈侵襲：あり

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 percocet であった。

The patient's past medications include:

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

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

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

CANASA for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS, WORSENING OF ULCERATIVE COLITIS SYMPTOMS, DIFFUSE ARTHRALGIA AND ULCERATIVE COLITIS SYMPTOM RELAPSE and DIFFUSE ARTHRALGIA AND ULCERATIVE COLITIS SYMPTOM RELAPSE ([redacted])

Causality for UPADACITINIB (Open Label)

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1) Testicular seminoma (pure) (10062124) (Testicular seminoma (pure) (10062124)) [v.23.1] [10062124]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of LEFT TESTICULAR SEMINOMA

- Investigator: History of benign testicular lump

- AbbVie: Event not consistent with study drug's mechanism of action. Exact etiology of seminoma is unknown. Instead, typical known risk factors include cryptorchidism, a personal or family history of testicular cancer, infertility or subfertility, and HIV infection.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **SCROTAL ULTRASOUND:** Suspicious for malignancy

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	MALE	WHITE

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
OTHER: ALLERGY TO SULFA'S	19[redacted]
OTHER: BILATERAL ADENOIDECTOMY	19[redacted]
OTHER: BILATERAL PRESSURE EQUALIZER SURGERY	19[redacted]
OTHER: DECREASED APPETITE	20[redacted]
OTHER: DENTAL IMPLANT	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: INTERMITTENT CHILLS	20[redacted]
OTHER: INTERMITTENT SWEATING	20[redacted]
OTHER: PILONDIAL CYST SURGERY	20[redacted]
OTHER: WISDOM TEETH REMOVAL	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	QD	[redacted] / 57	[redacted] / 372	316
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 372	[redacted] / 1248	877

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	9 mg	OTHER: QOD	Y-M: [redacted]
MESALAZINE	4 g	QD	Y-M: [redacted]
AZATHIOPRINE	150 mg	QD	Y-M: [redacted]
AZATHIOPRINE	50 mg	QID	Y-M: [redacted]
MESALAZINE	1.6 g	TID	Y-M: [redacted] / -62
MESALAZINE	1.5 mg	QD	Y: [redacted]
PREDNISONE	NOT REPORTED	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
PAROXETINE	20 mg	QD	Y-M: [redacted] / 429	ONGOING
ETODOLAC	400 mg	BID	Y-M: [redacted] / 580	Y-M: [redacted] / 581
CEFTRIAXONE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: [redacted] / 610	Y-M: [redacted] / 621
CLINDAMYCIN	600 mg	OTHER: EVERY 6 HOURS	Y-M: [redacted] / 610	Y-M: [redacted] / 621
GUAIFENESIN	10 mL	PRN	Y-M: [redacted] / 610	Y-M: [redacted] / 621
LEVOFLOXACIN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: [redacted] / 610	Y-M: [redacted] / 621
METRONIDAZOLE	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: [redacted] / 610	Y-M: [redacted] / 621
SULFAMETHOXAZOLE;TRIMETHOPRIM	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: [redacted] / 610	Y-M: [redacted] / 621
ATOVAQUONE	750 mg	BID	Y-M: [redacted] / 621	Y-M: [redacted] / 634

BIFIDOBACTERIUM NOS;LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS PARACASEI;STREPTOCOCCUS THERMOPHILUS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 621 Y-M: 20[redacted] / 634
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 621 Y-M: 20[redacted] / 697
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 621 Y-M: 20[redacted] / 625
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 626 Y-M: 20[redacted] / 697

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 981 / 610
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 610): NPTST138-INFLUENZA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST187-PNEUMOCYSTIS JIROVECI PNEUMONIA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST216-RESPIRATORY CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST262-VIRAL PCR PANEL: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 615): NPTST015-ACIDE-FAST BACILLI: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 610): CHEST X-RAY: BILATERAL BASILAR LUNG INFILTRATES; [redacted]20[redacted] (RX DAY 615): BRONCH W/LAVAGE: COULD NOT GET BIOPSIES WITH PERSISTENT STRONG COUGHING; COMPUTERIZED TOMOGRAPHY ABDOMEN: "MILDLY THICKENED DISTAL COLONIC WALL, LIKELY RELATED TO HISTORY OF ULCERATIVE COLITIS. NO EVIDENCE OF ACUTE INFLAMMATORY CHANGES. NO ACUTE INTRA-ABDOMINAL/PELVIC FINDING. BIBASILAR AIRSPACE OPACITIES . PLEASE CORRELATE CLINICALLY FOR PNEUMONIA."

AE Stopped Initial Rx Day / Rx Day	1042 / 671
Duration of AE	62 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

Generated: [redacted]20[redacted]:06:46
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 2[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺炎の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与981日後＊　，被験者は肺炎を発現した。投与1042日後＊，肺炎は消失した

投与981日後＊，被験者は，本事象発現の前に発熱を発現し，非重篤と判断された。

投与981日後＊　，被験者は発熱，悪心及び嘔吐があり，入院した。当初，潰瘍性大腸炎の再燃が原因であると考えられた。腹部 CT 検査が実施され，急性の炎症が否定された。 投与986日後＊，洗浄を伴う気管支鏡検査が実施された後，両側の肺炎が明らかとなったが，検査中の咳嗽のため生検検体は採取できなかった。被験者は，抗生物質を投与された。気管支鏡検査でニューモシスチス・イロベチイ肺炎は否定された。被験者が最後に電子タバコを使用したのは，2–3週間前であった。投与992日後＊ ，被験者は退院した。

投与された薬剤は，アトバコン，risaquad，prednisone，クリンダマイシン，robitussin，ロセフィン，levaquin，フラジール，bactrim であった。

The patient's past medications include:

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

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

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

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

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

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

ETODOLAC for BACK ARTHRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SULFA for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ACIDE-FAST BACILLI TEST (SPUTUM):** Negative

[redacted] **20[redacted] BRONCH W/LAVAGE:** COULD NOT GET BIOPSIES WITH PERSISTENT STRONG COUGHING

[redacted] **20[redacted] BRONCHOSCOPY:** Positive for bilateral pneumonia, negative for PJ pneumonia.

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

[redacted] **20[redacted] COMPUTERIZED TOMOGRAPHY ABDOMEN:** "MILDLY THICKENED DISTAL COLONIC WALL, LIKELY RELATED TO HISTORY OF ULCERATIVE COLITIS. NO EVIDENCE OF

ACUTE INFLAMMATORY CHANGES. NO ACUTE INTRA-ABDOMINAL/PELVICFINDING. BIBASILAR AIRSPACE OPACITIES. PLEASE CORRELATE CLINICALLY FOR PNEUMONIA."

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

[redacted] **20[redacted] PNEUMOCYSTIS JIROVECI PNEUMONIA TEST:** Negative

[redacted] **20[redacted] RESPIRATORY CULTURE (SPUTUM):** Negative

[redacted] **20[redacted] VIRAL PCR PANEL:** Negative

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
潰瘍性大腸炎		X		
敗血症	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 15 mg	2[redacted]	MALE	MULTIPLE

Medical History	Onset Year
ASTHMA	19[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
OSTEOPOROSIS	20[redacted]
OTHER: ALLERGIC TO CEPHALEXIN	20[redacted]
OTHER: ALLERGIC TO LEGUMES	19[redacted]
OTHER: ALLERGIC TO MILK	19[redacted]
OTHER: ALLERGIC TO PEANUT OIL	19[redacted]
OTHER: ALLERGIC TO SOY	19[redacted]
OTHER: COLONOSCOPY	20[redacted]
OTHER: COLONOSCOPY	20[redacted]
OTHER: COLONSCOPY	20[redacted]
OTHER: GASTRIC ULCER	20[redacted]
OTHER: HIATIAL HERNIA	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: NAUSEA	20[redacted]
OTHER: SIGMOIDOSCOPY	20[redacted]
OTHER: SLEEP APNEA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: GANGLION CYST REMOVED FROM LEFT WRIST	20[redacted]
SURGERY: 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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted] / 1	[redacted] / 55	55
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 56	[redacted] / 84	29
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 84	[redacted] / 967	884

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CETIRIZINE	10 mg	QD	Y-M: [redacted]
MONTELUKAST	10 mg	QD	Y-M: [redacted]
COLECALCIFEROL	2000 OTHER: UNITS	QD	Y-M: [redacted]
DICYCLOVERINE	20 mg	PRN	Y-M: [redacted]
MESALAZINE	4.8 g	QD	Y-M: [redacted]
ADALIMUMAB	40 mg	OTHER: EVERY 2 WEEKS	Y-M: [redacted]
MERCAPTOPURINE	50 mg	QD	Y-M: [redacted]
METHOTREXATE	25 mg	OTHER: WEEKLY	Y-M: [redacted]
INFLIXIMAB	5 OTHER	OTHER: EVERY 8 WEEKS	Y-M: [redacted]
TRAZODONE	50 mg	QD	Y-M: [redacted]
PANTOPRAZOLE	40 mg	BID	Y-M: [redacted]
PROMETHAZINE	25 mg	PRN	Y-M: [redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: [redacted]

BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -284
RISEDRONIC ACID	150 mg	OTHER: MONTHLY	Y-M: 20[redacted] / -139
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / -111
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -9
SALBUTAMOL	90 ug/m2	PRN	Y: 20[redacted]
BUDESONIDE;FORMOTEROL	160-4.5 ug	BID	Y: 20[redacted]
TRIAMCINOLONE	55 ug/m2	BID	Y: 20[redacted]
PROBIOTICS NOS	10 BILLION CELL OTHER: CAPSULE	BID	Y: 20[redacted]
CALCIUM CARBONATE	1500 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 / Stop Year-Month / RX Day	
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	2000 OTHER: UNITS	QD	Y-M: 20[redacted]	ONGOING
DICYCLOVERINE	20 mg	PRN	Y-M: 20[redacted]	ONGOING
TRAZODONE	50 mg	QD	Y-M: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted]	ONGOING
PROMETHAZINE	25 mg	PRN	Y-M: 20[redacted]	ONGOING
RISEDRONIC ACID	150 mg	OTHER: MONTHLY	Y-M: 20[redacted] / -139	ONGOING
LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / -111	ONGOING
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 21	ONGOING
HYOSCYAMINE	0.125 mg	PRN	Y-M: 20[redacted] / 743	ONGOING
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 784	Y-M: 20[redacted] / 798
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / 799	Y-M: 20[redacted] / 806
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 807	Y-M: 20[redacted] / 814
CALCIUM CHLORIDE;POTASSIUM;SODIUM LACTATE	1000 mL	OTHER: ONE DOSE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
GLUCOSE;POTASSIUM;SODIUM CHLORIDE	1000 mL	OTHER: ONE BAG AT 100 ML HR	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
HYDROXYZINE	25 mg	OTHER: 1 DOSE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 817	ONGOING
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 820

PARACETAMOL	1000 mg	OTHER: X1 DOSE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
PIPERACILLIN;TAZOBACTAM	4.5 g	PRN	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 820
PROMETHAZINE	12.5 mg	OTHER: ONE DOSE	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
SODIUM CHLORIDE	1000 mL	OTHER: 1 BAG	Y-M: 20[redacted] / 817	Y-M: 20[redacted] / 817
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 884	Y-M: 20[redacted] / 934
TOFACITINIB	10 mg	QD	Y-M: 20[redacted] / 904	ONGOING
SALBUTAMOL	90 ug/m2	PRN	Y: 20[redacted]	ONGOING
BUDESONIDE;FORMOTEROL	160-4.5 ug	BID	Y: 20[redacted]	ONGOING
TRIAMCINOLONE	55 ug/m2	BID	Y: 20[redacted]	ONGOING
PROBIOTICS NOS	10 BILLION CELL OTHER: CAPSULE	BID	Y: 20[redacted]	ONGOING
CALCIUM CARBONATE	1500 mg	BID	Y: 20[redacted]	ONGOING

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

Event Description	SEPSIS DUE TO UNSPECIFIED ORGANISM
Preferred term	敗血症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 899 / 816
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 817): CHEST X-RAY: PENDING; CT OF ABDOMEN: SUGGESTIVE OF DIARRHEAL ILLNESS AND DIFFUSE COLITIS; [redacted]20[redacted] (RX DAY 820): FLEXIBLE SIGMOIDOSCOPY WITH BIOPSY: NORMAL SIGMOID COLON RECTUM	
AE Stopped Initial Rx Day / Rx Day	903 / 820
Duration of AE	5 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 #2: AE Leading to Discontinuation of Study Drug

Event Description	ULCERATIVE COLITIS EXACERBATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 964 / 881
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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	YES
SAE Criteria	NONE

Generated: [redacted]20[redacted]:06:46
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 2[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，詳細不明の病原体による敗血症の事象を発現した。関連する病歴は，胃食道逆流性疾患，潰瘍性大腸炎，胃潰瘍，悪心，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899日後＊　，被験者は詳細不明の病原体による敗血症を発現した。投与903日後＊，詳細不明の病原体による敗血症は消失した。

本事象発現前の 投与806日後＊　，被験者は潰瘍性大腸炎の悪化（非重篤）を発現し始め，prednisone 25 mg の 2 週間の投与を開始し，その後漸減した。

投与899日後＊　，被験者は下痢，悪心，嘔吐，腹部痛，発熱及び頻脈を発現した。被験者は救急治療室を受診し，投与900日後＊に入院した。投与900日後＊　，被験者は腹部 CT 検査を受け，下痢性疾患及びびまん性大腸炎が示唆された。投与903日後＊，被験者は退院した。

投与された薬剤は，モルヒネ，塩化ナトリウム，ラクトリンゲル，アセトアミノフェン，ブドウ糖水和物 5%・塩化ナトリウム 0.9%・塩化カリウム 20 mEq 合剤及びゾシンであった。

The patient's past medications include:

LIALDA for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

6 MERCAPTOPURINE for ULCERATIVE COLITIS ([redacted])

METHOTREXATE for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

UCERIS for ULCERATIVE COLITIS ([redacted])

AZITHROMYCIN for SINUS INFECTION ([redacted])

CEPHALEXIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Open Label)

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1)　Sepsis (10040047)　(Sepsis (10040047))　[v.22.1]　[10040047]

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 SEPSIS DUE TO UNSPECIFIED ORGANISM

- Investigator: Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CREATINE:** increased

[redacted] **20[redacted] CT SCAN:** SUGGESTIVE OF DIARRHEAL ILLNESS AND SUGGESTIVE OF DIFFUSE COLITIS

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** biopsy taken: normal sigmoid colon, rectum

[redacted] **20[redacted] GLUCOSE:** increased

[redacted] **20[redacted] WBC:** increased

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
クロストリジウム・ディフィシレ感染	X			X
帯状疱疹				X
四肢痛	X			

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
INFLAMMATORY BOWEL DISEASE: ULCERATIVE COLITIS	20[redacted]
OSTEOARTHRITIS: ANKLE PAIN	20[redacted]
OTHER: CHICKEN POX	19[redacted]

Prior Procedures	Procedure Year
SURGERY: FECAL MATTER TRANSPLANT FOR TREATMENT OF RECURRENT C-DIFFICILE	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	FORMER	Less than 2 DRINKS

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58

M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 261	204

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2.4 g	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	5 mg/kg	OTHER: 4 WEEKS	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	40 mg	OTHER: BI WEEL;Y	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: 4	Y-M: 20[redacted]-[redacted]
METHOTREXATE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
BUDESONIDE	9 mg	OTHER: WEEKLY	Y-M: 20[redacted]-[redacted]
PREDNISONE	50 mg	QD	Y-M: 20[redacted]-[redacted] / -142
VANCOMYCIN	125 mg	QID	Y-M: 20[redacted]-[redacted] / -148

