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] / 53	53
M14-234 SS3 Placebo (MAIN)		QD	[redacted] / 54	[redacted] / 433	380
M14-533 Placebo (LTE)		QD	[redacted] / 434		

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	800 mg	TID	Y-M: [redacted]
MULTIVITAMINS, COMBINATIONS	1 OTHER: TABLET	QD	Y-M: [redacted]
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: [redacted]
LORATADINE	10 mg	PRN	Y-M: [redacted] / -226
SALBUTAMOL	90 ug	PRN	Y-M: [redacted] / -234
ASCORBIC ACID	500 mg	QD	Y-M: [redacted] / -7
ZINC	15 mg	QD	Y-M: [redacted] / -7

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MULTIVITAMINS, COMBINATIONS	1 OTHER: TABLET	QD	Y-M: [redacted]	Not reported
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: [redacted]	Not reported
LORATADINE	10 mg	PRN	Y-M: [redacted] / -226	Not reported
SALBUTAMOL	90 ug	PRN	Y-M: [redacted] / -234	Not reported
ASCORBIC ACID	500 mg	QD	Y-M: [redacted] / -7	Not reported
ZINC	15 mg	QD	Y-M: [redacted] / -7	Not reported
DICYCLOVERINE	10 mg	OTHER: ONCE	Y-M: [redacted] / 142	Y-M: [redacted] / 142
HYDROMORPHONE	0.5 mg	OTHER: EVERY 4 HOURS PRN	Y-M: [redacted] / 142	Y-M: [redacted] / 143
METHYLPREDNISOLONE	20 mg	OTHER: EVERY 6 HOURS	Y-M: [redacted] / 142	Y-M: [redacted] / 143
MORPHINE	4 mg	OTHER: EVERY 4 HRS PRN	Y-M: [redacted] / 142	Y-M: [redacted] / 142
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: [redacted] / 142	Y-M: [redacted] / 142
PARACETAMOL	650 mg	OTHER: EVERY 6 HOURS	Y-M: [redacted] / 142	Y-M: [redacted] / 143

PIPERACILLIN;TAZOBACTAM	3.375 g	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 143
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 142
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 143
SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143
CYCLOBENZAPRINE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 167

Event #1: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 434 / 1
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Initial Rx Day / Rx Day	469 / 36
Duration of AE	36 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

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

Event Description	ACUTE GASTROENTERITIS
Preferred term	胃腸炎
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 571 / 138
Age at AE Onset	3[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 142): Alanine Aminotransferase: 21 [16 - 61] U/L; Albumin: 36 [32 - 48] G/L; Alkaline Phosphatase: 53 [26 - 162] U/L; Aspartate Aminotransferase: 13 [15 - 37] U/L; Basophils/Leukocytes: 0 [0 - 2] %; Bilirubin: 8.551945 [3.420778 - 22.235057] UMOL/L; Calcium: 2.220639 [2.070933 - 2.470149] MMOL/L; Chloride: 105 [98 - 110] MMOL/L; Creatinine: 80.446967 [61.882282 - 114.924238] UMOL/L; Eosinophils/Leukocytes: 1 [0 - 5] %; Erythrocytes: 4.9 [4.5 - 5.9] 10^12/L; Glucose: 4.662588 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.442 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 147 [140 - 175] G/L; Leukocytes: 7.4 [4.5 - 11] 10^9/L; Lymphocytes/Leukocytes: 10 [15 - 49] %; Monocytes/Leukocytes: 14 [2 - 14] %; NPTST019-ALB/GLOB RATIO: 0.9 [1 - 2.2] UNIT NOT REPORTED;

NPTST050-BUN: 8 [6 - 20] MG/DL; NPTST078-CO2: 27 [21 - 32] MMOL/L; NPTST090-DIRECT BILIRUBIN: 0.1 [0 - 0.3] MG/DL; NPTST118-GFR, AFR. AMER: >60 [60 - NOT REPORTED] ML/MN; NPTST119-GFR, CAUCASIAN: >60 [60 - NOT REPORTED] ML/MN; NPTST122-GLOBULIN: 4.2 [2 - 4.2] G/DL; NPTST145-LACTIC ACID: 0.7 [0.4 - 2] MMOL/L; NPTST153-LIPASE: 98 [73 - 393] U/L; NPTST155-MAGNESIUM: 1.7 [1.6 - 2.5] MG/DL; NPTST157-MCH: 30.0 [25 - 32] PG; NPTST158-MCHC: 33.3 [31 - 37] G/DL; NPTST160-META, MYELO, PRO: 0 [0 - 5] %; NPTST165-MPV: 10.0 [8.2 - 12.2] FL; NPTST168-MVC: 90.2 [80 - 100] FL; NPTST174-NUCLEATED RBC'S: 0 [0 - 1] 100WBC; NPTST205-RDW CV: 13.2 [11 - 16] %; NPTST206-RDW SD: 43.2 [37 - 54] FL; NPTST221-SARS COV 2-RNA: NOT DETECTED [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST227-SEGS: 75 [29 - 66] %; Neutrophils: 5.53 [1.5 - 7] 10^9/L; Platelets: 198 [150 - 400] 10^9/L; Potassium: 3.6 [3.5 - 5.1] MMOL/L; Protein: 78 [64 - 83] G/L; Sodium: 138 [132 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 143): Calcium: 2.095884 [2.070933 - 2.470149] MMOL/L; Chloride: 107 [98 - 110] MMOL/L; Creatinine: 73.374706 [61.882282 - 114.924238] UMOL/L; Erythrocytes: 4.46 [4.5 - 5.9] 10^12/L; Glucose: 4.884616 [3.88549 - 5.5507] MMOL/L; Hematocrit: 0.403 [0.4 - 0.52] FRACTION OF 1; Hemoglobin: 137 [140 - 175] G/L; Leukocytes: 6.6 [4.5 - 11] 10^9/L; NPTST050-BUN: 8 [6 - 20] MG/DL; NPTST061-CARBON DIOXIDE: 24 [21 - 32] MMOL/L; NPTST103-ESTIMATED GFR: >60 [60 - NOT REPORTED] UNIT NOT REPORTED; NPTST104-ESTIMATED GFR FOR AF/AM: >60 [60 - NOT REPORTED] ML/MN; NPTST153-LIPASE: 101 [73 - 393] U/L; NPTST155-MAGNESIUM: 1.5 [1.6 - 2.5] MG/DL; NPTST157-MCH: 30.7 [25 - 32] PG; NPTST158-MCHC: 34.0 [31 - 37] G/L; NPTST159-MCV: 90.4 [80 - 100] FL; NPTST165-MPV: 9.9 [8.2 - 12.2] FL; NPTST173-NRBC: 0 [0 - 1] 100WBC; NPTST207-RDW-CV: 12.9 [11 - 16] %; NPTST208-RDW-SD: 42.3 [37 - 54] FL; NPTST237-STOOL CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST243-TOXIGENIC C DIFF: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST263-WESTERGREN SED RATE: 20 [0 - 15] MM/H; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Sodium: 138 [132 - 144] MMOL/L; [redacted]20[redacted] (RX DAY 152): Platelets: 181 [150 - 400] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 143): STOOL NPTST237-STOOL CULTURE: Negative; STOOL NPTST243-TOXIGENIC C DIFF: Negative

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 142): CT SCAN ABDOMEN/PELVIS: MID TO DISTAL SMALL BOWEL WITH ABNORMAL FLUID DISTENTION, MUCOSAL HYPER ENHANCEMENT AND DIFFUSE WALL THICKENING. IMPRESSION EXTENSIVE ENTERITIS, INFECTIOUS VERSUS INFLAMMATORY.

AE Stopped Initial Rx Day / Rx Day	577 / 144
Duration of AE	7 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #3: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 609 / 176
Age at AE Onset	3[redacted]

Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
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

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] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性胃腸炎の事象を発現した。関連する病歴は，十二指腸球部びらん，食道びらん，食道炎，胃食道逆流性疾患，悪心，潰瘍性大腸炎，非喫煙者及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与571日後＊　，被験者は急性胃腸炎を発現した。投与577日後＊　，急性胃腸炎は消失した。

投与575日後＊　，被験者は 5 日前からの悪心，嘔吐，頻繁な非血性の少量便，腹痛及び無力感のため，入院した。これらの症状は，カウンターの上に 12 時間置いてあったブリトーを食べてから 1 日以内に開始した。被験者は，CT 検査で認められた小腸閉塞の可能性を懸念され，入院した。入院翌日までに，被験者は痛みが軽減したことを報告し，清澄流動食を摂取できた。投与576日後＊　，被験者は退院した。

投与された薬剤は，メチルプレドニゾロン，モルヒネ，オンダンセトロン，ピペラシリン・タゾバクタム合剤，タイレノール，ヒドロモルフォン，ジサイクロミン，ソル・メドロール，ゾシン及び塩化ナトリウムであった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Acute gastroenteritis (10066762) (Gastroenteritis (10017888)) [v.24.0] [10066762]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of ACUTE GASTROENTERITIS

- Investigator: Not Applicable

- AbbVie: Event is more likely secondary to consumption of contaminated food as reported by PI. Additional risk factor includes pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ALANINE AMINO TRANSFERASE:** 21 U/L (normal 16 to 61)

[redacted] 20[redacted] **ALB/GLOB RATIO:** 0.9 NO UNITS (normal 1.0 to 2.2)

[redacted] 20[redacted] **ALBUMIN:** 3.6 G/DL (normal 3.2 to 4.8)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 53 U/L (normal 26 to 162)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 13 U/L (normal 15 to 37)

[redacted] 20[redacted] **BASOPHILS %:** 0 % (normal 0 to 2)

[redacted] 20[redacted] **BILIRUBIN:** 0.5 mg/dL (normal 0.2 to 1.3)

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

[redacted] 20[redacted] **BUN:** 8 mg/dL (normal 6 to 20)

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 2.9 mg/dL (normal >0.3)

[redacted] 20[redacted] **CALCIUM:** 8.9 mg/dL (normal 8.3 to 9.9)

[redacted] 20[redacted] **CALCIUM:** 8.4 mg/dL (normal 8.3 to 9.9)

[redacted] 20[redacted] **CHLORIDE:** 105 MMOL/L (normal 98 to 110)

[redacted] 20[redacted] **CHLORIDE:** 107 MMOL/L (normal 98 to 110)

[redacted] 20[redacted] **CO2:** 27 MMOL/L (normal 21 to 32)

[redacted] 20[redacted] **CO2:** 24 MMOL/L (normal 21 to 32)

[redacted] 20[redacted] **CREATININE:** 0.91 mg/dL (normal 0.70 to 1.30)

[redacted] 20[redacted] **CREATININE:** 0.83 mg/dL (normal 0.70 to 1.30)

[redacted] 20[redacted] **CT SCAN ABDOMEN/PELVIS:** MID TO DISTAL SMALL BOWEL WITH ABNORMAL FLUID DISTENTION, MUCOSAL HYPER ENHANCEMENT AND DIFFUSE WALL THICKENING. IMPRESSION EXTENSIVE ENTERITIS, INFECTIOUS VERSUS INFLAMMATORY.

[redacted] 20[redacted] **DIRECT BILIRUBIN:** 0.1 mg/dL (normal 0.0 to 0.3)

[redacted] 20[redacted] **EOSINOPHILS %:** 1 % (normal 0 to 5)

[redacted] 20[redacted] **GFR, CAUCASIAN:** >60 ML/MN

[redacted] 20[redacted] **GLOBULIN:** 4.2 G/DL (normal 2.0 to 4.2)

[redacted] 20[redacted] **GLUCOSE:** 84 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **GLUCOSE:** 88 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **HEMATOCRIT:** 44.2 % (normal 40.0 to 52.0)

[redacted] 20[redacted] **HEMATOCRIT:** 40.3 % (normal 40.0 to 52.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 14.7 G/DL (normal 14.0 to 17.5)

[redacted] 20[redacted] **HEMOGLOBIN:** 13.7 G/DL (normal 14.0 to 17.5)

[redacted] 20[redacted] **LACTIC ACID:** 0.7 MMOL/L (normal 0.4 to 2.0)

[redacted] 20[redacted] **LIPASE:** 98 U/L (normal 73 to 393)

[redacted] 20[redacted] **LIPASE:** 101 U/L (normal 73 to 393)

[redacted] 20[redacted] **LYMPHOCYTES %:** 10 % (normal 15 to 49)

[redacted] 20[redacted] **MAGNESIUM:** 1.7 mg/dL (normal 1.6 to 2.5)

[redacted] 20[redacted] **MAGNESIUM:** 1.5 mg/dL (normal 1.6 to 2.5)

[redacted] 20[redacted] **MCH:** 30.0 PG (normal 25.0 to 32.0)

[redacted] 20[redacted] **MCH:** 30.7 PG (normal 25.0 to 32.0)

[redacted] 20[redacted] **MCHC:** 33.3 G/DL (normal 31.0 to 37.0)

[redacted] 20[redacted] **MCHC:** 34.0 G/DL (normal 31.0 to 37.0)

[redacted] 20[redacted] **META, MYELO, PRO:** 0 % (normal 0 to 5)

[redacted] 20[redacted] **MONOCYTES %:** 14 % (normal 2 to 14)

[redacted] 20[redacted] **MPV:** 10.0 FL (normal 8.2 to 12.2)

[redacted] 20[redacted] **MPV:** 9.9 FL (normal 8.2 to 12.2)

[redacted] 20[redacted] **MVC:** 90.2 FL (normal 80.0 to 100.0)

[redacted] 20[redacted] **MVC:** 90.4 FL (normal 80.0 to 100.0)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 5.53 X10**3/MCL (normal 1.50 to 7.00)

[redacted] 20[redacted] **NUCLEATED RBC'S:** 0 (normal 0 to 1)

[redacted] 20[redacted] **NUCLEATED RBC'S:** 0 (normal 0 to 1)

[redacted] 20[redacted] **PLATELET COUNT:** 198 X10**3/MCL (normal 150 to 400)

[redacted] 20[redacted] **PLATELET COUNT:** 181 X10**3/MCL (normal 150 to 400)

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

[redacted] 20[redacted] **POTASSIUM:** 3.8 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **PROTEIN:** 7.8 G/DL (normal 6.4 to 8.3)

[redacted] 20[redacted] **RDW CV:** 13.2 % (normal 11.0 to 16.0)

[redacted] 20[redacted] **RDW CV:** 12.9 % (normal 11.0 to 16.0)

[redacted] 20[redacted] **RDW SD:** 43.2 FL (normal 37.0 to 54.0)

[redacted] 20[redacted] **RDW SD:** 42.3 FL (normal 37.0 to 54.0)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.90 X10**6/MCL (normal 4.50 to 5.90)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.46 X10**6/MCL (normal 4.50 to 5.90)

[redacted] 20[redacted] **SARS COV 2-RNA:NASOPHARYNGEAL:** Not Detected

[redacted] 20[redacted] **SEGS:** 75 % (normal 29 to 66)

[redacted] 20[redacted] **SODIUM:** 138 MMOL/L (normal 132 to 144)

[redacted] 20[redacted] **SODIUM:** 138 MMOL/L (normal 132 to 144)

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

[redacted] 20[redacted] **STOOL TOXIGENIC C DIFF:** Negative

[redacted] 20[redacted] **WESTERGREN SED RATE:** 20 MM/HR (normal 0 to 15)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 7.4 X10**3/MCL (normal 4.5 to 11.0)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 6.6 X10**3/MCL (normal 4.5 to 11.0)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血				X
横紋筋融解症	X	X		

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

Medical History	Onset Year
ABDOMINAL PAIN	20[redacted]
ACID REFLUX (GERD)	20[redacted]
ASTHMA	20[redacted]
CROHN'S DISEASE	20[redacted]
FIBROMYALGIA	20[redacted]
H. PYLORI INFECTION	20[redacted]
HYPERTENSION	20[redacted]
LEFT SIDED UC	20[redacted]
LORDOSIS	20[redacted]
PERIPHERAL ARTHROPATHY	20[redacted]

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

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 PACK	8	20[redacted]
CIGARS	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		QD	[redacted] / 1	[redacted] / 57	57
M14-675 ABT-494 (OL)	45 mg	QD	[redacted] / 58	[redacted] / 109	52
M14-234 SS3 ABT-494 (MAIN)	15 mg	QD	[redacted] / 110	[redacted] / 381	272
M14-533 ABT-494 (LTE)	15 mg	QD	[redacted] / 381	[redacted] / 483	103

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DIPHENHYDRAMINE	25 OTHER: CAPSULE	BID	Y-M: 20[redacted]
DIPHENHYDRAMINE	25 mg	BID	Y-M: 20[redacted]
PREDNISONE	20 mg	BID	Y-M: 20[redacted]
TRAMADOL	50 mg	BID	Y-M: 20[redacted]
ADALIMUMAB	40 mg	OTHER: Q2W	Y: 20[redacted]
MESALAZINE	1.5 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
DIPHENHYDRAMINE	25 OTHER: CAPSULE	BID	Y-M: 20[redacted]	ONGOING
DIPHENHYDRAMINE	25 mg	BID	Y-M: 20[redacted]	ONGOING
TRAMADOL	50 mg	BID	Y-M: 20[redacted]	ONGOING
LOPERAMIDE;SIMETICONE	125/2 mg	PRN	Y-M: 20[redacted] / 100	ONGOING
DIPHENHYDRAMINE	25 mg	PRN	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 107
MAGNESIUM SULFATE	2 OTHER: GM	OTHER: Q 1 HOUR 50 ML/HR PRN	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 107
ONDANSETRON	4 mg	OTHER: Q 6 HRS PRN	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 105
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 107
POTASSIUM	10 mEq	OTHER: Q 1 HOUR	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 107
POTASSIUM	20 mEq	OTHER: Q 2 HOURS	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 105

ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	491 mg	OTHER: ONCE	Y-M: 20[redacted] / 112	Y-M: 20[redacted] / 112
LIDOCAINE	70 mg	OTHER: ONCE	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
PROPOFOL	250 mg	OTHER: ONCE	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 113
DIPHENHYDRAMINE	25 mg	OTHER: ONCE	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143
MORPHINE	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143
ONDANSETRON	4 mg	OTHER: ONCE	Y-M: 20[redacted] / 143	Y-M: 20[redacted] / 143

Event #1: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day / Rx Day	[redacted]20[redacted] / 480 / 100
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
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	NO
SAE Criteria	NONE

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

Event Description	RHABDOMYOLYSIS
Preferred term	横紋筋融解症
AE Onset Date / Initial Rx Day / Rx	[redacted]JU[redacted]020 / 480 / 100
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 105): Creatine Kinase: 3698 [29 - 169] U/L; NPTST103-ESTIMATED GFR: 91 [60 - 90] ML/MIN; Occult Blood: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 106): Creatine Kinase: 2035 [29 - 169] U/L; Creatine Kinase: 2661 [29 - 169] U/L; [redacted]20[redacted] (RX DAY 107): Creatine Kinase: 948 [29 - 169] U/L; Creatine Kinase: 709 [29 - 169] U/L; NPTST103-ESTIMATED GFR: 95 [60 - 90] ML/MIN

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 105): CHEST RADIOGRAPH: NO RADIOGRAPHIC EVIDENCE OF ACUTE CARDIOPULMONARY PATHOLOGY.

AE Stopped Initial Rx Day / Rx Day	493 / 113 (10 DAYS AFTER LAST TREATMENT)
Duration of AE	14 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	ACUTE RHABDOMYOLYSIS NONTRAUMATIC
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]: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，横紋筋融解症の事象を発現した。関連する病歴は，喘息，元喫煙者（1 日 20 箱を 8 年間），腹痛，胃酸逆流，クローン病，線維筋痛，高血圧，末梢性関節障害，潰瘍性大腸炎及び現飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与480日後＊，被験者は横紋筋融解症を発現した。投与493日後＊，横紋筋融解症は消失した。

治験責任医師によると，被験者は投与の約6ヵ月後＊にCK上昇（非重篤）を発現し，その際に治験薬の投与は中断されなかった。

投与485日後＊　，被験者はCK上昇のため医療機関を受診するよう医師に指示された。同日，腹痛，下痢，背部痛及び直腸出血で入院した。身体検査では，覚醒，意識清明及び見当識ありで，心音（S1及びS2）は正常洞調律で，聴診では心雑音はなかった。被験者は，胸部X線検査を受け，心肺の急性病理学的所見は認められなかった。投与486日後＊　，被験者はCPK上昇のため受診した。気分は良好であり，閉塞性の排尿症状はなく，血尿，排尿障害又は排尿困難もなかった。また，胸部痛，息切れ，悪心又は嘔吐もなかった。被験者は，下痢と便秘を断続的に発現していた。直近に転倒はなく，直近の外傷の報告はなかった。投与487日後＊　，被験者は，硫酸マグネシウム及び塩化カリウムを処方され，退院した。

本事象により治験薬の投与は完全に中止された。

投与された薬剤は，硫酸マグネシウム，アセトアミノフェン及び塩化カリウムであった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Open Label)

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1)　Rhabdomyolysis (10039020)　(Rhabdomyolysis (10039020))　[v.23.1]　[10039020]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of RHABDOMYOLYSIS

- Investigator: Acute rhabdomyolysis nontraumatic

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** NO RADIOGRAPHIC EVIDENCE OF ACUTE CARDIOPULMONARY PATHOLOGY.

[redacted] **20[redacted] CK:** 93 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 142 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 1733 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 73 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 69 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 75 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 1515 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 3698 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 2661 U/L (normal 26 to 192)

[redacted] **20[redacted] CK:** 116 U/L (normal 26 to 192)

[redacted] **20[redacted] HCT:** 33.9 %

[redacted] **20[redacted] HCT:** 32.3 %

[redacted] **20[redacted] HGB:** 11.1 G/DL

[redacted] **20[redacted] HGB:** 10.3 G/DL

[redacted] **20[redacted] HGB:** 10.1 G/DL

[redacted] **20[redacted] PLATELETS:** 422 No units

NON SERIOUS EVENTS and **OTHER AREAS OF SAFETY INTEREST

Anaemia: Intermittent. Rectal bleed reported on [redacted]20[redacted].

M14-234 試験 Substudy 3（最終報告書）

治験の標題： 中等症から重症の活動性潰瘍性大腸炎患者を対象としたウパダシチニブ（ABT-494）の導入療法及び維持療法における安全性及び有効性を評価する多施設共同無作為化二重盲検プラセボ対照試験	
施設数 / 実施国名： 299 施設（アルゼンチン，オーストラリア，オーストリア，ベルギー，ボスニア・ヘルツェゴビナ，ブラジル，カナダ，チリ，中国，コロンビア，クロアチア，チェコ共和国，エストニア，フィンランド，フランス，ドイツ，ギリシャ，ハンガリー，アイルランド，イスラエル，イタリア，日本，韓国，ラトビア，リトアニア，マレーシア，メキシコ，オランダ，ノルウェー，ポーランド，ポルトガル，ロシア，セルビア，シンガポール，スロバキア，南アフリカ，スペイン，スイス，台湾，トルコ，ウクライナ，イギリス及び米国［プエルトリコを含む］）	
治験調整医師： [redacted], MD	
公表文献（参考資料）： 1 報（概要）	
治験期間： 最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日	開発のフェーズ： 第 III 相
目的： M14-234 試験 Substudy（以下「SS」）1，M14-234 試験 SS 2 又は M14-675 試験でのウパダシチニブの導入療法により臨床的改善（Adapted Mayo スコアによる）を達成した中等症から重症の活動性潰瘍性大腸炎（以下「UC」）患者を対象として，寛解維持（Adapted Mayo スコアによる）におけるウパダシチニブ 15 mg 及び 30 mg 投与の有効性及び安全性をプラセボと比較して評価することを主要目的とした。 本報告書では，M14-234 試験 SS 3（第 III 相維持療法試験）での維持療法におけるウパダシチニブの安全性を要約した。治験実施計画書に規定したとおり，52 週間の有効性データの最終解析は，本申請のために 20[redacted] 年 [redacted] 月に行ったデータベースロック及び非盲検解析で実施しており，その結果は中間報告書（5.3.5.1-3 項）に示した。	
被験者数（計画時と登録時）： 計画時：約 750 例，登録時：1046 例	
診断と主要な組入れ基準： M14-234 試験 SS 1，M14-234 試験 SS 2 又は M14-675 試験での 8 週間の導入療法期又は延長治療期の終了後に Adapted Mayo スコアによる臨床的改善を達成した被験者を適格とした。新型コロナウイルス感染症（以下「COVID-19」）パンデミックの期間，投与 8 週時及び/又は 16 週時の内視鏡検査が欠測している被験者は，M14-234 試験 SS 3 への組入れに不適格とした。M14-675 試験を完了した被験者は，M14-234 試験 SS 3 に参加する前に M14-234 試験の同意が必要とした。 M14-234 試験 SS 1，M14-234 試験 SS 2 又は M14-675 試験では，以下の被験者を適格とした：年齢が 16 歳以上 75 歳以下（M14-234 試験 SS 1 組入れ時は 18 歳以上 75 歳以下）の男女で，経口アミノサリチル酸製剤（M14-234 試験 SS 2 及び M14-675 試験のみ），副腎皮質ステロイド，免疫調節薬及び/又は生物学的製剤のいずれかひとつ以上に対して効果不十分，効果減弱又は不耐容であった被験者。ベースラインの 90 日以上前に UC と診断され，スクリーニング期間中に全大腸内視鏡検査で診断が確認されると共に，現在の特定のタイプの感染症，上皮異形成及び/又は悪性腫瘍が除外された被験者。Adapted Mayo スコアが 5–9，かつ内視鏡サブスコアが 2–3（中央判定による評価）の中等症から重症の活動性 UC を有する被験者。	
治験方法： M14-234 試験 SS 3 は，M14-234 試験 SS 1，M14-234 試験 SS 2 又は M14-675 試験での導入療法により臨床的改善	