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
METHOTREXATE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]	Not reported
VANCOMYCIN	125 mg	QID	Y-M: 20[redacted]-[redacted] / 133	Y-M: 20[redacted]-[redacted] / 142
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]-[redacted] / 141	ONGOING
PREDNISONE	50 mg	QD	Y-M: 20[redacted]-[redacted] / 144	Y-M: 20[redacted]-[redacted] / 150
PREDNISONE	20 mg	TID	Y-M: 20[redacted]-[redacted] / 204	Y-M: 20[redacted]-[redacted] / 211
VALACICLOVIR	1 mg	QD	Y-M: 20[redacted]-[redacted] / 204	Y-M: 20[redacted]-[redacted] / 211
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted]-[redacted] / 244	Y-M: 20[redacted]-[redacted] / 252
VANCOMYCIN	125 mg	QID	Y-M: 20[redacted]-[redacted] / 244	Y-M: 20[redacted]-[redacted] / 252

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

Event Description	C-DIFFICILE INFECTION
Preferred term	クロストリジウム・ディフィシレ感染
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 189 / 132
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY -234): NPTST185-PLATELETS: 532 [130 - 400] KMCL; [redacted]20[redacted] (RX DAY 132): Leukocytes: 11.5 [4.8 - 10.8] 10^9/L; NPTST020-ALK PHOS: 0.4 [0.1 - 1.3] MG/DL; NPTST022-ALT: 5 [7 - 52] IU/L; NPTST035-AST: 26 [15 - 41] U/L; NPTST057-C-DIFFICILE: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST062-CHEMISTRY- BUN: 6 [7 - 25] MG/DL; NPTST063-CHEMISTRY- POTASSIUM: 3.0 [3.5 - 5.3] MMOL/L; NPTST064-CHEMISTRY-ALBUMIN: 3.0 [3.3 - 4.6] G/DL; NPTST065-CHEMISTRY-CALCIUM: 8.8

[8.6 - 10.3] MG/DL; NPTST068-CHEMISTRY-CREATININE: 0.75 [0.6 - 1.1] MG/DL; NPTST069-CHEMISTRY-SODIUM: 132 [136 - 144] MMOL/L; NPTST071-CHEMISTRYTOTAL PROTEIN: 7.4 [6 - 8.1] G/DL; NPTST078-CO2: 26 [22 - 32] MMOL/L; NPTST125-GLUCOSE: 98 [75 - 110] MG/DL; NPTST128-HEMOCRIT: 32.6 [37 - 47] %; NPTST129-HEMOGLOBIN: 10.4 [12 - 16] G/DL; NPTST185-PLATELETS: 532 [130 - 400] K/MCL

Microbiology

[redacted]20[redacted] (RX DAY 133): STOOL NPTST056-C-DIFF: Positive-C DIFFICILE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 133): CT ABDOMEN AND PELVIS W CONTRAST: NORMAL

AE Stopped Initial Rx Day / Rx Day	199 / 142
Duration of AE	11 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	L FOOT PAIN
Preferred term	四肢痛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 198 / 141
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 142): Albumin: 24 [35 - 50] G/L; Calcium: 2.095884 [2.095884 - 2.619855] MMOL/L; NPTST050-BUN: 16 [9 - 20] MG/DL; NPTST066-CHEMISTRY-CARBON DIOXIDE: 26 [21 - 31] MEQ/L; NPTST067-CHEMISTRY-CHLORIDE: 99 [98 - 110] MEQ/L; NPTST068-CHEMISTRY-CREATININE: 0.5 [0.5 - 1.4] MG/DL; NPTST070-CHEMISTRY-UREA NITROGEN: 8 [7 - 22] MG/DL; NPTST125-GLUCOSE: 90 [60 - 99] MG/DL; Potassium: 3.9 [3.5 - 5.1] MMOL/L; Sodium: 137 [135 - 148] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 142): ULTRASOUND LOWER L EXTREMITIES: NO EVIDENCE OF DEEP VEIN THROMBOSIS; [redacted]20[redacted] (RX DAY 144): X- RAY OF L FOOT: NO ACUTE OSSEOUS ABNORMALITIES

AE Stopped Initial Rx Day / Rx Day	202 / 145
Duration of AE	5 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PARTICIPANT HOSPITALIZED ON [redacted]/[redacted]/[redacted] FOR SEVERE FOOT PAIN RELATING TO ARTHRALGIA FROM ULCERATIVE COLITIS
Discontinued Study Drug Due to the	NO

Event	
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: 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] / 261 / 204
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	306 / 249 (45 DAYS AFTER LAST TREATMENT)
Duration of AE	46 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]:06:46
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，クロストリジウム・ディフィシレ感染の事象を発現した。関連する病歴は，潰瘍性大腸炎，クロストリジウム・ディフィシレ感染再発の治療のための糞便移植，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与189日後＊　　，被験者はクロストリジウム・ディフィシレ感染を発現した。投与199日後＊，クロストリジウム・ディフィシレ感染は消失した。

投与189日後＊　，被験者は嘔吐，悪心及び腹痛があり，入院した。クロストリジウム・ディフィシレ感染と診断された。免疫抑制が危険因子であると考えられた。投与194日後＊　，被験者は退院した。

投与された薬剤は，バンコマイシンであった。

Causality for ABT-494 (Open Label)

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1) Clostridium difficile infection (10054236) (Clostridium difficile infection (10054236)) [v.21.0] [10054236]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Open Label)

Event of C-DIFFICILE INFECTION

- Investigator: Not applicable.

- AbbVie: Event is more likely related to recurrence of pre-existing Clostridium difficile infection. Ulcerative colitis is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:**3.0 G/DL (normal 3.3 to 4.6)

[redacted] 20[redacted] **ALT:** 5 IU/L (normal 7 to 52)

[redacted] 20[redacted] **CT ABDOMEN AND PELVIS W IV CONTRAST:** Normal

[redacted] 20[redacted] **HEMATOCRIT:** 32.6 % (normal 37 to 47)

[redacted] 20[redacted] **HEMOGLOBIN:** 10.4 G/DL (normal 12.0 to 16.0)

[redacted] 20[redacted] **PLATELETS:** 532 X10**3/MCL (normal 130 to 400)

[redacted] 20[redacted] **POTASSIUM:** 3.0 MMOL/L (normal 3.5 to 5.3)

[redacted] 20[redacted] **SODIUM:** 132 MMOL/L (normal 136 to 144)

[redacted] 20[redacted] **STOOL TEST:** Positive C. difficile

[redacted] 20[redacted] **STOOL TEST:** Positive C. difficile

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 11.5 X10**3/MM**3 (normal 4.8 to 10.8)
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，左足痛の事象を発現した。関連する病歴は，足関節痛，足痛及び変形性関節症であった。

Event 2 の臨床経過：

投与198日後＊　，被験者は左足痛を発現した。

投与198日後＊　　，被験者は重度の急性左足痛及び足関節痛があり，入院した。投与202日後＊，被験者は退院した。投与202日後＊，左足痛は消失した。

投与された薬剤は，トラマドール及び prednisone であった。

Causality for ABT-494 (Open Label)

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1)　Foot pain (10016974)　(Pain in extremity (10033425))　[v.23.1]　[10016974]

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 LEFT FOOT PAIN

- Investigator: PARTICIPANT HOSPITALIZED ON [redacted] FOR SEVERE FOOT PAIN RELATING TO ARTHRALGIA FROM ULCERATIVE COLITIS.

- AbbVie: EVENT IS MORE LIKELY RELATED TO PRE-EXISTING OSTEOARTHRITIS AND ANKLE PAIN.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BUN:** 16 mg/dL (normal 9 to 20)

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

[redacted] **20[redacted] CHEMISTRY-CARBON DIOXIDE:** 26 MEQ/L (normal 21 to 31)

[redacted] **20[redacted] CHEMISTRY-CHLORIDE:** 99 MEQ/L (normal 98 to 110)

[redacted] **20[redacted] CHEMISTRY-CREATININE:** 0.5 mg/dL (normal 0.5 to 1.4)

[redacted] **20[redacted] CHEMISTRY-UREA NITROGEN:** 8 mg/dL (normal 7 to 22)

[redacted] **20[redacted] GLUCOSE:** 90 mg/dL (normal 60 to 99)

[redacted] **20[redacted] POTASSIUM:** 3.9 MEQ/L (normal 3.5 to 5.1)

[redacted] **20[redacted] SODIUM:** 137 MEQ/L (normal 135 to 149)

[redacted] **20[redacted] ULTRASOUND LOWER L EXTREMITIES:** NO EVIDENCE OF DEEP VEIN THROMBOSIS

[redacted] **20[redacted] X- RAY OF L FOOT:** NO ACUTE OSSEOUS ABNORMALITIES

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
膵腺癌	X	X	X	X
血中クレアチンホスホキナーゼ増加				X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	7[redacted]	FEMALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERLIPIDEMIA: TAKES TRICOR	19[redacted]
HYPOTHYROIDISM: TAKES SYNTHROID	19[redacted]
OTHER: ARTHRITIS, MOST DISCOMFORT IN HANDS, FEET, BACK. OCCASIONAL TYLENOL	20[redacted]
OTHER: BENIGN MOLES/LESIONS REMOVAL	20[redacted]
OTHER: C.DIFFICILE	20[redacted]
OTHER: GAS	20[redacted]
OTHER: INFERIOR VENA CAVA THROMBUS	20[redacted]
OTHER: LATERAL, MEDIAL MENISCUS TEAR	20[redacted]
OTHER: PAROXYSMAL ATRIAL FIBRILLATION	20[redacted]
OTHER: RECTAL POLYPS REMOVED	20[redacted]
OTHER: VARIOUS BENIGN CYSTS REMOVED FROM RIGHT ARM AND FINGERS	19[redacted]
OTHER: VITAMIN D DEFICIENCY	20[redacted]

Prior Procedures	Procedure Year
SURGERY: HYSTERECTOMY	19[redacted]
SURGERY: LUMPECTOMY RIGHT BREAST,BENIGN LUMP (TIMES 2) RIGHT BREAST	19[redacted]
SURGERY: PARTIAL COCCYX REMOVAL	19[redacted]
SURGERY: RIGHT EYE CATARACT SURGERY	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 57	[redacted] / 365	309
M14-533 ABT-494 (LTE)	30 mg	QD	[redacted] / 429	[redacted] / 836	408

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
MERCAPTOPURINE	100 mg	QD	Y-M: [redacted]
INFLIXIMAB	5 mg/kg	OTHER: 8 WEEKS	Y-M: [redacted]
VEDOLIZUMAB	300 mg	OTHER: 8 WEEKS	Y-M: [redacted]
METHOTREXATE	25 mg	1 time per week	Y-M: [redacted]
CALCIUM CARBONATE	500 mg	PRN	Y-M: [redacted]
MESALAZINE	1000 mg	QD	Y-M: [redacted]
PREDNISONE	5 mg	QD	Y-M: [redacted]
ESTROGENS CONJUGATED	1 OTHER: APPLICATOR	PRN	Y-M: [redacted]
LOPERAMIDE	2 OTHER: TABLETS	PRN	Y-M: [redacted]
METOPROLOL	25 mg	QD	Y-M: [redacted] / -327
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y-M: [redacted] / -290
POTASSIUM	595 mg	BID	Y-M: [redacted] / -240
POTASSIUM	595 mg	QD	Y-M: [redacted] / -226
VITAMIN E NOS	400 OTHER: UNITS	QD	Y-M: [redacted] / -8
WARFARIN	2.5-5 mg	QD	Y-M: [redacted] / -8

PARACETAMOL	650 mg	PRN	Y: 19[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y: 19[redacted]
FENOFIBRATE	145 mg	QD	Y: 20[redacted]
VITAMIN D NOS	4000 IU	QD	Y: 20[redacted]
CALCIUM	500 mg	BID	Y: 20[redacted]
FOLIC ACID	400 ug	QD	Y: 20[redacted]
MAGNESIUM	250 mg	QD	Y: 20[redacted]
LEVOTHYROXINE	88 ug	QD	Y: 20[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY OTHER WEEK	Y: 20[redacted]
PREDNISONE	5 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
ESTROGENS CONJUGATED	1 OTHER: APPLICATOR	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 434
LOPERAMIDE	2 OTHER: TABLETS	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 434
METOPROLOL	25 mg	QD	Y-M: 20[redacted] / -327	Y-M: 20[redacted] / 434
SALBUTAMOL	2 OTHER: PUFFS	PRN	Y-M: 20[redacted] / -290	Y-M: 20[redacted] / 434
POTASSIUM	595 mg	QD	Y-M: 20[redacted] / -226	Y-M: 20[redacted] / 402
WARFARIN	2.5-5 mg	QD	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 330
BISACODYL	20 mg	QD	Y-M: 20[redacted] / 335	Y-M: 20[redacted] / 335
MACROGOL 3350	238 mg	QD	Y-M: 20[redacted] / 335	Y-M: 20[redacted] / 335
SIMETICONE	180 mg	QD	Y-M: 20[redacted] / 335	Y-M: 20[redacted] / 335
FENTANYL	100 OTHER: MCG	QD	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
MIDAZOLAM	7.5 mg	QD	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
WARFARIN	2.5-5 mg	QD	Y-M: 20[redacted] / 337	Y-M: 20[redacted] / 434
CEFALEXIN	500 mg	BID	Y-M: 20[redacted] / 392	Y-M: 20[redacted] / 398
DOCUSATE	100 mg	PRN	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 434
MAGNESIUM	400 mg	QD	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 434
MAGNESIUM HYDROXIDE	30 mL	PRN	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 434
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 408
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 408
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 408
POTASSIUM	40 mEq	QD	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 408
SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 408
VITAMIN E NOS	400 IU	QD	Y-M: 20[redacted] / 403	Y-M: 20[redacted] / 434

CYCLOBENZAPRINE	5 mg	TID	Y-M: 20[redacted] / 408	Y-M: 20[redacted] / 434
PARACETAMOL	650 mg	PRN	Y: 19[redacted]	Y-M: 20[redacted] / 434
VITAMINS NOS	1 OTHER: TABLET	QD	Y: 19[redacted]	Y-M: 20[redacted] / 434
FENOFIBRATE	145 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 434
VITAMIN D NOS	4000 IU	QD	Y: 20[redacted]	Y-M: 20[redacted] / 434
CALCIUM	500 mg	BID	Y: 20[redacted]	Y-M: 20[redacted] / 434
FOLIC ACID	400 ug	QD	Y: 20[redacted]	Y-M: 20[redacted] / 434
MAGNESIUM	250 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 402
LEVOTHYROXINE	88 ug	QD	Y: 20[redacted]	Y-M: 20[redacted] / 434

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

Event Description	ELEVATED CPK
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] / 764 / 336
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	862 / 434 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	99 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 #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Death, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC

Event Description	PANCREATIC ADENOCARCINOMA
Preferred term	膵腺癌
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 831 / 403
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 407): NPTST079-CORE BIOPSY: METASTATIC ADENOCARC [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 403): CT ABD/PELVIS W/O ALL CONTRAST: PANCREATIC LESION, MULTIPLE LIVER LESIONS; [redacted]20[redacted] (RX DAY 404): MRI MRCP W/O CONTRAST: FINDINGS WORRISOME FOR METASTATIC PANCREATIC ADENOCARCINOMA

AE Stopped Initial Rx Day / Rx Day	862 / 434 (26 DAYS AFTER LAST TREATMENT)
Duration of AE	32 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	AGE RELATED CANCER
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, DEATH OF SUBJECT

Generated: [redacted]20[redacted]:06:46

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）の治験で盲検化された治験薬が投与され，致死性の膵腺癌の事象を発現した。関連する病歴は，高脂血症，甲状腺機能低下症，子宮摘出，右乳房腫瘤摘除，右乳房良性腫瘤（2 回），右腕及び指から切除された種々の良性嚢胞，ビタミン D 欠乏，発作性心房細動，潰瘍性大腸炎，良性ほくろ及び良性病変の切除，胃食道逆流性疾患，直腸ポリープ切除，関節炎，多数の不快感（手，足，背部），下大静脈血栓症，非喫煙者，現飲酒者（1 日 2 杯未満）及び肺癌の家族歴（母親）であった。

Event 2 の臨床経過：

投与831日後＊　，被験者は膵腺癌を発現した。投与862日後＊　　，被験者は死亡した。死因は，膵臓病変–膵腺癌であると報告された。剖検が行われたかは不明である。

入院以前の 4 週間，被験者は上腹部に痛みを経験していた。胸やけの薬物治療を開始しており，それが関連していると考えていた。更に，被験者は，腹部痛が持続し，下腹部痛も自覚したと報告した。被験者は，2 週間前（投与820日後＊　）にクリニックを受診し，尿路感染（非重篤）と診断され，尿路感染は 投与826日後＊　に抗生物質により消失した。しかしながら，腹部痛は持続した。

投与831日後＊　，被験者は間欠的な腹部痛，浮動性めまい及び悪心（発熱又は悪寒はなし）を訴え，救急治療室を受診した。CT 検査及び MRI 検査を受け，検査結果は消化管科及び腫瘍科で評価された。投与836日後＊　，被験者は外来での生検結果の計画を立て，退院した。鎮痛薬，腸の薬剤及びプロトンポンプ阻害薬を処方され，帰宅した。

カルテによると，被験者は，肝臓の広範な転移性病変を伴う転移性膵癌を発現した。全身状態が急速に悪化し，ゲムシタビンとアブラキサン併用の化学療法を受けていた。被験者は，凝血異常，高カルシウム血症，高血圧，消化管出血，急性腎障害，汎血球減少症及び低ナトリウム血症も発現した。消化管科及び腫瘍科の診察を受け，最大限の治療を受けたにもかかわらず，改善しなかった。被験者は緩和ケア科に移され，腫瘍科及び緩和ケア科での蘇生処置を拒否した。緩和のための薬物治療に切り替えられ，緩和ケア科によってフォローされた。被験者は死亡前の数日間，経口摂取しなかった。痛み，不安，息切れ及び便秘に対処するための薬剤を処方された。緩和ケア科によると，被験者は昏迷状態，覚醒不可能であり，おそらく無意識であった。その後，被験者は死亡した。

胆嚢摘出術，回旋筋腱板修復，結腸内視鏡検査，子宮内容除去術，円錐切除術，右膝関節鏡検査及び結腸手術を含む病歴が追加された。

投与された薬剤は，アブラキサン及びゲムシタビンであった。

The patient's past medications include:

6-MERCAPTOPURINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - 20[redacted])

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Pancreatic adenocarcinoma (10051971) (Adenocarcinoma pancreas (10052747)) [v.24.0] [10051971]

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 PANCREATIC ADENOCARCINOMA

- Investigator: Age related cancer

- AbbVie: Advancing age is a risk factor. In addition, per Johns Hopkins researchers, conservative estimates are that an average of 11.7 years elapses before the first cancer cell develops within a high grade pancreatic lesion, then another 6.8 years as the cancer grows and at least one cell has the potential to spread.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BIOPSY: ULTRASOUND GUIDED BIOPSY:** Right lobe liver lesion core biopsy: metastatic carcinoma

[redacted] **20[redacted] BLOOD PRESSURE:** 145/59 mmHg

[redacted] **20[redacted] CA 19-9:** 10575 NO UNITS

[redacted] **20[redacted] CT ABD/PELVIS W/O ALL CONTRAST:** Pancreatic lesion, multiple liver lesions

[redacted] **20[redacted] CT ABDOMEN/PELVIS:** showed new atrophy of the pancreas body and tail with 3 cm probable mass at the junction of the pancreas head and body, consistent with neoplastic disease, prominent lymph node, nodal metastases, numerous scattered lesions in the liver.

[redacted] **20[redacted] HEART RATE:** 83 /min

[redacted] **20[redacted] MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY:** worrisome for metastatic pancreatic adenocarcinoma.

[redacted] **20[redacted] MRI MRCP W/O CONTRAST:** Findings worrisome for metastatic pancreatic adenocarcinoma

[redacted] **20[redacted] RESPIRATORY RATE:** 16 /min

[redacted] **20[redacted] SPO2:** 93 %

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

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
扁平上皮癌				X
皮膚有棘細胞癌				X

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

Medical History	Onset Year
CHOLELITHIASIS	20[redacted]
DIABETES MELLITUS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERLIPIDEMIA: HYPERLIPIDEMIA IS THE DIAGNOSIS	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: CHOLELITHTIASIS WITHOUT OBSTRUCTION	20[redacted]
OTHER: DEPRESSION	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: RHEUMATOID ARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
SURGERY: DILATION AND CURETTAGE FOR MENORRHAGIA	19[redacted]
SURGERY: SEPTOPLASY FOR DEVIATED SEPTUM	19[redacted]
SURGERY: TUBAL LIGATION	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	25	19[redacted]
CIGARS	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	UNKNOWN	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 58		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted]-[redacted]
METOPROLOL	50 mg	BID	Y-M: 20[redacted]-[redacted]
MESALAZINE	2.4 g	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]-[redacted]
SIMVASTATIN	40 mg	QD	Y-M: 20[redacted]-[redacted]
AMITRIPTYLINE	25 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]-[redacted]
HERPES ZOSTER IMMUNIZATION	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]-[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]-[redacted]
FLUOXETINE	40 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]-[redacted]
SULFASALAZINE	3 g	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	2.4 g	BID	Y-M: 20[redacted]-[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]-[redacted]
PIOGLITAZONE	15 mg	QD	Y-M: 20[redacted]-[redacted]
MERCAPTOPURINE	50 mg	QD	Y-M: 20[redacted]-[redacted]
MESALAZINE	2.4 g	BID	Y-M: 20[redacted]-[redacted]
BUDESONIDE	3 mg	QD	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY 2 WEEKS	Y-M: 20[redacted]-[redacted]

PREDNISONE	5 mg	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted]
HYDROXYCHLOROQUINE	200 mg	QD	Y-M: 20[redacted]
INSULIN GLARGINE	32 OTHER: UNITS	QD	Y-M: 20[redacted]
METFORMIN	500 mg	QD	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
HYDROCHLOROTHIAZIDE	12.5 mg	QD	Y-M: 20[redacted]	ONGOING
METOPROLOL	50 mg	BID	Y-M: 20[redacted]	ONGOING
SIMVASTATIN	40 mg	QD	Y-M: 20[redacted]	ONGOING
AMITRIPTYLINE	25 mg	QD	Y-M: 20[redacted]	ONGOING
FLUOXETINE	40 mg	QD	Y-M: 20[redacted]	ONGOING
PIOGLITAZONE	15 mg	QD	Y-M: 20[redacted]	ONGOING
HYDROXYCHLOROQUINE	200 mg	QD	Y-M: 20[redacted]	ONGOING
INSULIN GLARGINE	32 OTHER: UNITS	QD	Y-M: 20[redacted]	ONGOING
METFORMIN	500 mg	QD	Y-M: 20[redacted]	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]	ONGOING
POTASSIUM	250 mg	QID	Y-M: 20[redacted] / 604	Not reported
DEXAMETHASONE	NOT KNOWN OTHER: NOT KNOWN	OTHER: NOT KNOWN	Y-M: 20[redacted] / 977	Y-M: 20[redacted] / 1006
REMDESIVIR	NOT KNOWN OTHER: NOT KNOWN	OTHER: NOT KNOWN	Y-M: 20[redacted] / 977	Y-M: 20[redacted] / 1006
CORTISONE	ONE OTHER: INJECTION	OTHER: ONCE	Y-M: 20[redacted] / 1044	Y-M: 20[redacted] / 1044

Event #1: Event of Interest - Possible Malignancies, Event of Interest - Malignancy, Event of Interest - Malignancies Excluding NMSC

Event Description	SQUAMOUS CELL CARCINOMA, FACE
Preferred term	扁平上皮癌
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 607 / 550
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	607 / 550
Duration of AE	1 DAY
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 - Serious Infections

Event Description	COVID-19 PNEUMONIA
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1057 / 1000
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 996): Blood Urea Nitrogen: 15.70668 [2.85576 - 7.1394] MMOL/L; Creatinine: 141.445216 [44.20163 - 79.562934] UMOL/L; Leukocytes: 5.3 [4 - 11] 10^9/L; NPTST225-SARS-COV2 PCR: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 996): CHEST XRAY: FINDINGS CONSISTENT WITH PNEUMONIA IN SETTING OF + COVID TESTING

AE Stopped Initial Rx Day / Rx Day	1063 / 1006
Duration of AE	7 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	COVID-19
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Event of Interest - Possible Malignancies, Event of Interest - Malignancy, Event of Interest - Non-melanoma Skin Cancer (NMSC)

Event Description	SQUAMOUS CELL CARCINOMA, SKIN
Preferred term	皮膚有棘細胞癌
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1129 / 1072
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1129 / 1072
Duration of AE	1 DAY
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

Generated: [redacted]20[redacted]:06:46
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，COVID-19 肺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 25 年間），高血圧，糖尿病，潰瘍性大腸炎，高脂血症及び関節リウマチであった。

Event 2 の臨床経過：

投与1057日後＊　，被験者はCOVID-19肺炎を発現した。投与1063日後＊　，COVID-19肺炎は消失した。

本事象発現前，被験者に症状が現れる前に被験者の娘が COVID 検査で陽性となった。被験者は予防的に隔離され，投与1053日後＊に病院を受診する 1 週間前に，頭痛，浮動性めまい，悪心，下痢及び咳嗽を発現した。

投与1053日後＊　　，被験者は入院した。症状及び徴候は，頭痛，咳嗽，下痢，悪心，食欲不振及び乏尿であった。入院時，被験者は COVID 検査で陽性となり，低酸素状態で体力が減退していた。被験者は，治療及び観察のため 10 日間入院した。身体検査，検体検査及び胸部 X 線検査が実施された。被験者は，COVID に関連する市中肺炎があることも判明した。被験者はレムデシビル及びデカドロンを 1 クール投与され，軽快した。投与1063日後＊　，被験者は退院した。

投与された薬剤は，デカドロン及びレムデシビルであった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS ([redacted])

ROWASA for ULCERATIVE COLITIS ([redacted])

LIALDA for ULCERATIVE COLITIS ([redacted])

PREDNISONE forULCERATIVE COLITIS ([redacted])

SULFASALAZINE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

MERCAPTOPURINE for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

UCERIS for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

SHINGRIX for PREVENTATIVE MEASURE ([redacted])

Causality for UPADACITINIB (Open Label)

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1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.23.1] [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 (Open Label)

Event of COVID-19 PNEUMONIA

- Investigator: COVID-19

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

COVID-19 Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 44 mg/dL (normal 8 to 20)

[redacted] **20[redacted] BMI:** 37.8 kg/m2

[redacted] **20[redacted] CHEST X-RAY:** Findings consistent with pneumonia in setting of +COVID testing

[redacted] **20[redacted] CREATININE:** 1.6 mg/dL (normal 0.5 to 0.9)

[redacted] **20[redacted] SARS-COV2 PCR TEST:** Nasopharyngeal swab: Positive for COVID-19

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.3 X10**3/MCL (normal 4 to 11)

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Squamous cell carcinoma ([redacted]20[redacted]): Surgical excision, uncomplicated.
Squamous cell carcinoma ([redacted]20[redacted]): Dermatology treated with liquid nitrogen.

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
胃腸炎	X			X
細菌性肺炎	X			X

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

Medical History	Onset Year
CHOLECYSTITIS: CHOLECYSTECTOMY	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
EYE DISEASE/DISORDER: CATARACT	20[redacted]
EYE DISEASE/DISORDER: LATTICE DEGENERATION OF THE R EYE	20[redacted]
EYE DISEASE/DISORDER: PERIPHERAL NEUROPATHY	20[redacted]
EYE DISEASE/DISORDER: RETINAL DETACHMENT	20[redacted]
OTHER: ENLARGED HEART	20[redacted]
OTHER: GRADE 2 INTERNAL HEMORRHOIDS	20[redacted]
OTHER: PROSTATE ENLARGEMENT	20[redacted]
OTHER: SLEEP APNEA	20[redacted]

Prior Procedures	Procedure Year
SURGERY: BURSITIS OF SHOULDER	20[redacted]
SURGERY: CATARACT REPAIR	20[redacted]
SURGERY: MICRO DISCECTOMY FOR BACK PAIN AND BULGING DISC	20[redacted]
SURGERY: RETINAL SURGERY	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	FORMER	Less than 2 DRINKS

Study Drug Administration

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

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VITAMINS NOS	UNKNOWN mg	QD	Y-M: [redacted]
AZATHIOPRINE	50 mg	QID	Y-M: [redacted]
ADALIMUMAB	80 mg	OTHER: EVERY OTHER WEEK	Y-M: [redacted]
HYDROCORTISONE	NOT REPORTED	NOT REPORTED	Y-M: [redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: [redacted]
MESALAZINE	1000 mg	QD	Y-M: [redacted]
USTEKINUMAB	NOT REPORTED	NOT REPORTED	Y-M: [redacted] / -331
SIMETICONE	UNKNOWN mg	PRN	Y-M: [redacted] / -239
PREDNISONE	UNKNOWN OTHER: UNKNOWN	QD	Y-M: [redacted] / -178
PREDNISONE	15 mg	QD	Y-M: [redacted] / -67
PROBIOTICS NOS	UNKNOWN mg	QD	Y-M: [redacted] / -42
SERENOA REPENS	UNKNOWN mg	QD	Y-M: [redacted] / -42
TIMOLOL	0.5 %	BID	Y-M: [redacted] / -56
FENTANYL	150 OTHER: MCG	OTHER: ONCE	Y-M: [redacted] / -1
MIDAZOLAM	6 mg	OTHER: ONCE	Y-M: [redacted] / -1
NIFEDIPINE	30 mg	QD	Y: [redacted]
BUDESONIDE	9 mg	QD	Y: [redacted]
MESALAZINE	4800 mg	OTHER: 6 TIMES PER 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
VITAMINS NOS	UNKNOWN mg	QD	Y-M: 20[redacted]	ONGOING
PROBIOTICS NOS	UNKNOWN mg	QD	Y-M: 20[redacted] / -42	Y-M: 20[redacted] / 261
SERENOA REPENS	UNKNOWN mg	QD	Y-M: 20[redacted] / -42	Not reported
ALPHA-D-GALACTOSIDASE	UNK OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 522
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 156
PREGABALIN	600 mg	QD	Y-M: 20[redacted] / 151	Y-M: 20[redacted] / 244
PREDNISONE	27.5 mg	QD	Y-M: 20[redacted] / 157	Y-M: 20[redacted] / 163
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / 164	Y-M: 20[redacted] / 170
PREDNISONE	22.5 mg	QD	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 178
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 179	Y-M: 20[redacted] / 185
PREDNISONE	17.5 mg	QD	Y-M: 20[redacted] / 186	Y-M: 20[redacted] / 192
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 193	Y-M: 20[redacted] / 210
CEFALEXIN	500 mg	QID	Y-M: 20[redacted] / 201	Y-M: 20[redacted] / 211
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 201	Y-M: 20[redacted] / 201
PREDNISONE	12.5 mg	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 222
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 223	Y-M: 20[redacted] / 229
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted] / 231	Y-M: 20[redacted] / 236
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 237	Y-M: 20[redacted] / 243
PREDNISONE	2.5 mg	QD	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 250
COLECALCIFEROL	5000 IU	QD	Y-M: 20[redacted] / 293	Y-M: 20[redacted] / 339
LOPERAMIDE	UNK OTHER: UNK	PRN	Y-M: 20[redacted] / 310	Y-M: 20[redacted] / 506
DOCOSANOL	10 mg	PRN	Y-M: 20[redacted] / 334	Not reported
FENTANYL	100 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
MIDAZOLAM	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 336
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 336	Y-M: 20[redacted] / 425
LORATADINE	10 mg	QD	Y-M: 20[redacted] / 348	Y-M: 20[redacted] / 505
PREDNISONE	27.5 mg	QD	Y-M: 20[redacted] / 426	Y-M: 20[redacted] / 453
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 450	Y-M: 20[redacted] / 451
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / 454	Y-M: 20[redacted] / 481
PREDNISONE	22.5 mg	QD	Y-M: 20[redacted] / 482	Y-M: 20[redacted] / 510
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 511	Y-M: 20[redacted] / 538
PREDNISONE	17.5 mg	QD	Y-M: 20[redacted] / 539	Y-M: 20[redacted] / 558
UNSPECIFIED HERBAL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 553	Y-M: 20[redacted] / 612
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 559	Y-M: 20[redacted] / 579