（Adapted Mayo スコアによる）を達成した中等症から重症の活動性 UC 患者を対象として，寛解維持（Adapted Mayo スコアによる）におけるウパダシチニブ 15 mg 及び 30 mg 1 日 1 回投与の有効性及び安全性をプラセボと比較して評価した第 III 相維持療法試験であった。なお，M14-675 試験は中等症から重症の活動性 UC 患者を対象とした導入療法試験であった。

M14-234 試験 SS 1，M14-234 試験 SS 2 又は M14-675 試験での 8 週間の導入療法期又は延長治療期の終了後に Adapted Mayo スコアによる臨床的改善を達成した被験者 1046 例を M14-234 試験 SS 3 に組み入れ，1044 例に盲検下での投与割付けに従い最長 52 週間まで治験薬を投与した。被験者が M14-675 試験から M14-234 試験 SS 3 に移行するために必要な適格性の確認は，M14-234 試験 SS 3 に同意していること，M14-675 試験の投与 8 週時又は 16 週時に臨床的改善を達成していること，いずれの中止基準にも抵触していないことのみであった。この移行の時点で M14-234 試験の治験実施計画書に記載された選択基準及び除外基準を満たす必要はないこととした。適格被験者は，M14-234 試験 SS 3 のベースライン来院を導入療法期の最終来院（投与 8 週時又は 16 週時のいずれか）と同日に実施した。M14-234 試験 SS 3 への再割付けには，投与 8 週時（M14-234 試験 SS 1，M14-234 試験 SS 2 Part 1 又は M14-675 試験 Part 1）又は投与 16 週時（M14-234 試験 SS 2 Part 2 又は M14-675 試験 Part 2）の実施医療機関判定による内視鏡サブスコアをベースラインでの中央判定による内視鏡サブスコアと比較し，M14-234 試験 SS 3 への組入れのための臨床的改善を判定した。ウパダシチニブ及びプラセボのすべての用量は，1 日 1 回投与とした。

M14-234 試験 SS 3 には以下の 4 つのコホートが含まれた。

Cohort 1：

M14-234 試験 SS 1，M14-234 試験 SS 2 又は M14-675 試験で以下のいずれかを投与し，臨床的改善を達成した被験者 847 例を 1：1：1 の比率で Cohort 1 の投与群のいずれかに再ランダム化した。

- M14-234 試験 SS 1 でのウパダシチニブ 30 mg 又は 45 mg 1 日 1 回投与
- M14-234 試験 SS 2 Part 1 でのウパダシチニブ 45 mg 1 日 1 回投与
- M14-675 試験 Part 1 でのウパダシチニブ 45 mg 1 日 1 回投与
- M14-234 試験 SS 2 Part 1 でプラセボを 1 日 1 回投与後，Part 2 でウパダシチニブ 45 mg を 1 日 1 回投与
- M14-675 試験 Part 1 でプラセボを 1 日 1 回投与後，Part 2 でウパダシチニブ 45 mg を 1 日 1 回投与

Cohort 1 の投与群

- Group 1：ウパダシチニブ 15 mg 1 日 1 回
- Group 2：ウパダシチニブ 30 mg 1 日 1 回
- Group 3：プラセボ 1 日 1 回

M14-234 試験 SS 1 でウパダシチニブ 15 mg を 1 日 1 回投与し，臨床的改善を達成した場合は，ウパダシチニブ 15 mg 1 日 1 回（Group 1）又はプラセボ 1 日 1 回（Group 3）のいずれかのみに 1：1 の比率で再ランダム化した。

Cohort 2：

M14-234 試験 SS 1，M14-234 試験 SS 2 Part 1 又は M14-675 試験 Part 1 で，二重盲検下でプラセボを 8 週間 1 日 1 回投与し，臨床的改善を達成した被験者 104 例は，Cohort 2 でも引き続き盲検下でプラセボを 1 日 1 回投与した。

Cohort 3：

導入療法期でウパダシチニブ 45 mg を 1 日 1 回投与し，臨床的改善を達成しなかった被験者のうち，M14-234 試験 SS 2 Part 2 又は M14-675 試験 Part 2 の延長治療期にウパダシチニブ 45 mg を 1 日 1 回投与し，投与 16 週時に臨床的改善を達成した被験者 75 例を 1：1 の比率で再ランダム化し，Cohort 3 で盲検下にてウパダシチニブ

15 mg 又は 30 mg を 1 日 1 回投与した。

Cohort 4：

M14-234 試験 SS 1 で，二重盲検下でウパダシチニブ 7.5 mg を 8 週間 1 日 1 回投与し，臨床的改善を達成した被験者 20 例は，Cohort 4 でも引き続き盲検下でウパダシチニブ 7.5 mg を 1 日 1 回投与した。

UC に関連する併用薬（経口副腎皮質ステロイド，抗菌薬，アミノサリチル酸製剤及び/又はメトトレキサート［以下「MTX」］）：

M14-234 試験 SS 3 のベースライン時（M14-234 試験 SS 1，M14-234 試験 SS 2 及び M14-675 試験の投与 8 週時又は 16 週時）に副腎皮質ステロイドを投与中の被験者は，推奨される漸減スケジュールに従って副腎皮質ステロイドの漸減を開始することとした。UC に関連する抗菌薬を投与中の被験者は，治験責任医師の判断で M14-234 試験 SS 3 の投与 0 週時から投与を中止できることとした。投与 0 週時に UC に関連する抗菌薬（中止しなかった場合），アミノサリチル酸製剤又は MTX を一定の用量で投与中の被験者は，本試験の終了時まで同用量で投与を継続することとした。これらの併用薬に関連する中等度から高度の毒性（白血球減少症又は肝酵素上昇など）が認められた場合は，治験責任医師の判断により併用薬を減量又は投与中止できることとした。

レスキュー治療：

M14-234 試験 SS 3 の投与 4 週時又はそれ以降に効果減弱が認められ，治療を要するものの，M14-533 試験の Cohort 1 への移行基準を満たさない被験者には，治験実施計画書の規定に従い，レスキュー治療を実施できることとした。

被験薬，用量，投与方法及びロット番号：

被験薬	用量	投与方法	バルクロット番号
ウパダシチニブ	7.5 mg	経口	[redacted]
ウパダシチニブ	15 mg	経口	[redacted]
ウパダシチニブ	30 mg	経口	[redacted]

治療期間：

最長 52 週間

対照薬，用量，投与方法及びロット番号：

ウパダシチニブに対応するプラセボの経口フィルムコート錠 バルクロット番号：[redacted]

評価基準：

有効性：

M14-234 試験 SS 3 の有効性データの最終解析結果は，中間報告書（5.3.5.1-3 項）に示した。治験実施計画書の規定に従い，最終報告書では有効性の解析は更新しなかった。

薬物動態：

ウパダシチニブの血漿中濃度の平均値（標準偏差）を，用量及び前回投与からの時間ごとに要約した。

安全性： 有害事象，バイタルサイン，身体検査，臨床検査値（血液学的検査，血液生化学検査及び尿検査）及び治験薬に係る苦情を評価した。
統計手法： 薬物動態： 各来院時での被験者別のウパダシチニブの血漿中濃度を一覧表にし，適切な統計手法を用いて要約した。 安全性： 安全性解析対象集団（治験薬を投与した全被験者，以下「SA 集団」）のうち，ウパダシチニブ 45 mg 1 日 1 回 8 週間投与の導入療法で臨床的改善を達成し，維持療法期を 44 週間又は 52 週間とした治験実施計画書に基づき Cohort 1 に組み入れた被験者を SAC 集団と定義し，安全性は主に SAC 集団を対象として解析した。また，その他の SA 集団での安全性の要約も示した。 標準的な安全性解析として，有害事象，特に注目すべき有害事象，臨床検査値及びバイタルサインを評価した。有害事象については，投与群ごとの発現割合及び 100 人年あたりの発現件数を ICH 国際医薬用語集（MedDRA）version 23.0 の器官別大分類（SOC）別及び基本語（PT）別に示した。安全性評価項目の連続変数（各来院時の臨床検査値及びバイタルサイン）は，投与群ごとに要約した。臨床的な意義があると判断した臨床検査値異常及びバイタルサインが認められた被験者の割合は，投与群ごとに示した。

薬物動態の結果

ウパダシチニブの血漿中濃度の平均値は，投与後 24 時間以内では，ウパダシチニブ 7.5 mg 1 日 1 回群（7.5 mg 群）で 1.23–5.38 ng/mL，ウパダシチニブ 15 mg 1 日 1 回群（以下「15 mg 群」）で 4.72–30.0 ng/mL，ウパダシチニブ 30 mg 1 日 1 回群（以下「30 mg 群」）で 12.2–81.1 ng/mL の範囲であった。ウパダシチニブの血漿中濃度は，中間報告書及び過去に実施したウパダシチニブの第 III 相試験で認められた薬物動態と一致していた。