PREDNISONE	12.5 mg	QD	Y-M: 20[redacted] / 580	Y-M: 20[redacted] / 600
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 601	Y-M: 20[redacted] / 628
PREDNISONE	7.5 mg	QD	Y-M: 20[redacted] / 629	Y-M: 20[redacted] / 656
NEPAFENAC	1 gtt	QD	Y-M: 20[redacted] / 636	Y-M: 20[redacted] / 664
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 657	Y-M: 20[redacted] / 704
DIFLUPREDNATE	3 gtt	QD	Y-M: 20[redacted] / 664	Y-M: 20[redacted] / 687
AMOXICILLIN;CLAVULANIC ACID	875-125 mg	BID	Y-M: 20[redacted] / 761	Y-M: 20[redacted] / 768
BENZONATATE	100 mg	PRN	Y-M: 20[redacted] / 761	Y-M: 20[redacted] / 768
AZITHROMYCIN	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 768
CEFTRIAXONE	1 g	OTHER: ONCE	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 768
CODEINE;PROMETHAZINE	6.25-10 mg	OTHER: Q6H PRN	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 772
HEPARIN	500 mg	OTHER: Q12H	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 772
IBUPROFEN	600 mg	OTHER: ONCE	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 768
KETOROLAC	60 mg	OTHER: ONCE	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 768
METHYLPREDNISOLONE	125 mg	OTHER: ONCE	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 768
METHYLPREDNISOLONE	60 mg	OTHER: Q6H	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 772
ONDANSETRON	4 mg	OTHER: Q6H PRN	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 772
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 772
PARACETAMOL	650 mg	OTHER: Q6H PRN	Y-M: 20[redacted] / 768	Y-M: 20[redacted] / 772
CEFDINIR	300 mg	BID	Y-M: 20[redacted] / 772	Y-M: 20[redacted] / 774
VANCOMYCIN	125 mg	QID	Y-M: 20[redacted] / 772	Not reported
CYANOCOBALAMIN	500 mg	QD	Y-M: 20[redacted] / 782	Not reported
ATORVASTATIN	20 mg	QD	Y-M: 20[redacted] / 1301	Not reported
NIFEDIPINE	30 mg	QD	Y: 20[redacted]	ONGOING

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

Event Description	ELEVATED CPK
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] / 226 / 170
Age at AE Onset	5[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	392 / 336
Duration of AE	167 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 - Creatine Phosphokinase (CPK) Elevation

Event Description	ELEVATED CPK
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] / 478 / 422
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

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

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

Event Description	BACTERIAL PNEUMONIAE
Preferred term	細菌性肺炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 824 / 768
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 769): BLOOD NPTST077-CMV IGG: Positive-CMVIGG REACTIVE; BLOOD NPTST133-HISTOPLASMA PNEUMONIAE IGG, ICM: Positive-3.02; [redacted]20[redacted] (RX DAY 770): STOOL NPTST244-TOXINGENIC C DIFFICILE BY AMPLI: Positive-POSITIVE

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 768): CHEST CT WO CONTRAST: NO CARDIOPULMONARY PROCESS; CHEST XRAY: NO ACUTE CARDIOPULMONARY PROCESS

AE Stopped Initial Rx Day / Rx Day	838 / 782
Duration of AE	15 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PI DETERMINED NOT DRUG RELATED. CAUSE IS BACTERIAL PER PI ASSESSMENT
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

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

Event Description	SEVERE GASTROENTERITIS
Preferred term	胃腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 941 / 885
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 768): CT CHEST WITHOUT CONTRAST: NO CARDIOPULMONARY PROCESS

AE Stopped Initial Rx Day / Rx Day	972 / 916
Duration of AE	32 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECT WAS AROUND SICK FAMILY MEMBER
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46

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，細菌性肺炎の事象を発現した。関連する病歴は，心肥大，広範囲な潰瘍性大腸炎（全大腸炎型），睡眠時無呼吸，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 3 の臨床経過：

投与824日後＊　，被験者は細菌性肺炎を発現した。投与838日後＊　，細菌性肺炎は消失した。

本事象発現の約 10 日前，被験者は建築作業中にコウモリの糞に曝露した。2–3 日後，被験者は咳嗽を伴う発熱の悪化を発現した。被験者は緊急医療センターを受診し，非重篤な気管支炎及び副鼻腔感染と診断された。被験者は薬物療法を開始した。被験者は，息切れの悪化，咳嗽及び粘稠性の緑色痰の排出困難のため緊急医療センターを再受診した。被験者は薬物療法により改善しなかった。被験者は疲労，発汗し，体温は華氏 103°F 超であり，心拍数上昇が認められた。

投与824日後＊，被験者は入院した。投与825日後＊　，ヒストプラスマ肺炎抗体の血液検査では陽性であったが，血液培養では陰性であった。入院中に，被験者は診断され，非重篤なクロストリジウム・ディフィシレに対する治療を受けた。投与828日後＊，被験者は退院した。

治験責任医師は，CMV IgG 検査陽性は遠い過去（6 ヵ月超前）の CMV 曝露を示していたと述べた。活動性感染は示されず，臨床的に重大ではなかった。治験責任医師は，肺炎の結果を示す画像はなかったとも述べた。

投与された薬剤は，アジスロマイシン，ketorolac，プロメタジン-コデイン，オンダンセトロン，アセトアミノフェン，パントプラゾール，ヘパリン，メチルプレドニゾロン，イブプロフェン，セフジニル，バンコマイシン及びセフトリアキソンであった。

The patient's past medications include:

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

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

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

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

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

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

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

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

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

Causality for UPADACITINIB (Open Label)

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1) Pneumonia bacterial (10060946) (Pneumonia bacterial (10060946)) [v.22.0] [10060946]

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 BACTERIAL PNEUMONIAE

- Investigator: PI DETERMINED NOT DRUG RELATED. CAUSE IS BACTERIAL PER PI ASSESSMENT

- AbbVie: Risk factors include obesity, sleep apnea and Inflammatory bowel disease , conditions that increase the risk to develop pneumonia

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **BLOOD CULTURE:** Culture negative for sepsis

20[redacted] **BODY TEMPERATURE:** 103 F

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

[redacted] 20[redacted] **CHEST CT:** No cardiopulmonary process

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

[redacted] 20[redacted] **CHEST XRAY:** No acute cardiopulmonary process

[redacted] 20[redacted] **CMV IGG:** positive: CMVIGG Reactive

[redacted] 20[redacted] **FLEXIBLE SIGMOIDOSCOPY:** No normal mucosa (pancolitis).

[redacted] 20[redacted] **HEART RATE:** 120 /min

[redacted] 20[redacted] **HISTOPLASMA PNEUMONIAE IGG, ICM AB:** positive- 3.02

[redacted] 20[redacted] **STOOL TOXINGENIC C DIFFICILE BY AMPLIFIED DNA:** Positive
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，高度の胃腸炎の事象を発現した。関連する病歴は，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 4 の臨床経過：

投与941日後＊　，被験者は高度の胃腸炎を発現した。投与972日後＊　，高度の胃腸炎は消失した。

入院前日に，被験者は来訪した胃腸症状を呈する家族 1 名と接触した。接触の翌日，被験者は下痢及び大量嘔吐の症状を発症し，嘔吐は改善しているようであった。被験者は身震い及び悪寒を発現したため，体を温めるために温浴した。看護師である被験者の娘は，被験者の指が青いことに気付き，被験者の酸素飽和度は 80%台と低かった。同日（投与941日後＊　），救急車が出動要請され，被験者は救急治療室へ搬送された。

投与941日後＊　，被験者は嘔吐及び下痢のため入院した。被験者は，胸痛，動悸，息切れ，湿性咳嗽，ふくらはぎ痛，下肢浮腫，起坐呼吸又は発作性夜間呼吸困難を否定した。被験者は，吐血，血便，メレナ又は泌尿器系愁訴を否定した。静脈内輸液が投与された。薬剤は投与され

なかった。投与943日後＊　，被験者は退院した。

The patient's past medications include:

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

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

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

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

CANASA for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 2

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

PREDNISONE for ULCERATIVE COLITIS and UC FLARE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [

Event of SEVERE GASTROENTERITIS

- Investigator: Patient was around sick family member.

- AbbVie: Event is more likely due to contact with family member with similar gastrointestinal symptoms. Additionally, event is common in general population

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT SCAN:** NOT REPORTED

[redacted] **20[redacted] SPO2:** in the 80s

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Blood creatine phosphokinase increased ([redacted]/20[redacted]): Asymptomatic, related to vigorous physical activity.
Blood creatine phosphokinase increased ([redacted]/20[redacted]): Asymptomatic, related to vigorous physical activity.
Blood creatine phosphokinase increased ([redacted]/20[redacted]): Symptom of muscle pain, related to exercise or other vigorous physical activity.
Blood creatine phosphokinase increased ([redacted]/20[redacted]): Symptom of muscle pain, related to exercise or other vigorous physical activity. 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
大腸菌感染	X			X
敗血症	X			X

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

Medical History	Onset Year
ANEMIA: SUBJECT IS CURRENTLY TAKING IRON SUPPLEMENTS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GASTROESOPHAGEAL REFLUX DISEASE: ACID REFLUX	20[redacted]
HYPERTENSION	20[redacted]
OTHER: ANXIETY	20[redacted]
OTHER: DX'D WITH CERVICAL CANCER AND SUCCESSFULLY TREATED AT THE AGE OF 25.	19[redacted]
OTHER: HEMORRHOIDS	20[redacted]
OTHER: JOINT PAIN	20[redacted]
OTHER: RIGHT SIDE FLANK PAIN	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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted] / 1	[redacted] / 63	63
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 63	[redacted] / 420	358

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ALPRAZOLAM	0.5 mg	OTHER: AT BEDTIME	Y-M: [redacted]
QUETIAPINE	25 mg	OTHER: AT BEDTIME	Y-M: [redacted]
INFLIXIMAB	10 mg	OTHER: EVERY 4 WEEKS	Y-M: [redacted]
MESALAZINE	3200 mg	QD	Y-M: [redacted]
PREDNISONE	5 mg	QD	Y-M: [redacted]
HYDROCODONE;PARACETAMOL	7.5-325 mg	PRN	Y-M: [redacted] / -158
PANTOPRAZOLE	40 mg	BID	Y-M: [redacted] / -51

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ALPRAZOLAM	0.5 mg	OTHER: AT BEDTIME	Y-M: [redacted]	ONGOING
QUETIAPINE	25 mg	OTHER: AT BEDTIME	Y-M: [redacted]	ONGOING
HYDROCODONE;PARACETAMOL	7.5-325 mg	PRN	Y-M: [redacted] / -158	ONGOING
IRON	325 mg	QD	Y-M: [redacted] / 57	ONGOING
PANTOPRAZOLE	20 mg	BID	Y-M: [redacted] / 88	Y-M: [redacted] / 341
BUDESONIDE	9 mg	QD	Y-M: [redacted] / 266	Y-M: [redacted] / 342
AMOXICILLIN	500 mg	TID	Y-M: [redacted] / 330	Y-M: [redacted] / 339
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: [redacted] / 342	Y-M: [redacted] / 342
PROCHLORPERAZINE	10 mg	PRN	Y-M: [redacted] / 342	Y-M: [redacted] / 350
CEFEPIME	2000 mg	OTHER: ONCE	Y-M: [redacted] / 343	Y-M: [redacted] / 343
CEFTRIAXONE	1000 mg	QD	Y-M: [redacted] / 343	Y-M: [redacted] / 343
DICYCLOVERINE	20 mg	OTHER: ONCE	Y-M: [redacted] / 343	Y-M: [redacted] / 343
DIPHENHYDRAMINE	25 mg	OTHER: ONCE	Y-M: [redacted] / 343	Y-M: [redacted] / 343
ENOXAPARIN	40 mg	QD	Y-M: [redacted] / 343	Y-M: [redacted] / 350

FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 348
LORAZEPAM	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 343
METHYLPREDNISOLONE	125 mg	OTHER: ONCE	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 344
METRONIDAZOLE	500 mg	OTHER: Q8H	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 343
MORPHINE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 343
MUPIROCIN	2 %	OTHER: ONCE	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 343
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 350
VANCOMYCIN	2000 mg	OTHER: ONCE	Y-M: 20[redacted] / 343	Y-M: 20[redacted] / 343
CEFTRIAXONE	1000 mg	QD	Y-M: 20[redacted] / 345	Y-M: 20[redacted] / 350
CALCIUM CARBONATE	500 mg	OTHER: Q4H	Y-M: 20[redacted] / 348	Y-M: 20[redacted] / 350
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 348	ONGOING
CEFAZOLIN	2000 mg	OTHER: Q8H	Y-M: 20[redacted] / 349	Y-M: 20[redacted] / 350
CEFALEXIN	500 mg	OTHER: Q8H	Y-M: 20[redacted] / 350	Y-M: 20[redacted] / 355

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

Event Description	SEPSIS, E. COLI
Preferred term	大腸菌感染，敗血症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 404 / 342
Age at AE Onset	4[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 342): BLOOD NPTST102-ESCHERICHIA COLI: Positive-CULTURE RESULT POSITIVE DURING INPT STAY

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 343): CHEST CT: NO DISTINCT CT FINDING OF PULMONARY EMBOLISM; CHEST X-RAY: NONSPECIFIC, NONOBSTRUCTIVE INTESTINAL GAS PATTERN AGAIN NOTED, WITH RELATIVE PAUCITY OF INTESTINAL GAS AGAIN SEEN. NO ACUTE CARDIOPULMONARY ABNORMALITIES IDENTIFIED.; [redacted]20[redacted] (RX DAY 345): ABDOMINAL X-RAY: NO EVIDENCE OF ACUTE PROCESS WITHIN THE CHEST OR ABDOMEN. ADYNAMIC ILEUS IS SUSPECT.; [redacted]20[redacted] (RX DAY 346): CHEST X-RAY: EXAMINATION DEMONSTRATES A NONSPECIFIC BOWEL GAS PATTERN. NO EVIDENCE OF INTESTINAL OBSTRUCTION. THERE IS NO EVIDENCE OF DILATION OF LARGE OR SMALL BOWEL

AE Stopped Initial Rx Day / Rx Day	412 / 350
Duration of AE	9 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	EXACT CAUSE OF INFECTION IS UNKNOWN. THERE ARE MULTIPLE WAYS THE SUBJECT COULD HAVE GOTTEN E. COLI
Discontinued Study Drug Due to the Event	NO

SAE Criteria HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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，敗血症（大腸菌）の事象を発現した。関連する病歴は，貧血，潰瘍性大腸炎，高血圧，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与404日後＊　，被験者は敗血症（大腸菌）を発現した。投与412日後＊　，敗血症（大腸菌）は消失した。

被験者は高熱，悪寒，嘔吐及び脱水があり，救急治療室を受診した。投与404日後＊　，被験者は入院した。血液培養では大腸菌陽性であった。投与412日後＊　，被験者は退院した。

治験薬の投与は本事象により完全に中止された。

投与された薬剤は，benadryl，pepcid，セファゾリン，ソル・メドロール，zofran，フラジール，tums，ケフレックス，セフトリアキソン，セフェピム，モルヒネ，バンコマイシン，ムピロシン，bentyl，タイレノール，lovenox，compazine 及び ativan であった。

The patient's past medications include:

ASACOL 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])

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

UCERIS for UC ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Sepsis (10040047) (Sepsis (10040047)) [v.23.0] [10040047]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Escherichia infection (10061126) (Escherichia infection (10061126)) [v.23.0] [10061126]

Causality as per reporter (Drug/Vaccine): No 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 SEPSIS, E COLI

- Investigator: Exact cause of infection is unknown. There are multiple ways the subject could have gotten E. Coli

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL X-RAY:** no evidence of acute process within the chest or abdomen. Adynamic ileus is suspect.

[redacted] **20[redacted] BLOOD CULTURE:** Escherichia Coli Positive. Culture result positive during inpatient stay

[redacted] **20[redacted] CHEST CT:** No distinct CT finding of pulmonary embolism

[redacted] 20[redacted] **CHEST XRAY:** Nonspecific, nonobstructive intestinal gas pattern again noted, with relative paucity of intestinal gas again seen. No acute cardiopulmonary abnormalities identified.

[redacted] [redacted] 20[redacted] **CHEST XRAY:** Examination demonstrates a nonspecific bowel gas pattern. No evidence of intestinal obstruction. There is no evidence of dilation of large or small bowel

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
アラニンアミノトランスフェラーゼ増加				X
アスパラギン酸アミノトランスフェラーゼ増加				X
肩回旋筋腱板症候群	X			

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

Medical History	Onset Year
DEPRESSION: DEPRESSION	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ANXIETY	20[redacted]
OTHER: BACK PAIN FROM CAR ACCIDENT IN 20[redacted]	20[redacted]
OTHER: HYPERTENSION	20[redacted]
OTHER: LOW IRON	20[redacted]
OTHER: MITRAL VALVE PROLAPSE	20[redacted]
OTHER: NECK PAIN FROM CAR ACCIDENT IN 20[redacted]	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	UNKNOWN	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 57		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SULFASALAZINE	1500 mg	BID	Y-M: 20[redacted]
HYDROCHLOROTHIAZIDE;LISINOPRIL	20 12.5 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	10 mg	OTHER: Q6WEEKS	Y-M: 20[redacted]
IRON	142 mg	QD	Y-M: 20[redacted]
SERTRALINE	150 mg	QD	Y-M: 20[redacted]
VITAMIN B COMPLEX	1000 mg	QD	Y-M: 20[redacted]
CIPROFLOXACIN	250 mg	BID	Y-M: 20[redacted] / -352
AZATHIOPRINE	75 mg	BID	Y-M: 20[redacted] / -271
MESALAZINE	1000 mg	PRN	Y-M: 20[redacted] / -216
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / -192
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / -119
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted] / -135
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / -28
GUAIFENESIN	600 mg	QD	Y-M: 20[redacted] / -45

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
HYDROCHLOROTHIAZIDE;LISINOPRIL	20 12.5 mg	QD	Y-M: 20[redacted]	ONGOING
SERTRALINE	150 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 923
VITAMIN B COMPLEX	1000 mg	QD	Y-M: 20[redacted]	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / -192	ONGOING
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted] / -135	ONGOING
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / -28	ONGOING
GUAIFENESIN	600 mg	QD	Y-M: 20[redacted] / -45	ONGOING
CYCLOBENZAPRINE	5 mg	PRN	Y-M: 20[redacted] / 485	Y-M: 20[redacted] / 661
CYCLOBENZAPRINE	5 mg	TID	Y-M: 20[redacted] / 513	Y-M: 20[redacted] / 570
SIMVASTATIN	20 mg	QD	Y-M: 20[redacted] / 533	Not reported

BETAMETHASONE;SODIUM PHOSPHATE	2 mL	PRN	Y-M: 20[redacted] / 540	Y-M: 20[redacted] / 540
ROPIVACAINE	4 mL	PRN	Y-M: 20[redacted] / 540	Y-M: 20[redacted] / 540
BETAMETHASONE;SODIUM PHOSPHATE	2 mL	OTHER: ONCE	Y-M: 20[redacted] / 661	Y-M: 20[redacted] / 661
ROPIVACAINE	4 mL	OTHER: ONCE	Y-M: 20[redacted] / 661	Y-M: 20[redacted] / 661
FENTANYL	50 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 675	Y-M: 20[redacted] / 675
MIDAZOLAM	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 675	Y-M: 20[redacted] / 675
POTASSIUM	UNKNOWN mg	QD	Y-M: 20[redacted] / 742	Not reported
BETAMETHASONE;SODIUM PHOSPHATE	2 mL	PRN	Y-M: 20[redacted] / 757	Y-M: 20[redacted] / 757
ROPIVACAINE	4 mL	PRN	Y-M: 20[redacted] / 757	Y-M: 20[redacted] / 757
ONDANSETRON	8 mg	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 813
OXYCODONE;PARACETAMOL	5-325 mg	OTHER: EVERY 4 HOURS	Y-M: 20[redacted] / 806	Y-M: 20[redacted] / 813
SERTRALINE	200 mg	QD	Y-M: 20[redacted] / 924	ONGOING
HYDROCODONE;PARACETAMOL	5-325 mg	OTHER: Q6H	Y-M: 20[redacted] / 980	Not reported
TRAZODONE	50 mg	QD	Y-M: 20[redacted] / 980	Not reported
FENTANYL	100 OTHER: MCG	OTHER: ONCE	Y-M: 20[redacted] / 1014	Y-M: 20[redacted] / 1014
MIDAZOLAM	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 1014	Y-M: 20[redacted] / 1014
DICYCLOVERINE	10 mg	TID	Y-M: 20[redacted] / 1031	Y-M: 20[redacted] / 1099
HYOSCYAMINE	0.125 mg	QD	Y-M: 20[redacted] / 1031	Y-M: 20[redacted] / 1099
ZOLPIDEM	5 mg	QD	Y-M: 20[redacted] / 1174	Not reported
BUPIVACAINE	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 1175	Y-M: 20[redacted] / 1175
DICLOFENAC	1 %	OTHER: ONCE	Y-M: 20[redacted] / 1175	Y-M: 20[redacted] / 1175
LIDOCAINE	200 mg	OTHER: ONCE	Y-M: 20[redacted] / 1175	Y-M: 20[redacted] / 1175
TRIAMCINOLONE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 1175	Y-M: 20[redacted] / 1175
DICYCLOVERINE	10 mg	TID	Y-M: 20[redacted] / 1256	Not reported
HYOSCYAMINE	0.125 mg	PRN	Y-M: 20[redacted] / 1256	Not reported

Event #1: Event of Interest - Hepatic Disorder

Event Description	ELEVATED ALT AND AST
Preferred term	アラニンアミノトランスフェラーゼ増加，アスパラギン酸アミノトランスフェラーゼ増加
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 562 / 506
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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

Event #2: Serious Adverse Event

Event Description	RIGHT SHOULDER IMPINGEMENT SYNDROME DIAGNOSED ON [redacted]20[redacted]
Preferred term	肩回旋筋腱板症候群
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 569 / 513
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 798): CORRECTIVE SURGERY FOR RIGHT SHOULDER IMPINGEMENT SYNDROME: SUBJECT REQUIRES TIME OFF WORK AND PROLONGED PHYSICAL THERAPY	
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	UNKNOWN

Discontinued Study Drug Due to the Event NO

SAE Criteria IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:06:46

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 [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投与597日後＊　に診断された右肩インピンジメント症候群の事象を発現した。関連する病歴は，事故による頚部痛（19[redacted] 年），潰瘍性大腸炎，非喫煙者及び禁酒であった。

Event 2 の臨床経過：

投与569日後＊　，被験者は右肩インピンジメント症候群を発現し，投与597日後＊ に診断された。

手術前，被験者は 投与の約19ヵ月後＊に右肩痛を発現し始め，右肩インピンジメント症候群及び変形性関節症と診断された。

投与854日後＊　，被験者は手術のため入院した。同日，被験者は右肩インピンジメント症候群の矯正手術を受けた。投与854日後＊ ，被験者は退院した。被験者は 12 週間の術後理学療法を開始した。

被験者は環境サービス業に従事しており，ゴミの交換，清掃の反復運動を行っていた。

投与された薬剤は，percocet，flexeril，bethamethasone acetate sodium PHOS 及び naropin であった。

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])

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

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

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

PREDNISONE for UC FLARE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Open Label)

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1) Impingement syndrome shoulder (10049039) (Rotator cuff syndrome (10039227)) [v.24.0] [10049039]

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 RIGHT SHOULDER IMPINGEMENT SYNDROME DIAGNOSED ON [redacted]20[redacted]

- Investigator: Unknown

- AbbVie: Shoulder impingement syndrome (SIS) is attributed to the compression of structures around the glenohumeral joint that occur with shoulder elevation. Event not consistent with study drug's mechanism of action. Additional risk factor includes patient's occupation which involves repetitive motion for cleaning, sweeping, and changing trash.

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Aspartate aminotransferase increased: Intermittent.
Aspartate aminotransferase increased: 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
貧血				X
血中クレアチンホスホキナーゼ増加				X
脳損傷	X	X	X	
ヘマトクリット減少				X
ヘモグロビン減少				X
リンパ球数減少				X
片頭痛	X			
好中球数減少				X
過量投与	X			

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

Medical History	Onset Year
GASTROESOPHAGEAL REFLUX DISEASE	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	19[redacted]
NEPHROLITHIASIS	19[redacted]
OSTEOPOROSIS	20[redacted]
OTHER: BENZO ADDICTION	20[redacted]
OTHER: BIPOLAR DISORDER	20[redacted]
OTHER: BOWEL OBSTRUCTION	20[redacted]
OTHER: ENDOMETRIOSIS	19[redacted]
OTHER: FIBROMYALGIA	20[redacted]
OTHER: IRRITABLE BOWEL SYNDROME	19[redacted]
OTHER: RECURRENT UTIS	20[redacted]
OTHER: SCREENING PHYSICAL EXAM: DIFFUSE POSTERIOR THORAX AND BACK TENDERNESS	20[redacted]
OTHER: SCREENING PHYSICAL EXAM: MODERATE DIFFUSE ABDOMINAL TENDERNESS. NO MASSES. NO REBOUND	20[redacted]

Prior Procedures	Procedure Year
SURGERY: APPENDECTOMY	20[redacted]
SURGERY: C-SECTION	19[redacted]
SURGERY: C-SECTION	19[redacted]
SURGERY: CHOLECYSTECTOMY	20[redacted]
SURGERY: HERNIA REPAIR	20[redacted]
SURGERY: HYSTERECTOMY	20[redacted]
SURGERY: LEFT ANKLE SURGERY	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	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 60	[redacted]20[redacted] / 371	312
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted]20[redacted] / 372	[redacted]20[redacted] / 1558	1187

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5 mg/kg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]
AZITHROMYCIN	97.5 mg	PRN	Y-M: 20[redacted]
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
GABAPENTIN	600 mg	TID	Y-M: 20[redacted]

METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
PROMETHAZINE	25 mg	PRN	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	TID	Y-M: 20[redacted]
BISACODYL	5 mg	PRN	Y-M: 20[redacted] / -256
LORAZEPAM	1 mg	BID	Y-M: 20[redacted] / -261
HYOSCYAMINE	.125 mg	QD	Y-M: 20[redacted] / -176
APIXABAN	5 mg	QD	Y-M: 20[redacted] / -146
BUPROPION	300 mg	QD	Y-M: 20[redacted] / -87
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted] / -87
OXYCODONE;PARACETAMOL	10 mg	QID	Y-M: 20[redacted] / -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
AZITHROMYCIN	97.5 mg	PRN	Y-M: 20[redacted]	ONGOING
GABAPENTIN	600 mg	TID	Y-M: 20[redacted]	ONGOING
PROMETHAZINE	25 mg	PRN	Y-M: 20[redacted]	ONGOING
BISACODYL	5 mg	PRN	Y-M: 20[redacted] / -256	ONGOING
LORAZEPAM	1 mg	BID	Y-M: 20[redacted] / -261	ONGOING
HYOSCYAMINE	.125 mg	QD	Y-M: 20[redacted] / -176	ONGOING
APIXABAN	5 mg	QD	Y-M: 20[redacted] / -146	ONGOING
BUPROPION	300 mg	QD	Y-M: 20[redacted] / -87	ONGOING
ZOLPIDEM	10 mg	QD	Y-M: 20[redacted] / -87	Y-M: 20[redacted] / 427
OXYCODONE;PARACETAMOL	10 mg	QID	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / 135
ESOMEPRAZOLE	20 mg	PRN	Y-M: 20[redacted] / 28	ONGOING
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TABLET	BID	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 62
OXYCODONE	15 mg	PRN	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 319
AZITHROMYCIN	500 mg	BID	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 147
FLUTICASONE	1 OTHER: SPRAY	QD	Y-M: 20[redacted] / 147	Y-M: 20[redacted] / 151
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 148	Y-M: 20[redacted] / 151
ACETYLSALICYLIC ACID;CAFFEINE	1 OTHER: PACKET	PRN	Y-M: 20[redacted] / 173	Y-M: 20[redacted] / 333
BUTALBITAL;CAFFEINE;PARACETAMOL	50/325/40 mg	PRN	Y-M: 20[redacted] / 311	ONGOING

PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 311	ONGOING
KETAMINE	50 mg	TID	Y-M: 20[redacted] / 380	Y-M: 20[redacted] / 746
LISINOPRIL	20 mg	QD	Y-M: 20[redacted] / 470	Y-M: 20[redacted] / 523
HYOSCYAMINE	0.125 mg	PRN	Y-M: 20[redacted] / 497	Y-M: 20[redacted] / 917
LISINOPRIL	40 mg	QD	Y-M: 20[redacted] / 523	ONGOING
CEFALEXIN	500 mg	QD	Y-M: 20[redacted] / 537	Y-M: 20[redacted] / 551
MORPHINE	4 mg	QD	Y-M: 20[redacted] / 537	Y-M: 20[redacted] / 537
PROMETHAZINE	25 mg	QD	Y-M: 20[redacted] / 537	Y-M: 20[redacted] / 537
RISPERIDONE	1 mg	QD	Y-M: 20[redacted] / 543	ONGOING
BISACODYL	4 DF	OTHER: ONCE	Y-M: 20[redacted] / 682	Y-M: 20[redacted] / 682
MACROGOL 3350	238 g	OTHER: ONCE	Y-M: 20[redacted] / 682	Y-M: 20[redacted] / 683
PROPOFOL	300 mg	OTHER: ONCE	Y-M: 20[redacted] / 683	Y-M: 20[redacted] / 683
OXYCODONE	10 mg	QD	Y-M: 20[redacted] / 811	Y-M: 20[redacted] / 1015
BISACODYL	4 DF	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 1014	Y-M: 20[redacted] / 1014
MACROGOL 3350	238 g	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 1014	Y-M: 20[redacted] / 1015
LIDOCAINE	40 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 1015	Y-M: 20[redacted] / 1015
PROPOFOL	350 mg	OTHER: SINGLE DOSE	Y-M: 20[redacted] / 1015	Y-M: 20[redacted] / 1015
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted] / 1096	ONGOING
ATORVASTATIN	1 DF	QD	Y-M: 20[redacted] / 1096	ONGOING
CITALOPRAM	40 mg	QD	Y-M: 20[redacted] / 1096	ONGOING
METOPROLOL	2 DF	QD	Y-M: 20[redacted] / 1096	ONGOING
NALOXONE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 1181	Y-M: 20[redacted] / 1181
NALOXONE	2 mg	OTHER: ONCE	Y-M: 20[redacted] / 1186	Y-M: 20[redacted] / 1186

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

Event Description	ELEVATED CK LEVELS
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] / 462 / 91
Age at AE Onset	4[redacted]
Laboratory Testing	

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	557 / 186
Duration of AE	96 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	DECREASED NEUTROPHIL LEVELS
Preferred term	好中球数減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 462 / 91
Age at AE Onset	4[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	557 / 186
Duration of AE	96 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 - Neutropenia

Event Description	DECREASED TOTAL ANC LEVELS
Preferred term	好中球数減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 462 / 91
Age at AE Onset	4[redacted]

Laboratory Testing
NOT APPLICABLE
Microbiology
NOT APPLICABLE
SAE Supplemental Procedure
NOT APPLICABLE

AE Stopped Initial Rx Day / Rx Day	557 / 186
Duration of AE	96 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

Event Description	WORSENING OF MIGRAINE HEADACHES
Preferred term	片頭痛
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 681 / 310
Age at AE Onset	4[redacted]

Laboratory Testing
NOT REPORTED
Microbiology
NOT REPORTED
SAE Supplemental Procedure
NOT REPORTED

AE Stopped Initial Rx Day / Rx Day	682 / 311
Duration of AE	2 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

Event #5: Event of Interest - Anemia

Event Description	LOW HGB, HCT, AND RBC
Preferred term	ヘマトクリット減少，ヘモグロビン減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 818 / 447
Age at AE Onset	4[redacted]

Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1054 / 683
Duration of AE	237 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 #6: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 987 / 616
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1054 / 683
Duration of AE	68 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 #7: Event of Interest - Lymphopenia

Event Description	LOW LYMPHOCYTES
Preferred term	リンパ球数減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1054 / 683
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	1138 / 767
Duration of AE	85 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 #8: Event of Interest - Lymphopenia

Event Description	LOW LYMPHOCYTES
Preferred term	リンパ球数減少
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1386 / 1015
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	ONGOING
Duration of AE	ONGOING
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 #9: Serious Adverse Event

Event Description	OPIOD OVERDOSE
Preferred term	過量投与
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1552 / 1181
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 1181): Albumin: 44 [35 - 49] G/L; Alkaline Phosphatase: 61 [36 - 108] U/L; Basophils: 0 [0 - 0.2] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 1.3] %; Bilirubin: 6.841556 [0 - 25.655835] UMOL/L; Blood Urea Nitrogen: 4.99758 [2.49879 - 8.92425] MMOL/L; Calcium: 2.345394 [2.220639 - 2.569953] MMOL/L; Chloride: 105 [100 - 111] MMOL/L; Creatinine: 67.186478 [41.549532 - 119.344401] UMOL/L; Eosinophils: 0 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 0.2 [0 - 5] %; Erythrocytes: 3.68 [3.57 - 4.97] 10^12/L; Glucose: 5.828235 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.347 [0.326 - 0.434] FRACTION OF 1; Hemoglobin: 118 [110 - 149] G/L; Leukocytes: 4.5 [3.7 - 10.6] 10^9/L; Lymphocytes: 0.8 [1 - 3.4] 10^9/L; Lymphocytes/Leukocytes: 19 [15.7 - 45.3] %; Monocytes: 0.3 [0.2 - 0.9] 10^9/L; Monocytes/Leukocytes: 7.3 [3.5 - 11.1] %; NPTST005-A/G RATIO: 2.3 [0.9 - 2.4] RATIO; NPTST023-ALT (SGPT): 38 [8 - 39] IU/L; NPTST027-ANION GAP: 6 [6 - 13] MMOL/L; NPTST035-AST: 33 [12 - 33] IU/L; NPTST052-BUN/CREATININE RATIO: 18 [8 - 23] RATIO; NPTST078-CO2: 28.3 [23 - 32.6] MMOL/L; NPTST122-GLOBULIN: 1.9 [2 - 4.5] G/DL; NPTST157-MCH: 31.9 [26.9 - 34.1] PG; NPTST158-MCHC: 33.9 [32.9 - 35.4] G/DL; NPTST159-MCV: 94.3 [80.1 - 98.4] FL; NPTST173-NRBC: 0.1 [0 - 0] 10^9/L; NPTST176-OSMOLALITY CALC: 278 [270 - 350] MOSM/KG; NPTST204-RDW: 14.3 [11.8 - 15.2] %; NPTST247-TROPONIN I: 0.02 [0 - 0.04] NG/ML; Neutrophils: 3.3 [1 - 8] 10^9/L; Neutrophils/Leukocytes: 73.2 [43.4 - 75.7] %; Platelets: 188 [141 - 359] 10^9/L; Potassium: 4.4 [3.5 - 5.2] MMOL/L; Protein: 63 [61 - 80] G/L; Sodium: 139 [133 - 146] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 1181): EKG: SINUS RHYTHM; XR CHEST 1 VW: RESULTS NOT LISTED ON REPORT

AE Stopped Initial Rx Day / Rx Day	1552 / 1181
Duration of AE	1 DAY
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DRUG OVERDOSE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #10: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Death

Event Description	ANOXIC BRAIN INJURY
Preferred term	脳損傷
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 1558 / 1187
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 1186): Albumin: 39 [35 - 49] G/L; Alkaline Phosphatase: 203 [36 - 108] U/L; Basophils: 0 [0 - 0.2] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 1.3] %; Bilirubin: 8.551945 [0 - 25.655835] UMOL/L; Blood Urea Nitrogen: 5.71152 [2.49879 - 8.92425] MMOL/L; Calcium: 2.045982 [2.220639 - 2.569953] MMOL/L; Chloride: 106 [100 - 111] MMOL/L; Creatinine: 107.851977 [41.549532 - 119.344401] UMOL/L; Eosinophils: 0 [0 - 0.4] 10^9/L; Eosinophils/Leukocytes: 0.3 [0 - 5] %; Erythrocytes: 3.6 [3.57 - 4.97] 10^12/L; Glucose: 20.426576 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.356 [0.326 - 0.434] FRACTION OF 1; Hemoglobin: 114 [110 - 149] G/L; Leukocytes: 6.9 [3.7 - 10.6] 10^9/L; Lymphocytes: 1.7 [1 - 3.4] 10^9/L; Lymphocytes/Leukocytes: 25 [15.7 - 45.3] %; Monocytes: 0.2 [0.2 - 0.9] 10^9/L; Monocytes/Leukocytes: 2.8 [3.5 - 11.1] %; NPTST005-A/G RATIO: 2.2 [0.9 - 2.4] RATIO; NPTST023-ALT (SGPT): 355 [8 - 39] IU/L; NPTST027-ANION GAP: 16 [6 - 13] MMOL/L; NPTST035-AST: 617 [12 - 33] IU/L; NPTST051-BUN/ CREATININE RATIO: 13 [8 - 23] RATIO; NPTST078-CO2: 15.9 [23 - 32.6] MMOL/L; NPTST122-GLOBULIN: 1.8 [2 - 4.5] G/DL; NPTST153-LIPASE: 82 [10 - 140] U/L; NPTST155-MAGNESIUM: 2.5 [1.7 - 2.2] MG/DL; NPTST157-MCH: 31.7 [26.9 - 34.1] PG; NPTST158-MCHC: 32.0 [32.9 - 35.4] G/DL; NPTST159-MCV: 98.8 [80.1 - 98.4] FL; NPTST173-NRBC: 0.0 [0 - 0] 10^9/L; NPTST176-OSMOLALITY CALC: 292 [270 - 350] MOSM/KG; NPTST204-RDW: 14.6 [11.8 - 15.2] %; NPTST247-TROPONIN I: 0.03 [0 - 0.04] NG/ML; Neutrophils: 4.9 [1 - 8] 10^9/L; Neutrophils/Leukocytes: 71.6 [43.4 - 75.7] %; Platelets: 171 [141 - 359] 10^9/L; Potassium: 4.4 [3.5 - 5.2] MMOL/L; Protein: 57 [61 - 81] G/L; Sodium: 138 [133 - 146] MMOL/L; [redacted]20[redacted] (RX DAY 1190): Albumin: 34 [35 - 49] G/L; Alkaline Phosphatase: 128 [36 - 108] U/L; Bilirubin: 8.551945 [0 - 25.655835] UMOL/L; Blood Urea Nitrogen: 6.42546 [2.49879 - 8.92425] MMOL/L; Calcium: 2.24559 [2.220639 - 2.569953] MMOL/L; Chloride: 112 [100 - 111] MMOL/L; Creatinine: 60.114217 [41.549532 - 119.344401] UMOL/L; Glucose: 10.046767 [3.88549 - 5.5507] MMOL/L; NPTST005-A/G RATIO: 1.5 [0.9 - 2.4] RATIO; NPTST018-ALANINE TRANSAMINASE: 94 [8 - 39] IU/L; NPTST027-ANION GAP: 8 [6 - 13] MMOL/L; NPTST034-ASPARTATE TRANSAMINASE: 45 [12 - 33] IU/L; NPTST052-BUN/CREATININE RATIO: 26 [8 - 23] RATIO; NPTST078-CO2: 27.7 [23 - 32.6] MMOL/L; NPTST123-GLOBULIN TOTAL: 2.2 [2 - 4.5] G/DL; NPTST176-OSMOLALITY CALC: 301 [270 - 350] MOSM/KG; Potassium: 3.9 [3.5 - 5.2] MMOL/L; Protein: 56 [61 - 80] G/L; Sodium: 148 [133 - 146] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 1186): CT CERVICAL SPINE WITHOUT CONTRAST: NO ACUTE FRACTURE OR TRAUMATIC LISTHESIS SEEN; CT CHEST ABDOMEN PELVIS WITH IV CONTRAST ONLY: NO ACUTE FINDING IN THE CHEST, ONLY MILD BIBASILAR DEPENDENT ATELECTASIS. NO CLEARLY ACUTE INTRA-ABDOMINAL OR PELVIS FINDING, SURGERY CHANGES SEEN. THERE MAY BE AN EARLY DEVELOPING BOWEL ILEUS.; CT HEAD WITHOUT CONTRAST: ABNORMAL EXAM- APPEARANCE VERY WORRISOME FOR DIFFUSE ANOXIC INJURY WITH CEREBRAL/CEREBELLAR EDEMA; 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; XR CHEST 1 VW: ENDOTRACHEAL TUBE RESIDES IN GOOD LOCATION 3 CM ABOVE CARINA; [redacted]20[redacted] (RX DAY 1187): EKG: SINUS RHYTHM, LOW QRS VOLTAGE IN CHEST LEADS, NONSPECIFIC T WAVE ABNORMALITY; [redacted]20[redacted] (RX DAY 1190): XR CHEST 1 VW- ORGAN DONATION: NO ACUTE ABNORMALITY

AE Stopped Initial Rx Day / Rx Day	1558 / 1187
Duration of AE	1 DAY
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	ACUTE RESPIRATORY FAILURE WITH HYPOXIA
Discontinued Study Drug Due to the Event	YES

SAE Criteria HOSPITALIZATION OR PROLONGED HOSPITALIZATION, DEATH OF SUBJECT

Generated: [redacted]20[redacted]:06:46
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，片頭痛の悪化の事象を発現した。関連する病歴は，子宮内膜症，過敏性腸症候群，双極性障害，元喫煙者（1 日 0.5 箱を 1 年間），ベンゾ系薬剤嗜癖，線維筋痛，高血圧，片頭痛，軽度両側浮腫，肺塞栓症，不眠症及び潰瘍性大腸炎であった。

Event 4 の臨床経過：

投与681日後＊　，被験者は片頭痛の悪化を発現した。投与682日後＊　，片頭痛の悪化は消失した。

投与681日後＊　，被験者は入院した。被験者は激しい右側の頭痛を経験し，不明瞭発語，顔面全体のしびれ感，右顔面のピリピリ感及び右腕のピリピリ感を伴っていた。被験者の NIH 脳卒中スケール/スコア（NIHSS）は 2 及び 4 であった。被験者は診断検査を受け，脳卒中は否定された。投与682日＊　　，被験者は退院した。被験者は，頭部外傷，嘔吐又は脳卒中の病歴はなかった。

投与された薬剤は，fioricet 及びアセトアミノフェンであった。

Causality for UPADACITINIB (Open Label)

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1)　Migraine aggravated (10027600)　(Migraine (10027599))　[v.23.1]　[10027600]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of WORSENING OF MIGRAINE HEADACHES

- Investigator: NOT APPLICABLE.

- AbbVie: RISK FACTORS INCLUDE PRE-EXISTING MIGRAINE HEADACHE, FIBROMYALGIA AND OBESITY.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD UREA NITROGEN:** 11 mg/dL (normal 7 to 21)

[redacted] **20[redacted] CALCIUM:** 9.6 mg/dL (normal 8.9 to 10.7)

[redacted] **20[redacted] CARBON DIOXIDE:** 23 MMOL/L (normal 20 to 30)

[redacted] **20[redacted] CHLORIDE:** 108 MMOL/L (normal 101 to 111)

[redacted] **20[redacted] COLONOSCOPY:** No inflammation seen

[redacted] **20[redacted] CREATININE:** 0.75 mg/dL (normal 0.72 to 1.25)

[redacted] **20[redacted] CT SCAN-HEAD:** NO EVIDENCE FOR ACUTE HEMORRHAGE OR EDEMA.

[redacted] **20[redacted] ECG 12 LEAD:** NORMAL SINUS RHYTHM WITHOUT ACUTE ST-T WAVE CHANGES

[redacted] **20[redacted] ECHO:** TECHNICALLY DIFFICULT STUDY DUE TO PATIENTS BODY HABITUS. THE LEFT VENTRICULAR SYSTOLIC FUNCTION IS NORMAL (55-65%). MILD AORTIC VALVA REGURGITATION. THERE IS A PATENT FORAMEN OVALE PRESENT WITH RIGHT TO LEFT SHUNTING INDICATED BY BUBBLE STUDY. THE EXAM WAS COMPARED TO THE STUDY PERFORMED ON [redacted]/20[redacted]. NO SIGNIFICANT CHANGES COMPARED TO PRIOR STUDY. THIS STUDY DID INCLUDE A SALINE BUBBLE CONTRAST STUDY WHICH IS POSITIVE.

[redacted] **20[redacted] GLUCOSE:** 94 mg/dL (normal 74 to 99)

[redacted] **20[redacted] HEMATOCRIT:** 34.3 % (normal 41.0 to 53.0)

[redacted] **20[redacted] HEMOGLOBIN:** 11.7 G/DL (normal 13.5 to 17.5)

[redacted] 20[redacted] **MRI ANGIOGRAM HEAD WITHOUT CONTRAST:** NO ABNORMALITY IS IDENTIFIED WITHIN THE MAJOR INTRACRANIAL ARTERIAL VASCULATURE

[redacted] 20[redacted] **MRI ANGIOGRAM NECK WITH AND WITHOUT CONTRAST:** LOSS OF SIGNAL WITHIN THE BILATERAL VERTEBRAL ARTERIES, PROXIMAL RIGHT COMMON ARTERY AND LEFT SUBCLAVIAN ARTERY LIMITING EVALUATION. THESE ARE MOST LIKE ARTIFACTUAL. NO DEFINITIVE AREAS OF OCCLUSION OR INTRACRANIAL STENOSIS ARE IDENTIFIED. IF THERE IS CONTINUED CLINICAL CONCERN, MAY CONSIDER CTA OF THE NECK

[redacted] 20[redacted] **MRI BRAIN WITHOUT CONTRAST:** 1. NO EVIDENCE OF INTRACRANIAL HEMORRHAGE. 2. NO EVIDENCE OF ACUTE OR EVOLVING CEREBRAL INFARCTION. 3. MILD PERIVENTRICULAR WHITE MATTER CHANGES

[redacted] 20[redacted] **NIH STROKE SCALE/SCORE (NIHSS):** 2 no units

[redacted] 20[redacted] **NIH STROKE SCALE/SCORE (NIHSS):** 4 no units

[redacted] 20[redacted] **PLATELET COUNT:** 197 TH/CUMM (normal 125 to 415)

[redacted] 20[redacted] **POTASSIUM:** 4.1 MMOL/L (normal 3.4 to 5.1)

[redacted] 20[redacted] **SODIUM:** 142 MEQ/L (normal 135 to 145)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.9 TH/MM3 (normal 4.0 to 11.5)
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，死亡に至った無酸素性脳損傷及びオピオイド過量投与の事象を発現した。関連する病歴は，潰瘍性大腸炎，腸閉塞，ベンゾ系薬剤嗜癖，高血圧，元喫煙者（1 日 0.5 箱を 1 年間），肺塞栓症及び非飲酒者であった。

Event 9 及び 10 の臨床経過：

投与1552日後＊，被験者はオピオイド過量投与を発現した。投与1552日後＊ ，オピオイド過量投与は消失した。投与1558日後＊，被験者は無酸素性脳損傷を発現した。投与1558日後＊ ，被験者は死亡した。死因は無酸素性脳損傷と報告された。剖検は実施されなかった。

投与1552日後＊ ，被験者は narcan の投与を必要とする過量投与のため，救急治療室に搬送された。

同日，被験者は退院した。

投与1557日後＊　，被験者は心停止後状態で救急医療サービスを介して救急治療室へ搬送された。被験者は家族により無反応状態で発見された。被験者は約 45 分間から 1 時間蘇生が試みられ，挿管された。病院到着時，被験者はnarcanを複数回投与されたが反応がなく，瞳孔は固定し散大しており，グラスゴーコーマスケール（GCS）は鎮静剤の使用なしで 3 であった。CT 検査でびまん性酸素欠乏障害が認められた。被験者は脳死検査実施まで入院となった。入院 24 時間後に，集中治療室で正式な脳死検査が実施された。被験者は正常体温であり，電解質異常はなかった。投与1558日後＊ ，10 時 20 分，被験者は死亡宣告された。

治験責任医師によると，本事象に関連する危険因子はオピオイド乱用の病歴であった。

投与された薬剤は，narcan であった。

The patient's past medications include:

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

SOLUMEDROL for ULCERATIVE COLITIS ([redacted])

SULFASALAZINE for ULCERATIVE COLITIS ([redacted])

CIPRO for ULCERATIVE COLITIS ([redacted])

FLAGYL for ULCERATIVE COLITIS ([redacted])

PREDNISONE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Open Label)

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1)　Anoxic brain damage (10002663)　(Brain injury (10067967))　[v.23.1]　[10002663]

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

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

Dechallenge: Not Applicable

2) Drug overdose (10068719) (Overdose (10033295)) [v.23.1] [10068719]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of ANOXIC BRAIN INJURY

- Investigator: Acute respiratory failure with hypoxia.