安全性の結果

本試験では，いずれの SA 集団でも死亡は認められなかった。SAC 集団では，有害事象の 100 人年あたりの発現件数について，すべての有害事象（15 mg 群 313.9 件/100 人年，30 mg 群 316.2 件/100 人年，以下同順），高度の有害事象（9.0 件/100 人年，10.5 件/100 人年）及び重篤な有害事象（12.0 件/100 人年，10.1 件/100 人年）で，15 mg 群と 30 mg 群でおおむね同程度であった。治験薬と関連ありの有害事象及び治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，15 mg 群（それぞれ 89.3 件/100 人年及び 5.5 件/100 人年）と比較して 30 mg 群（106.6 件/100 人年及び 8.7 件/100 人年）の方が多かった。いずれのカテゴリーの有害事象（すべての有害事象，高度の有害事象，重篤な有害事象，治験薬と関連ありの有害事象及び治験薬の投与中止に至った有害事象）の 100 人年あたりの発現件数も，プラセボ群と比較して両ウパダシチニブ群の方が少なかった。SAB 集団（SA 集団のうち，ウパダシチニブ 45 mg 1 日 1 回 16 週間投与の導入療法で臨床的改善を達成し，Cohort 3 に組み入れた被験者）では，被験者数は少なく，被験者の治験薬への曝露は限定的であった。SAB 集団では，いずれのカテゴリーの有害事象の 100 人年あたりの発現件数も，15 mg 群と比較して 30 mg 群の方が多かった。

SAC 集団では，全投与群で 100 人年あたりの発現件数が 10 件/100 人年以上であった有害事象は，上咽頭炎（15 mg 群 16.0 件/100 人年，30 mg 群 17.4 件/100 人年，プラセボ群 15.6 件/100 人年，以下同順）であった。その他，いずれかの投与群で 100 人年あたりの発現件数が 10 件/100 人年以上であった有害事象は，15 mg 群では潰瘍性大腸炎，30 mg 群では血中クレアチンホスホキナーゼ増加，プラセボ群では潰瘍性大腸炎及び関節痛であった。血中クレアチンホスホキナーゼ増加は，プラセボ群と比較してウパダシチニブ群で用量依存的に多く認められた（15 mg 群 8.0 件/100 人年，30 mg 群 10.1 件/100 人年，プラセボ群 3.7 件/100 人年）。いずれかの投与群で 100 人年あたりの発現件数が 5 件/100 人年以上であった有害事象のうち，帯状疱疹はウパダシチニブ群のみで認められ，100 人年あたりの発現件数は 30 mg 群で最も多かった（15 mg 群 5.5 件/100 人年，30 mg 群 6.9 件/100 人年）。発現割合（有害事象を発現した被験者の割合）においても，SAC 集団で多く認められた有害事象は同様であった。SAB 集団では，SAC 集団と同様に，多く認められた有害事象は，100 人年あたりの発現件数と発現割合で同様であった。潰瘍性大腸炎，血中クレアチンホスホキナーゼ増加及び上咽頭炎は，SAC 集団と同様に多く認められた。その他，ウパダシチニブ群で多く認められた有害事象は，頭痛，背部痛及び高血圧であった。頭痛は 30 mg 群でのみ認められた（17.9 件/100 人年）。背部痛の 100 人年あたりの発現件数は，30 mg 群（6.0 件/100 人年）と比較して 15 mg 群（12.4 件/100 人年）の方が多く，一方で，高血圧の 100 人年あたりの発現件数は，15 mg 群（8.3 件/100 人年）と 30 mg 群（9.0 件/100 人年）で同程度であった。

SAC 集団では，いずれかの投与群で 2 例以上に認められた重篤な有害事象は，15 mg 群で人工流産及び肺塞栓症，30 mg 群で潰瘍性大腸炎，子宮頚部上皮異形成，COVID-19 肺炎及びクリプトコッカス性肺炎，プラセボ群で潰瘍性大腸炎及び肺炎であった。SAB 集団では，重篤な有害事象は，15 mg 群で 1 例（2.9%，4.1 件/100 人年），30 mg 群で 4 例（10.0%，20.9 件/100 人年）に認められた。

SAC 集団では，いずれかの投与群で 2 例以上に認められた治験薬の投与中止に至った有害事象は，潰瘍性大腸炎（15 mg 群 5 例［2.0%］，30 mg 群 3 例［1.2%］，プラセボ群 13 例［5.3%］，以下同順）並びに帯状疱疹及びクリプトコッカス性肺炎（各 0 例，2 例［0.8%］，0 例）であった。SAB 集団では，治験薬の投与中止に至った有害事象として，潰瘍性大腸炎が 15 mg 群及び 30 mg 群で各 1 例，肺炎が 30 mg 群で 1 例に認められた。

特に注目すべき有害事象のうち，活動性結核及びリンパ腫は維持療法期に認められなかった。SAC 集団では，100 人年あたりの発現件数がプラセボ群と比較して 15 mg 群及び 30 mg 群の方が多かった特に注目すべき有害事象は，帯状疱疹（15 mg 群 6.0 件/100 人年，30 mg 群 7.3 件/100 人年，プラセボ群 0 件/100 人年，以下同順），クレアチンホスホキナーゼ増加（8.0 件/100 人年，10.1 件/100 人年，3.7 件/100 人年）及び薬剤に関連する肝障害（17.0 件/100 人年，9.2 件/100 人年，5.9 件/100 人年）であった。100 人年あたりの発現件数が 15 mg 群及びプラセボ群と比較して 30 mg 群の方が多かった特に注目すべき有害事象は，好中球減少症（5.5 件/100 人年，8.7 件/100 人年，5.2 件/100 人年）であった。貧血の 100 人年あたりの発現件数は，15 mg 群及び 30 mg 群と比較してプラセボ群の方が多く（15 mg 群 6.0 件/100 人年，30 mg 群 4.6 件/100 人年，プラセ

ボ群 14.1 件/100 人年，以下同順），重篤な感染症の 100 人年あたりの発現件数は，30 mg 群と比較してプラセボ群の方が多かった（5.0 件/100 人年，3.2 件/100 人年，5.9 件/100 人年）。悪性腫瘍，主要心血管事象及び静脈血栓塞栓症，日和見感染（結核及び帯状疱疹を除く）並びに腎機能障害は，発現件数が少なかったため投与群間の適切な比較はできなかった。消化管穿孔は，プラセボ群のみで認められた。SAB 集団で 2 例又は 3 例に認められた特に注目すべき有害事象は，15 mg 群ではクレアチンホスホキナーゼ増加及び貧血，30 mg 群では重篤な感染症，帯状疱疹，好中球減少症，クレアチンホスホキナーゼ増加，薬剤に関連する肝障害及び貧血であった。SAB 集団では，特に注目すべき有害事象の 100 人年あたりの発現件数は，いずれも 15 mg 群と比較して 30 mg 群の方が多かった。

SAC 集団では，ヘモグロビン量，リンパ球数及び血小板数の投与 52 週時の維持療法期ベースライン（投与 0 週時）からの平均変化量（最小二乗平均）は小さく，投与群間で顕著な差は認められなかった。好中球数の投与 0 週時からの平均変化量について，投与 4 週時，8 週時，12 週時，20 週時及び 28 週時にプラセボ群ではわずかな増加が認められたのに対し，ウパダシチニブ群では減少が認められた。アラニンアミノトランスフェラーゼ（以下「ALT」）及びアスパラギン酸アミノトランスフェラーゼ（以下「AST」）の投与 0 週時からの平均変化量は，ウパダシチニブ群で経時的に変動していた。AST の投与 52 週時の投与 0 週時からの平均変化量は，プラセボ群で–2.6 U/L であったのに対し，15 mg 群で 2.2 U/L，30 mg 群で 2.5 U/L であった。クレアチニンの投与 52 週時の投与 0 週時からの平均変化量は，プラセボ群で–3.6 µmol/L であったのに対し，15 mg 群で 1.5 µmol/L，30 mg 群で 1.4 µmol/L であった。コレステロールの投与 52 週時の投与 0 週時からの平均変化量は，15 mg 群で–0.056 mmol/L，プラセボ群で–0.958 mmol/L であったのに対し，30 mg 群で 0.108 mmol/L であった。クレアチンキナーゼの投与 52 週時の投与 0 週時からの平均変化量は，15 mg 群で–31.403 U/L，30 mg 群で–62.687 U/L であり，プラセボ群で–81.147 U/L であった。SAC 集団では，尿検査の平均変化量の顕著な変化は，認められなかった。