- AbbVie: Risk factors include pre-existing benzodiazepine addiction, polypharmacy, history of opioid abuse (per PI) and recent opioid overdose requiring Narcan administration.

Event of OPIOD OVERDOSE

- Investigator: Drug overdose

- AbbVie: Risk factors include pre-existing bipolar disorder, benzodiazepine addiction and history of opioid abuse (per PI).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] A/G RATIO:** 1.5 Ratio (normal 0.9 to 2.4)

[redacted] **20[redacted] ALANINE TRANSAMINASE:** 94 IU/L (normal 8 to 39)

[redacted] **20[redacted] ALBUMIN:** 3.4 G/DL (normal 3.5 to 4.9)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 203 IU/L (normal 36 to 108)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 128 IU/L (normal 36 to 108)

[redacted] **20[redacted] ALT:** 355 IU/L (normal 8to 39)

[redacted] 20[redacted] **ANION GAP:** 16 MMOL/L (normal 6 to 13)

[redacted] 20[redacted] **ANION GAP:** 8 MMOL/L (normal 6 to 13)

[redacted] 20[redacted] **ASPARTATE TRANSAMINASE:** 45 IU/L (normal 12 to 33)

[redacted] 20[redacted] **AST:** 617 IU/L (normal 12 to 33)

[redacted] 20[redacted] **BILIRUBIN:** 0.5 mg/dL (normal 0.0 to 1.5)

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 18 mg/dL (normal 7 to 25)

[redacted] 20[redacted] **BODY WEIGHT:** 6[redacted]KG

[redacted] 20[redacted] **BUN:** 16 mg/dL (normal 7 to 25)

[redacted] 20[redacted] **BUN/CREATININE RATIO:** 26 RATIO (normal 8 to 23)

[redacted] 20[redacted] **CALCIUM:** 9.0 mg/dL (normal 8.9 to 10.3)

[redacted] 20[redacted] **CHLORIDE:** 112 MMOL/L (normal 100 to 111)

[redacted] 20[redacted] **CO2:** 27.7 MMOL/L (normal 23.0 to 32.6)

[redacted] 20[redacted] **CREATININE:** 0.68 mg/dL (normal 0.47 to 1.35)

[redacted] 20[redacted] **CT CHEST ABDOMEN PELVIS WITH IV CONTRAST ONLY:** No acute finding in the chest, only mild bibasilar dependent atelectasis. No clearly acute intra-abdominal or pelvis finding, surgery changes seen. There maybe an early developing bowel ileus.

[redacted] 20[redacted] **CT HEAD WITHOUT CONTRAST:** Abnormalexam-appearance very worrisome for diffuse anoxic injury with cerebral/cerebellar edema.

[redacted] 20[redacted] **EKG:** RESULTS NOT LISTED ON REPORT

[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

Blood creatine phosphokinase increased ([redacted]/[redacted]/20[redacted]): Symptom of muscle pain, related to exercise or other vigorous physical activity.

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

Reason for Narrative

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

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted]20[redacted] / 56	[redacted]20[redacted] / 373	318
M14-533 ABT-494 (LTE)	15 mg	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
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	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 89): NEPHROLITHOTRIPSY: BREAK UP OF STONES	
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

Generated: [redacted]20[redacted]:06:46
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＊　　，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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	7.5 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	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]-[redacted]
ADALIMUMAB	40 mg	OTHER: WEEKLY	Y-M: 20[redacted]-[redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 4 WEEKS	Y-M: 20[redacted]-[redacted]
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted]-[redacted] / -309
UREA	40 %	BID	Y-M: 20[redacted]-[redacted] / -153
PREDNISONE	30 mg	QD	Y-M: 20[redacted]-[redacted] / -89
CALCIUM;VITAMIN D NOS	800 IU	QD	Y-M: 20[redacted]-[redacted] / -90
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]-[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	
SAE Supplemental Procedure	
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

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 149): LAPAROSCOPIC TOTAL PROCTOCOLECTOMY ILEOSTOMY: TOTAL PROCTOCOLECTOMY ILEOSTOMY; [redacted]20[redacted] (RX DAY 154): NG PLACEMENT: DECOMPRESSION OF ABDOMEN

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

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 154): CT 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 D ISTAL SMALL BOWEL IS DECOMPRESSED BUT SEVERAL LOOPS CONTAIN INTERNAL FLUID.; NG TUBE PLACED: DECOMPRESSION OF ABDOMEN

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]:06:46
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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 57	[redacted] / 359	303
M14-533 ABT-494 (LTE)	15 mg	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	9 mg	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	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	
SAE Supplemental Procedure	
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

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 783): CHEST XRAY: NEGATIVE; EKG: EP INTERP, NORMAL AXIS, NO ECTOPY SUBLTLE ST DEPRESSIONS V5 AND V6 NO T WAVE INVERSIONS

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

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 987): EP STUDY AND CARDIAC ABLATION: RECURRENT VENTRICULAR TACHYCARDIA IN NEED OF ICD IMPLANTATION; [redacted]20[redacted] (RX DAY 988): DUAL CHAMBER ICD IMPLANTATION: ICD IMPLANTATION WITHOUT COMPLICATION

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

Generated: [redacted]20[redacted]:06:46

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])

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) 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

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 54	54
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 55	[redacted] / 418	364
M14-533 ABT-494 (LTE)	15 mg	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): NPTST014-ACETAMINOPHEN LEVEL: 140.10 [10 - 30] UG/ML; NPTST014-ACETAMINOPHEN LEVEL: 77.80 [10 - 30] UG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 67): ECG: NORMAL SINUS RHYTHM

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]:06:46
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
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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 57	[redacted] / 365	309
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 365		

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: [redacted]
MESALAZINE	1.2 g	QD	Y-M: [redacted]
ALPRAZOLAM	0.5 mg	PRN	Y-M: [redacted]
ATORVASTATIN	20 mg	QD	Y-M: [redacted]
MESALAZINE	1.2 g	QD	Y-M: [redacted]
LOPERAMIDE	4 mg	NOT REPORTED	Y-M: [redacted]
PREDNISONE	5 mg	OTHER: ON AND OFF BETWEEN THE DATES LISTED DUE TO FLARES	Y-M: [redacted]
BALSALAZIDE	750 mg	TID	Y-M: [redacted]
ADALIMUMAB	40 mg	OTHER: EVERY 10 DAYS	Y-M: [redacted]
DICYCLOVERINE	10 mg	NOT REPORTED	Y-M: [redacted]
BUDESONIDE	3 mg	QD	Y-M: [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	Not reported
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
SALBUTAMOL	2 OTHER: PUFFS	OTHER: Q4HRS	Y-M: 20[redacted] / 441	Not reported
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	Not reported
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
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

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 260): LEFT CORONARY ANGIOGRAPHY: STENT PLACEMENT; LEFT HEART CATHETERIZATION: STENT PLACEMENT; RIGHT CORONARY ANGIOGRAPHY: STENT PLACEMENT; [redacted]20[redacted] (RX DAY 261): ECG: ABNORMAL

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	
SAE Supplemental Procedure	
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	
SAE Supplemental Procedure	
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

Generated: [redacted]20[redacted]:06:46
Program Source Code: [redacted]

Investigator No.: [redacted]#[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

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted] / 1	[redacted] / 57	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 58	[redacted] / 421	364
M14-533 ABT-494 (LTE)	15 mg	QD	[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: [redacted]
ETHINYLESTRADIOL;NORETHISTERONE	1 OTHER: TABLET	QD	Y-M: [redacted]
ESCITALOPRAM	20 mg	QD	Y-M: [redacted]
MESALAZINE	3.6 g	QD	Y-M: [redacted]
PLANTAGO OVATA	1 OTHER: TBL	QD	Y-M: [redacted]
PROBIOTICS NOS	10 BILLION CELLS OTHER: 1 CAPSULE	QD	Y-M: [redacted]
MESALAZINE	1600 mg	TID	Y-M: [redacted]
OMEPRAZOLE	20 mg	QD	Y-M: [redacted]
DICYCLOVERINE	20 mg	OTHER: Q 6 HOURS; PRN	Y-M: [redacted]
MESALAZINE	1.2 g	TID	Y-M: [redacted]
CETIRIZINE	10 mg	QD	Y-M: [redacted]
MESALAZINE	1600 mg	TID	Y-M: [redacted]
PREDNISONE	10 mg	QD	Y-M: [redacted]
PARACETAMOL	325 mg	PRN	Y-M: [redacted]
MOMETASONE	1 METERED DOSE IN EACH NOSTRIL OTHER: MICROGRAMS	QD	Y-M: [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: [redacted]	ONGOING
ETHINYLESTRADIOL;NORETHISTERONE	1 OTHER: TABLET	QD	Y-M: [redacted]	Y-M: [redacted] / 719
ESCITALOPRAM	20 mg	QD	Y-M: [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
BENZONATATE	100 mg	TID	Y-M: 20[redacted] / 719	ONGOING
CODEINE;GUAIFENESIN	10-100/5ML mg	TID	Y-M: 20[redacted] / 719	ONGOING
ETHINYLESTRADIOL;NORETHISTERONE	1/20 OTHER: MCG	QD	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	ONGOING

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): NPTST085-CRP: 4.8 [NOT REPORTED - 0.5] mg/dL

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 717): 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.; 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.; XR CHEST 1 VIEW: CARDIAC SIZE WITHIN NORMAL LIMITS; MILD BILATERAL AIRSPACE, RIGHT MORE THAN LEFT; NO SIGNIFICANT PLEURAL EFFUSION; NO PNEUMOTHORAX

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]:06:46
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
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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted] / 1	[redacted] / 63	63
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 64	[redacted] / 105	42
M14-533 ABT-494 (LTE)	15 mg	QD	[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	ONGOING
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	ONGOING
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
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	
SAE Supplemental Procedure	
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; NPTST089-D-DIMER: 2.44 [0.5 - 0.5] MG/DL; NPTST155-MAGNESIUM: 1.7 [1.8 - 2.4] MG/DL; NPTST191-PRO BNP: 279 [900 - 900] PG/ML; NPTST249-TROPONIN I QNT: > 200 [0 - 0.056] NG/ML; NPTST249-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): NPTST249-TROPONIN I QNT: 93.552 [0 - 0.056] NG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 323): EKG: ABNORMAL EKG WITH MINIMAL ST ELEVATION; LEFT HEART CATH: NSTEMI DUE TO ATHEROTHROMBOTIC DISEASE OF THE LEFT ANTERIOR DESCENDING ARTERY, SP THROMBECTOMY WITH PENUMBRA

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

Generated: [redacted]20[redacted]:06:46

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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-533 ABT-494 (LTE)	15 mg	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
ASCORBIC ACID;IRON;NICOTINAMIDE;RIBOFLAVIN;THIAMINE	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
ASCORBIC ACID;IRON;NICOTINAMIDE;RIBOFLAVIN;THIAMINE	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	
SAE Supplemental Procedure	
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	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 428): X-RAY OF THE CHEST AND ABDOMEN: NORMAL; [redacted]20[redacted] (RX DAY 429): ABDOMINAL ULTRASOUND: NORMAL	
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]:06:46
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)

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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
肝酵素上昇				X
帯状疱疹				X
平均赤血球容積増加				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]
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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	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]-[redacted]
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]-[redacted]
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted]-[redacted] / -162
PREDNISONE	10 mg	QD	Y-M: 20[redacted]-[redacted] / -115
PREDNISONE	15 mg	QD	Y-M: 20[redacted]-[redacted] / -1
PROPOFOL	300 mL	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / -2
RANITIDINE	150 mg	PRN	Y-M: 20[redacted]-[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]-[redacted]	Y-M: 20[redacted]-[redacted] / 907
AMLODIPINE	10 mg	QD	Y-M: 20[redacted]-[redacted]	ONGOING
BALSALAZIDE	2250 mg	TID	Y-M: 20[redacted]-[redacted] / -162	ONGOING

PREDNISONE	15 mg	QD	Y-M: 20[redacted] / -1	ONGOING
RANITIDINE	150 mg	PRN	Y-M: 20[redacted] / -8	Not reported
PANTOPRAZOLE	40 mg	BID	Y-M: 20[redacted] / 1	ONGOING
IRON	325 mg	QD	Y-M: 20[redacted] / 18	Not reported
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
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	Not reported
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	Not reported
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
OTHER VIRAL VACCINES	0.3 mL	OTHER: ONCE	Y-M: 20[redacted] / 1030	Y-M: 20[redacted] / 1060
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

CALCIUM CARBONATE	2 OTHER: TABLET	PRN	Y: 20[redacted]	ONGOING
TRIAMCINOLONE	UNK OTHER: UNKNOWN	PRN	Y: 20[redacted]	ONGOING
LISINOPRIL	12.5 mg	BID	Y: 20[redacted]	ONGOING

Event #1: 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	
SAE Supplemental Procedure	
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 #2: 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	
SAE Supplemental Procedure	
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 #3: 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	
SAE Supplemental Procedure	
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 #4: 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; NPTST093-EGFR NON AFRICAN/AMERICAN: 11 [15 - 60] ML/MIN; NPTST153-LIPASE: 506 [73 - 393] U/L; NPTST155-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: 33.55518 [3.5697 - 7.1394] MMOL/L; Blood Urea Nitrogen: 22.13214 [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; NPTST043-BILIRUBIN, DIRECT: 0.9 [0 - 0.2] MG/DL; NPTST044-BILIRUBIN, TOTAL: 1.4 [NOT REPORTED - 1.2] mg/dL; NPTST093-EGFR NON AFRICAN/AMERICAN: 20 [60 - NOT REPORTED] mL/min/1.73m2; NPTST153-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; NPTST044-BILIRUBIN, TOTAL: 1.2 [NOT REPORTED - 1.2] mg/dL; NPTST093-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; NPTST044-BILIRUBIN, TOTAL: 1.0 [NOT REPORTED - 1.2] mg/dL; NPTST093-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; NPTST044-BILIRUBIN, TOTAL: 1.0 [NOT REPORTED - 1.2] mg/dL; NPTST094-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; NPTST027-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; NPTST027-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; NPTST027-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

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 779): CT ABDOMEN AND PELVIS WO 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 PE LVIC SIDE WALL IS LIKELY SECONDARY TO CHOLECYSTITIS.; EKG 12 LEAD: SINUS RHYTHM ATRIAL PREMATURE COMPLEX LEFT ANTERIOR FASCICULAR BLOCK; US RUQ: THICKENED HYPERCHOIC GALLBLADDER WALL AND SMALL PERICHOLECYSTIC FLUID COLLECTION CONSISTENT ACUTE CHOLECYSTITIS, LIEKLY ASSOCIATED RUPTURE. NO OBSTRUCTING STONE IDENTIFIED; XR CHEST 1 VIEW: NO PNEUMOTHORAX OR PLEURAL EFFUSION. NORMAL HEART SIZE; [redacted]20[redacted] (RX DAY 780): IR CHOLECYSTOSTOMY TUBE PLACEMENT: SUCCESSFUL PLACEMENT OF CATHETER; [redacted]20[redacted]

(RX DAY 781): CHOLECYSTOGRAM: SUCCESSFUL CHOLECYSTOGRAM THROUGH EXISTING DRAIN SHOWS GOOD POSITION OF DRAIN WITH PATENT CYSTIC DUCT; [redacted]20[redacted] (RX DAY 782): IR CHOLECYSTOSTOMY CATHETER PLACEMENT: SUCCESSFUL CHOLECYSTOSTOGRAM OF CATHETER; [redacted]20[redacted] (RX DAY 785): CT ABDOMEN AND PELVIS WITH CONTRAST: PARACOLIC ABSCESS, BILOMA, AND RIGHT PLEURAL EFFUSION; [redacted]20[redacted] (RX DAY 786): RLQ IR DRAINAGE: SUCCESSFUL DRAINAGE OF CATHETER; [redacted]20[redacted] (RX DAY 817): CT ABDOMEN AND PELVIS W/ CONTRAST: 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 COMPL ICATION.; IR CHOLECYSTECTOMY TUBE CHANGE: SUCCESSFUL TUBE CHANGE; [redacted]20[redacted] (RX DAY 866): LAPAROSCOPIC CHOLECYSTECTOMY: SUCCESSFUL SUBTOTAL REMOVAL OF GALLBLADDER.