SAC 集団では，Grade 3 の好中球数減少が認められた被験者の割合は，15 mg 群で 0.8%，30 mg 群で 2.4%，プラセボ群で 0.8%であり，Grade 4 の好中球数減少は認められなかった。その他の血液学的検査パラメータについて，Grade 3 又は Grade 4 の減少が認められた被験者の割合は，いずれの投与群でも 2%未満であった。SAB 集団では，Grade 3 の白血球数減少が 15 mg 群の 1 例に，Grade 3 のリンパ球数減少が 15 mg 群及び 30 mg 群の各 1 例に認められた。SAC 集団では，Grade 3 のクレアチンキナーゼ増加が認められた被験者の割合は，15 mg 群で 2.8%，30 mg 群で 5.2%，プラセボ群で 0.8%であった。SAC 集団では，いずれかの投与群で 2%以上に認められた肝機能検査値の上昇は，ALT が基準値上限（以下「ULN」）の 3 倍以上，AST が ULN の 3 倍以上，総ビリルビンが ULN の 2 倍以上及びアルカリホスファターゼが ULN の 1.5 倍以上であった。

結論

中間報告書で報告したとおり，ウパダシチニブ 15 mg 及び 30 mg の 1 日 1 回投与は，従来の治療又は生物学的製剤に対して効果不十分，効果減弱又は不耐容であった中等症から重症の活動

性UC患者において，52週間までの維持療法としてプラセボと比較して有効であることが示された。

維持用量としてのウパダシチニブ15 mg及び30 mgの1日1回投与は，おおむね安全で忍容性は良好であった。安全性プロファイルは，中間報告書で報告したものと同様であった。ウパダシチニブの既知の安全性プロファイルと比較して，新たな安全性リスクは認められなかった。

本試験の結果は，中等症から重症の活動性UC患者を対象とした維持療法として，ウパダシチニブ15 mg及び30 mg 1日1回投与を裏付けるものであった。

<u>日本人部分集団の有害事象</u>

日本人部分集団について，SAC集団の有害事象の発現状況を以下に示す。

有害事象の100人年あたりの発現件数は，15 mg群で285.8件/100人年，30 mg群で359.7件/100人年，プラセボ群で525.5件/100人年であり，発現割合は15 mg群で75.6%（34/45例），30 mg群で91.1%（41/45例），プラセボ群で85.4%（35/41例）であった。100人年あたりの発現件数が20件/100人年以上であった有害事象は，15 mg群で上咽頭炎，30 mg群で上咽頭炎，プラセボ群で潰瘍性大腸炎及び上咽頭炎であった。

治験薬と関連ありの有害事象の100人年あたりの発現件数は，15 mg群で75.1件/100人年，30 mg群で129.0件/100人年，プラセボ群で120.6件/100人年であり，発現割合は15 mg群で35.6%（16例），30 mg群で48.9%（22例），プラセボ群で31.7%（13例）であった。発現割合が5%以上であった治験薬と関連ありの有害事象は，15 mg群で帯状疱疹及び上咽頭炎，30 mg群で帯状疱疹，血中クレアチンホスホキナーゼ増加，好中球数減少，アラニンアミノトランスフェラーゼ増加及び好中球減少症，プラセボ群で潰瘍性大腸炎であった。

高度の有害事象の100人年あたりの発現件数は，15 mg群で7.3件/100人年，30 mg群で7.4件/100人年，プラセボ群で25.8件/100人年であり，発現割合は15 mg群で4.4%（2例），30 mg群で6.7%（3例），プラセボ群で14.6%（6例）であった。いずれの投与群でも2例以上に認められた高度の有害事象はなかった。

死亡に至った有害事象は認められなかった。

重篤な有害事象の100人年あたりの発現件数は，15 mg群で12.1件/100人年，30 mg群で7.4件/100人年，プラセボ群で21.5件/100人年であり，発現割合は15 mg群で6.7%（3例），30 mg群で6.7%（3例），プラセボ群で12.2%（5例）であった。15 mg群及び30 mg群で2例以上に認められた重篤な有害事象はなかった。プラセボ群で2例以上に認められた重篤な有害事象は，潰瘍性大腸炎であった。

治験薬の投与中止に至った有害事象の100人年あたりの発現件数は，15 mg群で4.8件/100人年，30 mg群で14.9件/100人年，プラセボ群で17.2件/100人年であり，発現割合は15 mg群で2.2%（1例），30 mg群で11.1%（5例），プラセボ群で9.8%（4例）であった。15 mg群で治験薬の投与中止に至った有害事象が認められたのは1例のみであり，30 mg群で2例以上に認められた治験薬の投与中止に至った有害事象は，帯状疱疹であった。プラセボ群で2例以上に認められた治験薬の投与中止に至った有害事象は，潰瘍性大腸炎であった。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団	日本人部分集団
有害事象の概要（発現割合）	表 1 (TABLE 14.3__1.1.1.3)	表 10 (TABLE 14.3__1.1.1.3_J)
有害事象の概要 （100 人年あたりの発現件数）	表 2 (TABLE 14.3__1.1.2.3)	表 11 (TABLE 14.3__1.1.2.3_J)
すべての有害事象（発現割合）	表 3 (TABLE 14.3__1.2.1.1.3)	表 12 (TABLE 14.3__1.2.1.1.3_J)
すべての有害事象 （100 人年あたりの発現件数）	表 4 (TABLE 14.3__1.2.1.2.3)	表 13 (TABLE 14.3__1.2.1.2.3_J)
治験薬と関連ありの有害事象（発現割合）	表 5 (TABLE 14.3__1.3.1.1.3)	表 14 (TABLE 14.3__1.3.1.1.3_J)
高度の有害事象（発現割合）	表 6 (TABLE 14.3__1.3.3.3)	表 15 (TABLE 14.3__1.3.3.3_J)
死亡に至った有害事象（発現割合）	表 7 (TABLE 14.3__2.3.1.3)	表 16 (TABLE 14.3__2.3.1.3_J)
重篤な有害事象（発現割合）	表 8 (TABLE 14.3__2.1.1.3)	表 17 (TABLE 14.3__2.1.1.3_J)
治験薬の投与中止に至った有害事象 （発現割合）	表 9 (TABLE 14.3__2.2.1.3)	表 18 (TABLE 14.3__2.2.1.3_J)

表1

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__1.1.1.3

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA_C Population)

	Placebo (N=245) n (%) [SSA%]	UPA 15 mg QD (N=250) n (%) [SSA%]	UPA 30 mg QD (N=251) n (%) [SSA%]	- Treatment Comparison (95% CI) [A] - UPA 15 mg QD - Placebo	UPA 30 mg QD - Placebo
Subjects with:					
Any adverse event (AE)	186 (75.9) [75.5]	193 (77.2) [77.2]	198 (78.9) [78.9]	1.7 (-5.7, 9.1)	3.4 (-3.9, 10.7)
Any AE with reasonable possibility of being related to study drug$	84 (34.3) [33.8]	87 (34.8) [34.9]	96 (38.2) [38.3]	1.1 (-7.1, 9.4)	4.5 (-3.7, 12.7)
Any severe AE	23 (9.4) [9.3]	14 (5.6) [5.6]	20 (8.0) [8.0]	-3.7 (-8.4, 0.9)	-1.3 (-6.3, 3.7)
Any serious AE	23 (9.4) [9.3]	21 (8.4) [8.3]	21 (8.4) [8.4]	-1.0 (-6.0, 4.1)	-0.9 (-6.0, 4.1)
Any AE leading to discontinuation of study drug	25 (10.2) [10.1]	10 (4.0) [4.0]	18 (7.2) [7.2]	-6.2 (-10.7, -1.6)	-3.0 (-8.0, 2.0)
Any AE leading to death	0	0	0	0.0	0.0
Deaths#	0	0	0	0.0	0.0
Occurring <= 30 days after last dose	0	0	0	0.0	0.0
Occurring > 30 days after last dose	0	0	0	0.0	0.0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.

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表2

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__1.1.2.3

Overview of Treatment-Emergent Adverse Events and All Deaths per 100 Patient-Years (PYS)
(SA_C Population)

	Placebo (N=245) (PYS=135.0) Events (E/100PY) [SSA E/100PY]	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY) [SSA E/100PY]	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY) [SSA E/100PY]	-- Treatment Comparison (95% CI) [A] -- UPA 15 mg QD - Placebo	UPA 30 mg QD - Placebo
Any treatment-emergent:					
Any adverse event (AE)	674 (499.4) [494.1]	626 (313.9) [314.1]	691 (316.2) [315.6]	-180.1 (-224.9, -135.2)	-178.5 (-222.8, -134.2)
Any AE with reasonable possibility of being related to study drug$	192 (142.3) [137.5]	178 (89.3) [91.1]	233 (106.6) [106.6]	-46.5 (-70.2, -22.8)	-31.0 (-54.8, -7.1)
Any severe AE	29 (21.5) [21.3]	18 (9.0) [8.9]	23 (10.5) [10.5]	-12.5 (-21.3, -3.7)	-10.8 (-19.8, -1.9)
Any serious AE	28 (20.7) [20.8]	24 (12.0) [12.0]	22 (10.1) [10.0]	-8.8 (-17.9, 0.4)	-10.8 (-19.6, -2.0)
Any AE leading to discontinuation of study drug	26 (19.3) [19.1]	11 (5.5) [5.5]	19 (8.7) [8.7]	-13.6 (-21.7, -5.6)	-10.4 (-18.7, -2.0)
Any AE leading to death	0	0	0	0.0	0.0
Deaths#	0	0	0	0.0	0.0
Occurring <= 30 days after last dose	0	0	0	0.0	0.0
Occurring > 30 days after last dose	0	0	0	0.0	0.0

Note: PYS is defined as the sum of the study drug exposure of all subjects, normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.