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 #5: 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	
SAE Supplemental Procedure	
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 #6: 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	
SAE Supplemental Procedure	
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 #7: 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	
SAE Supplemental Procedure	
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 #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] / 1064 / 1008
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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 #9: 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	
SAE Supplemental Procedure	
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 #10: Event of Interest - Anemia

Event Description	ELEVATED MEAN CORPUSCULAR VOLUME
Preferred term	平均赤血球容積増加
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	
SAE Supplemental Procedure	
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 #11: 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] / 1131 / 1075
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
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 #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	
SAE Supplemental Procedure	
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

Generated: [redacted]20[redacted]:06:46
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.
Herpes zoster: ([redacted] 20[redacted]) One dermatome. History of shingles
Herpes zoster: ([redacted] 20[redacted]) One dermatome. History of shingles
Hepatic enzyme increased: Intermittent. Asymptomatic. User of alcohol, 4-8 oz of wine most nights.
Gamma-glutamyltransferase increased: Intermittent. Asymptomatic. User of Alcohol, 12 oz of wine daily.
Gamma-glutamyltransferase increased: Intermittent. Fatugue, dark urine, loss of appetite. User of Alcohol, 12 oz of wine daily.
Hepatic enzyme increased: Intermittent. Asymptomatic. User of Alcohol, 12 oz of wine daily. ABOVE [redacted]20[redacted] GGT INCREASE, THE HEPATIC SUPPLEMENTAL CONTRADICTS IF THE SUBJECT IS OR IS NOT SYMPTOMATIC. BOTH HAVE THE SAME ONSET DATE & . ONGOING DATE.
Acute kidney injury: Intermittent. Study drug interrupted. Symptoms of shortness of breath, chest pain, weakess, and fever. Vomiting preceding the event.

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
背部痛	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: 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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 Placebo (IND)		QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	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]-[redacted]
MESALAZINE	NOT REPORTED	QD	Y-M: 20[redacted]-[redacted]
INFLIXIMAB	10 mg/kg	OTHER: Q 8 WEEKS	Y-M: 20[redacted]-[redacted]
WARFARIN	5 mg	QD	Y-M: 20[redacted]-[redacted]
VITAMINS NOS	2 OTHER: CHEWS	QD	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: Q 8 WKS	Y-M: 20[redacted]-[redacted]
METHOTREXATE	15 mg	OTHER: WEEKLY	Y-M: 20[redacted]-[redacted] / -340
ADALIMUMAB	40 mg	OTHER: WEEKLY	Y-M: 20[redacted]-[redacted] / -284
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]-[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	ONGOING
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
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	4 L	OTHER: ONCE	Y-M: 20[redacted] / 1010	Y-M: 20[redacted] / 1011
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 1010	Y-M: 20[redacted] / 1011
FENTANYL	100 OTHER: MCGS	OTHER: ONCE	Y-M: 20[redacted] / 1011	Y-M: 20[redacted] / 1011
METHYLTHIONINIUM	250 OTHER: CC	OTHER: ONCE	Y-M: 20[redacted] / 1011	Y-M: 20[redacted] / 1011
PROPOFOL	560 mg	OTHER: ONCE	Y-M: 20[redacted] / 1011	Y-M: 20[redacted] / 1011
AZITHROMYCIN	250 mg	QD	Y-M: 20[redacted] / 1067	Y-M: 20[redacted] / 1071
OXYCODONE;PARACETAMOL	0.5 OTHER: TABLET	PRN	Y-M: 20[redacted] / 1067	Y-M: 20[redacted] / 1076
CEFALEXIN	250 mg	BID	Y-M: 20[redacted] / 1072	Y-M: 20[redacted] / 1080
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 1081	Y-M: 20[redacted] / 1090
OTHER VIRAL VACCINES	1 OTHER: DOSE	OTHER: ONCE	Y-M: 20[redacted] / 1175	Y-M: 20[redacted] / 1175
OTHER VIRAL VACCINES	1 OTHER: DOSE	OTHER: ONCE	Y-M: 20[redacted] / 1200	Y-M: 20[redacted] / 1200

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; NPTST006-A:G RATIO: 1.2 [NOT REPORTED - NOT REPORTED] N/A; NPTST007-ABS BASOS: 0.03 [0 - 0.2] K/UL; NPTST008-ABS EOS: 0.07 [0 - 0.4] K/UL; NPTST009-ABS IMMATURE GRANS: 0.06 [0 - 0.05] K/UL; NPTST010-ABS LYMPHS: 1.53 [0.8 - 3.3] K/UL; NPTST011-ABS MONOS: 1.09 [0.1 - 1] K/UL; NPTST012-ABS NEUTS: 9.43 [1.8 - 7.8] K/UL; NPTST013-ABS NRBCS: 0.00 [0 - 0] K/UL; NPTST028-ANION GAP W/O K: 15 [7 - 15] N/A; NPTST040-BASOS: 0.2 [NOT REPORTED - NOT REPORTED] %; NPTST042-BILIRUBIN TOTAL: 0.6 [0.2 - 1.4] MG/DL; NPTST050-BUN: 15 [8 - 24] MG/DL; NPTST073-CL: 106 [98 - 109] MMOL/L; NPTST078-CO2: 22 [21 - 28] MMOL/L; NPTST096-EOS: 0.6 [NOT REPORTED - NOT REPORTED] %; NPTST117-GFR NON AFRICAN AMERICAN: 74 [59 - NOT REPORTED] mL/min; NPTST124-GLOBULIN(CALC): 2.9 [2 - 4.5] G/DL; NPTST127-HCT: 36.2 [37 - 47] %; NPTST130-HGB: 11.8 [12 - 16] G/DL; NPTST136-IMMATURE GRANS: 0.5 [0 - 0.6] %; NPTST139-INR: 2.0 [0 - 3.5] N/A; NPTST141-K: 3.1 [3.6 - 5.3] MMOL/L; NPTST143-LACTATE: 2.9 [0.7 - 2] MMOL/L; NPTST143-LACTATE: 1.4 [0.7 - 2] MMOL/L; NPTST151-LEUKOCYTE ESTERASE: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; NPTST153-LIPASE: 21 [8 - 78] IU/L; NPTST154-LYMPHS: 12.5 [NOT REPORTED - NOT REPORTED] %; NPTST157-MCH: 28.3 [27 - 33] PG; NPTST158-MCHC: 32.6 [32 - 37] G/DL; NPTST159-MCV: 86.8 [80 - 98] FL; NPTST164-MONOS: 8.9 [NOT REPORTED - NOT REPORTED] %; NPTST170-NA: 143 [135 - 145] MMOL/L; NPTST172-NEUTS: 77.3 [NOT REPORTED - NOT REPORTED] %; NPTST173-NRBC: 0.0 [0 - 100] WBC; NPTST186-PLT: 276 [150 - 450] K/UL; NPTST197-PROTIME: 23.3 [11.3 - 15.2] SEC; NPTST204-RDW: 14.4 [11.5 - 15] %; NPTST229-SGOT/AST: 10 [5 - 40] IU/L; NPTST230-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

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 34): CT KUB STONE PROTOCOL W/O IV CONTRAST: MILD LEFT HYDROURETER AND HYDRONEPHROSIS RELATED TO TINY 3MM LEFT UVJ STONE; XR FLUOROSCOPY: FLUOROSCOPY IN OR FOR LEFT URETERAL STENT PLACEMENT

AE Stopped Initial Rx Day / Rx Day	92 / 36
Duration of AE	12 DAYS
Severity	MODERATE
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	BACK PAIN
Preferred term	背部痛
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; NPTST151-LEUKOCYTE ESTERASE: 3+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST236-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; NPTST058-C-REACTIVE PROTEIN: 0.9 [0 - 1] MG/DL; NPTST059-CALPROTECTIN: >500 [0 - 50] UG/G; NPTST060-CAMPYLOBACTER DNA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST095-ENTEROINVASIVE ECOLI: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST158-MCHC: 31.2 [32 - 37] G/DL; NPTST197-PROTIME: 35.4 [11.3 - 15.2] SEC; NPTST219-SALMONELLA SP DNA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST231-SHIGA TOXIN GENE DNA: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST232-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; NPTST028-ANION GAP W/O K: 6 [7 - 15] UNIT NOT REPORTED; NPTST158-MCHC: 31.5 [32 - 37] G/DL; NPTST226-SED RATE (ESR): 22 [0 - 30] MM/H; Protein: 55 [62 - 80] G/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 803): 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 NEPHROCA LCINOSIS. APPENDIX IS UPPER LIMITS OF MILDLY ENLARGED 7MM WITHOUT PERIAPPENDICEAL STRANDING OR FLUID.

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	COEXISTENT MEDICAL PROBLEM: KIDNEY STONES, BACK PAIN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:06:46
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，背部痛の事象を発現した。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＊ ，被験者は背部痛を発現した。

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＊ ，被験者は急性下痢及び急性潰瘍性大腸炎の再燃と診断され，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) Back pain (10003988) (Back pain (10003988)) [v.22.1] [10003988]

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 BACK PAIN

- Investigator: COEXISTENT MEDICAL PROBLEM: KIDNEY STONES, BACK PAIN

- AbbVie: Back pain is common in the general population. According to WHO, the lifetime prevalence of back pain is estimated at 60 to 70% in industrialized countries. Additional risk factor includes prior event of obstructive ureter stone.

Relevant Laboratory & Other Diagnostic Tests

20[redacted] CMP: Not reported

[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.

20[redacted] MG TEST: Not reported

20[redacted] SED RATE: Not reported

20[redacted] URINALYSIS: Not reported

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-533 ABT-494 (LTE)	15 mg	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	3000 mg	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 / 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]-[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

SAE Supplemental Procedure

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

SAE Supplemental Procedure

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

SAE Supplemental Procedure

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 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]20[redacted] / 771 / 715
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 715): NPTST139-INR: 1.1 [0.9 - 1.1] RATIO; NPTST199-PT: 11.1 [9.5 - 12] SEC; NPTST246-TROPONIN: 0.075 [0 - 0.039] NG/ML; [redacted]20[redacted] (RX DAY 716): NPTST203-PTT: 58 [22 - 32] SEC

Microbiology

[redacted]20[redacted] (RX DAY 715): OTHER NASAL SWAB NPTST224-SARS-COV-2, NAA LC: Negative; [redacted]20[redacted] (RX DAY 716): URINE NPTST148-LEGIONELLA AG: Negative; URINE NPTST238-STREPNEUMO AG: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 715): CHEST X RAY: MILD DIFFUSE PROMINENCE OF INTERSTITIAL LUNG MARKINGS; CTA CHEST: CT SCAN OF THE CHEST SHOWED PE IN LEFT AND RIGHT.; VENOUS DUPLEX SCAN LOWER EXTREMITY: NON OCCLUSIVE THROMBUS IN RIGHT POPLITEAL VEIN AND RIGHT PERONEAL VEIN; [redacted]20[redacted] (RX DAY 719): 2D ECHO: NORMAL LEFT VENTRICULAR SIZE AND LEFT VENTRICULAR SYSTOLIC FUNCTION, ESTIMATED EF 65-70 %

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]20[redacted]:06:46
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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 57	[redacted] / 421	365
M14-533 ABT-494 (LTE)	15 mg	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 / RX Day	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
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] %; NPTST131-HGBA1C: 6.2 [4.5 - 5.7] %; NPTST134-IG%: 0.40 [0 - 1.99] %; NPTST139-INR: 1.2 [0.8 - 1.2] RATIO; NPTST140-IPF: 0.0 [1.2 - 8.6] %; NPTST156-MBGLU: 131 [NOT REPORTED - NOT REPORTED] mg/dL; NPTST157-MCH: 28.0 [26.1 - 33.6] PG; NPTST158-MCHC: 30.6 [32.4 - 35.2] G/DL; NPTST159-MCV: 91.4 [79.1 - 97.9] FL; NPTST165-MPV: 10.0 [6.64 - 11.5] FL; NPTST199-PT: 12.2 [9.2 - 12.2] SEC; NPTST204-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; NPTST004-A/G: 0.5 [1 - 3] G/DL; NPTST029-ANIONGAP: 14 [3 - 19] UNIT NOT REPORTED; NPTST045-BILT: 0.50 [0 - 1] MG/DL; NPTST078-CO2: 25 [21 - 32] MMOL/L; NPTST122-GLOBULIN:

5.3 [2.2 - 4.2] G/DL; NPTST161-MG: 2.4 [1.8 - 2.4] MG/DL; NPTST175-OSMOC: 276 [250 - 300] MOSM/KG; NPTST254-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

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 15): CT CHEST: CT CHEST REVEALED INCREASED MINIMAL BILATERAL UPPER LOBE AND RIGHT MIDDLE LOBE PERIPHERAL ROUNDED TRIANGULAR SHAPED GROUND-GLASS OPACITIES. INCREASED MODERATE RIGHT AND MILD LEFT LOWER LOBE WEDGE-SHAP ED AREAS OF GROUND-GLASS OPACITY AND PATCHY CONSOLIDATION. THESE FINDINGS COULD BE CONSISTENT WITH WORSENING COVID 19

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]:06:46
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
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	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 142	86
M14-533 ABT-494 (LTE)	15 mg	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]-[redacted]
INFLIXIMAB	500 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
CERTOLIZUMAB PEGOL	0 mg	NOT REPORTED	Y-M: 20[redacted]-[redacted]
ADALIMUMAB	40 mg	OTHER: EVERY TWO WEEKS	Y-M: 20[redacted]-[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]-[redacted]
VEDOLIZUMAB	300 mg	OTHER: EVERY 8 WEEKS	Y-M: 20[redacted]-[redacted]
ATORVASTATIN	10 mg	QD	Y-M: 20[redacted]-[redacted]
PREDNISONE	10 mg	OTHER: EVERY TWO DAYS	Y-M: 20[redacted]-[redacted]
CETIRIZINE	10 mg	QD	Y-M: 20[redacted]-[redacted]
GABAPENTIN	600 mg	QD	Y-M: 20[redacted]-[redacted] / -228
MESALAZINE	1.2 g	BID	Y-M: 20[redacted]-[redacted] / -88
PREDNISONE	40 mg	QD	Y-M: 20[redacted]-[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
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): NPTST246-TROPONIN: 0.130 [0 - 0.045] NG/ML

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 79): CR CHEST AP: NO ACUTE DISEASE; [redacted]20[redacted] (RX DAY 80): ECHOCARDIOGRAM: EJECTION FRACTION=60; MILD MITRAL REGURGITATION; EKG: NORMAL SINUS RHYTHM, PR INTERVAL 140MS, QRS DURATION 86MS, QT/QTC334/375 MS, NO STEMI, UNDETERMINED RHYTHM; NONSPECIFIC TWAVE ABNORMALITY. ABNORMAL EKG; [redacted]20[redacted] (RX DAY 81): 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%

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]:06:46

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
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