Program Source Code: [redacted]

表3

TABLE 14.3__1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
Any adverse event	186 (75.9)	193 (77.2)	198 (78.9)
血液およびリンパ系障害	23 (9.4)	16 (6.4)	16 (6.4)
貧血	10 (4.1)	9 (3.6)	7 (2.8)
好酸球増加症	1 (0.4)	0	0
内出血発生の増加傾向	0	0	1 (0.4)
鉄欠乏性貧血	5 (2.0)	0	0
白血球増加症	1 (0.4)	0	0
白血球減少症	3 (1.2)	5 (2.0)	1 (0.4)
リンパ節症	0	0	1 (0.4)
リンパ球増加症	1 (0.4)	0	0
リンパ球減少症	2 (0.8)	2 (0.8)	1 (0.4)
小球性貧血	0	0	1 (0.4)
好中球減少症	3 (1.2)	3 (1.2)	6 (2.4)
脾腫	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
血液およびリンパ系障害 (Cont.)			
血小板減少症	1 (0.4)	0	0
血小板増加症	0	0	1 (0.4)
心臓障害	5 (2.0)	4 (1.6)	8 (3.2)
急性心筋梗塞	1 (0.4)	0	0
不整脈	0	1 (0.4)	0
心房細動	1 (0.4)	0	0
二束ブロック	0	0	1 (0.4)
心不全	0	0	1 (0.4)
うっ血性心不全	1 (0.4)	1 (0.4)	0
慢性左室不全	0	0	1 (0.4)
動悸	2 (0.8)	1 (0.4)	0
心膜炎	0	0	1 (0.4)
洞性徐脈	0	1 (0.4)	1 (0.4)
上室性頻脈	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
心臓障害 (Cont.)			
頻脈	1 (0.4)	0	0
心室性期外収縮	0	0	1 (0.4)
ウォルフ・パーキンソン・ホワイト症候群	0	0	1 (0.4)
先天性、家族性および遺伝性障害	0	1 (0.4)	2 (0.8)
皮様嚢腫	0	0	1 (0.4)
胃腸管動静脈奇形	0	0	1 (0.4)
ジルベール症候群	0	1 (0.4)	0
耳および迷路障害	3 (1.2)	4 (1.6)	1 (0.4)
感音性難聴	0	1 (0.4)	0
片耳難聴	0	0	1 (0.4)
耳痛	0	1 (0.4)	0
耳部腫脹	1 (0.4)	0	0
外耳道の外骨腫	1 (0.4)	0	0
中耳滲出液	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
耳および迷路障害 (Cont.)			
回転性めまい	0	2 (0.8)	0
内分泌障害	1 (0.4)	1 (0.4)	0
クッシング症候群	1 (0.4)	0	0
甲状腺腫	0	1 (0.4)	0
眼障害	12 (4.9)	7 (2.8)	9 (3.6)
眼瞼炎	1 (0.4)	0	2 (0.8)
白内障	1 (0.4)	2 (0.8)	2 (0.8)
霰粒腫	0	0	3 (1.2)
結膜充血	1 (0.4)	0	0
アレルギー性結膜炎	1 (0.4)	1 (0.4)	1 (0.4)
角膜混濁	1 (0.4)	0	0
ドライアイ	0	1 (0.4)	1 (0.4)
上強膜炎	1 (0.4)	0	0
眼刺激	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
眼障害 (Cont.)			
眼そう痒症	0	1 (0.4)	0
眼部腫脹	0	1 (0.4)	0
眼瞼障害	1 (0.4)	0	0
眼瞼発疹	1 (0.4)	0	0
角膜炎	1 (0.4)	0	1 (0.4)
流涙増加	0	1 (0.4)	0
眼充血	0	1 (0.4)	1 (0.4)
眼窩周囲腫脹	1 (0.4)	0	0
潰瘍性角膜炎	1 (0.4)	0	0
ぶどう膜炎	1 (0.4)	0	0
胃腸障害	110 (44.9)	62 (24.8)	58 (23.1)
腹部膨満	1 (0.4)	2 (0.8)	5 (2.0)
腹部腫瘤	1 (0.4)	0	0
腹痛	6 (2.4)	6 (2.4)	4 (1.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
胃腸障害 (Cont.)			
下腹部痛	3 (1.2)	0	0
上腹部痛	2 (0.8)	3 (1.2)	2 (0.8)
腹部圧痛	0	0	2 (0.8)
異常便	1 (0.4)	0	0
裂肛	1 (0.4)	1 (0.4)	0
痔瘻	0	0	1 (0.4)
肛門の炎症	0	0	1 (0.4)
肛門そう痒症	2 (0.8)	0	0
アフタ性潰瘍	2 (0.8)	1 (0.4)	3 (1.2)
大腸炎	3 (1.2)	2 (0.8)	0
虚血性大腸炎	0	1 (0.4)	0
潰瘍性大腸炎	74 (30.2)	29 (11.6)	19 (7.6)
結腸異形成	0	1 (0.4)	0
便秘	2 (0.8)	3 (1.2)	6 (2.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
胃腸障害 (Cont.)			
便意切迫	0	0	1 (0.4)
齲歯	1 (0.4)	1 (0.4)	0
歯嚢胞	0	0	1 (0.4)
下痢	2 (0.8)	2 (0.8)	2 (0.8)
口内乾燥	0	0	1 (0.4)
消化不良	3 (1.2)	1 (0.4)	1 (0.4)
嚥下障害	1 (0.4)	1 (0.4)	1 (0.4)
小腸炎	0	1 (0.4)	2 (0.8)
変色便	0	0	1 (0.4)
大腿ヘルニア	1 (0.4)	0	0
鼓腸	3 (1.2)	0	2 (0.8)
胃潰瘍	0	1 (0.4)	0
胃炎	0	3 (1.2)	1 (0.4)
胃食道逆流性疾患	3 (1.2)	1 (0.4)	3 (1.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
胃腸障害 (Cont.)			
歯肉腫脹	1 (0.4)	0	0
舌痛	1 (0.4)	0	0
血便排泄	1 (0.4)	0	0
痔出血	2 (0.8)	1 (0.4)	0
痔核	1 (0.4)	2 (0.8)	2 (0.8)
血栓性痔核	1 (0.4)	0	0
単径ヘルニア	0	1 (0.4)	0
腸閉塞	0	1 (0.4)	0
過敏性腸症候群	0	0	1 (0.4)
大腸穿孔	1 (0.4)	0	0
大腸ポリープ	2 (0.8)	0	1 (0.4)
口唇腫脹	0	0	1 (0.4)
口腔嚢胞	1 (0.4)	0	0
口腔内潰瘍形成	2 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
胃腸障害 (Cont.)			
粘液便	1 (0.4)	0	0
悪心	5 (2.0)	4 (1.6)	5 (2.0)
非感染性歯肉炎	0	0	1 (0.4)
嚥下痛	1 (0.4)	0	0
食道炎	0	1 (0.4)	0
口腔障害	0	0	1 (0.4)
膵炎	1 (0.4)	0	0
歯周病	1 (0.4)	0	1 (0.4)
肛門周囲痛	0	1 (0.4)	0
直腸炎	1 (0.4)	0	0
直腸分泌物	0	0	1 (0.4)
直腸出血	1 (0.4)	0	1 (0.4)
直腸攣縮	1 (0.4)	0	0
直腸しぶり	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
胃腸障害 (Cont.)			
口内炎	3 (1.2)	1 (0.4)	2 (0.8)
埋伏歯	0	1 (0.4)	0
歯の脱落	0	0	1 (0.4)
歯痛	0	4 (1.6)	3 (1.2)
臍ヘルニア	1 (0.4)	0	0
嘔吐	1 (0.4)	1 (0.4)	1 (0.4)
一般・全身障害および投与部位の状態	22 (9.0)	16 (6.4)	28 (11.2)
胸部不快感	0	1 (0.4)	0
胸痛	1 (0.4)	2 (0.8)	2 (0.8)
悪寒	2 (0.8)	1 (0.4)	0
医療機器に対する不耐性	1 (0.4)	0	0
薬効欠如	1 (0.4)	0	0
疲労	5 (2.0)	2 (0.8)	4 (1.6)
全身性浮腫	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
高体温症	1 (0.4)	0	0
炎症	0	0	1 (0.4)
インフルエンザ様疾患	1 (0.4)	0	2 (0.8)
注射部位疼痛	0	1 (0.4)	2 (0.8)
倦怠感	1 (0.4)	0	2 (0.8)
腫瘤	0	0	1 (0.4)
粘膜乾燥	1 (0.4)	0	0
小結節	0	0	1 (0.4)
非心臓性胸痛	1 (0.4)	0	0
浮腫	0	1 (0.4)	0
末梢性浮腫	3 (1.2)	1 (0.4)	1 (0.4)
疼痛	1 (0.4)	1 (0.4)	0
末梢腫脹	1 (0.4)	1 (0.4)	1 (0.4)
発熱	7 (2.9)	8 (3.2)	15 (6.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
異物感	1 (0.4)	0	0
腫脹	0	0	1 (0.4)
顔面腫脹	0	0	1 (0.4)
肝胆道系障害	3 (1.2)	6 (2.4)	2 (0.8)
薬物性肝障害	0	1 (0.4)	1 (0.4)
肝機能異常	2 (0.8)	1 (0.4)	0
脂肪肝	0	2 (0.8)	0
高トランスアミナーゼ血症	0	1 (0.4)	0
肝障害	0	0	1 (0.4)
肝損傷	1 (0.4)	1 (0.4)	0
免疫系障害	1 (0.4)	2 (0.8)	1 (0.4)
薬物過敏症	1 (0.4)	0	0
季節性アレルギー	0	2 (0.8)	1 (0.4)
感染症および寄生虫症	92 (37.6)	98 (39.2)	105 (41.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
腹部膿瘍	1 (0.4)	0	0
ダニ皮膚炎	0	2 (0.8)	0
急性心内膜炎	1 (0.4)	0	0
肛門膿瘍	0	1 (0.4)	0
肛門直腸感染	1 (0.4)	0	0
細菌性関節炎	0	1 (0.4)	0
細菌感染	0	0	1 (0.4)
細菌性膣症	1 (0.4)	0	0
乳房膿瘍	0	1 (0.4)	0
気管支炎	3 (1.2)	5 (2.0)	1 (0.4)
感染性滑液包炎	0	0	1 (0.4)
カンピロバクター感染	0	1 (0.4)	0
カンジダ感染	1 (0.4)	0	0
蜂巣炎	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
クロストリジウム・ディフィシレ感染	2 (0.8)	1 (0.4)	2 (0.8)
結膜炎	0	2 (0.8)	1 (0.4)
ＣＯＶＩＤ－１９	8 (3.3)	5 (2.0)	10 (4.0)
ＣＯＶＩＤ－１９肺炎	1 (0.4)	1 (0.4)	2 (0.8)
膀胱炎	0	3 (1.2)	2 (0.8)
サイトメガロウイルス感染	1 (0.4)	1 (0.4)	0
毛嚢虫症	0	3 (1.2)	2 (0.8)
皮膚糸状菌症	1 (0.4)	0	0
憩室炎	0	0	1 (0.4)
耳感染	0	1 (0.4)	2 (0.8)
感染性腸炎	0	0	1 (0.4)
エンテロウイルス感染	0	0	1 (0.4)
大腸菌性尿路感染	0	1 (0.4)	0
毛包炎	4 (1.6)	4 (1.6)	9 (3.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
真菌感染	0	0	1 (0.4)
皮膚真菌感染	0	0	2 (0.8)
せつ	0	1 (0.4)	0
胃腸炎	4 (1.6)	5 (2.0)	3 (1.2)
ウイルス性胃腸炎	0	0	2 (0.8)
歯肉膿瘍	0	0	1 (0.4)
歯肉炎	0	1 (0.4)	0
ヘモフィルス感染	1 (0.4)	0	0
ヘルペス性皮膚炎	0	1 (0.4)	0
単純ヘルペス	0	2 (0.8)	1 (0.4)
帯状疱疹	0	11 (4.4)	14 (5.6)
帯状疱疹性髄膜炎	0	0	1 (0.4)
麦粒腫	3 (1.2)	0	2 (0.8)
膿痂疹	1 (0.4)	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
感染性皮膚嚢腫	0	1 (0.4)	0
インフルエンザ	3 (1.2)	7 (2.8)	8 (3.2)
大腸感染	0	1 (0.4)	0
喉頭炎	1 (0.4)	0	1 (0.4)
潜伏結核	0	0	2 (0.8)
下気道感染	1 (0.4)	1 (0.4)	0
乳腺炎	0	1 (0.4)	0
伝染性軟属腫	1 (0.4)	0	0
上咽頭炎	20 (8.2)	23 (9.2)	26 (10.4)
食道カンジダ症	0	1 (0.4)	0
爪真菌症	2 (0.8)	1 (0.4)	1 (0.4)
口腔カンジダ症	2 (0.8)	1 (0.4)	1 (0.4)
口腔ヘルペス	3 (1.2)	5 (2.0)	7 (2.8)
外耳炎	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
乳頭腫ウイルス感染	0	0	1 (0.4)
爪囲炎	0	1 (0.4)	0
歯周炎	1 (0.4)	0	2 (0.8)
咽頭炎	4 (1.6)	2 (0.8)	1 (0.4)
レンサ球菌性咽頭炎	1 (0.4)	2 (0.8)	1 (0.4)
毛巣嚢胞	0	1 (0.4)	0
胸膜感染	0	0	1 (0.4)
ニューモシスチス・イロベチイ肺炎	1 (0.4)	0	0
肺炎	4 (1.6)	1 (0.4)	2 (0.8)
クリプトコッカス性肺炎	0	0	2 (0.8)
ウイルス性肺炎	0	0	1 (0.4)
歯髄炎	0	1 (0.4)	1 (0.4)
膿疱	1 (0.4)	0	1 (0.4)
腎盂腎炎	1 (0.4)	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
膿皮症	0	0	1 (0.4)
ウイルス性気道感染	1 (0.4)	4 (1.6)	0
鼻炎	3 (1.2)	1 (0.4)	2 (0.8)
セラチア感染	1 (0.4)	0	0
副鼻腔炎	4 (1.6)	2 (0.8)	3 (1.2)
ブドウ球菌感染	1 (0.4)	0	0
白癬感染	2 (0.8)	0	0
足部白癬	2 (0.8)	3 (1.2)	1 (0.4)
癜風	0	1 (0.4)	1 (0.4)
扁桃炎	1 (0.4)	2 (0.8)	3 (1.2)
歯膿瘍	0	1 (0.4)	1 (0.4)
歯感染	2 (0.8)	0	3 (1.2)
トリコモナス症	1 (0.4)	0	0
上気道感染	8 (3.3)	12 (4.8)	11 (4.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
尿路感染	6 (2.4)	7 (2.8)	3 (1.2)
水痘帯状疱疹ウイルス感染	0	1 (0.4)	0
ウイルス血症	1 (0.4)	0	0
ウイルス感染	0	1 (0.4)	2 (0.8)
ウイルス性上気道感染	3 (1.2)	1 (0.4)	3 (1.2)
外陰部腟カンジダ症	1 (0.4)	1 (0.4)	1 (0.4)
外陰腟真菌感染	1 (0.4)	1 (0.4)	1 (0.4)
傷害、中毒および処置合併症	11 (4.5)	12 (4.8)	12 (4.8)
動物による引っかき傷	1 (0.4)	0	0
骨挫傷	1 (0.4)	0	1 (0.4)
挫傷	0	0	3 (1.2)
毒性物質曝露	0	1 (0.4)	0
眼外傷	0	0	1 (0.4)
熱中症	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
傷害、中毒および処置合併症 (Cont.)			
損傷	1 (0.4)	0	0
関節損傷	0	2 (0.8)	0
靱帯捻挫	1 (0.4)	1 (0.4)	1 (0.4)
四肢損傷	1 (0.4)	1 (0.4)	0
四肢外傷性切断	0	0	1 (0.4)
腰椎骨折	0	0	1 (0.4)
筋断裂	0	0	1 (0.4)
肉離れ	1 (0.4)	1 (0.4)	0
外傷後疼痛	0	2 (0.8)	0
肺挫傷	0	1 (0.4)	0
肋骨骨折	1 (0.4)	0	0
交通事故	1 (0.4)	0	0
皮膚裂傷	1 (0.4)	3 (1.2)	0
脊椎圧迫骨折	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
傷害、中毒および処置合併症 (Cont.)			
皮下血腫	1 (0.4)	0	0
胸椎骨折	0	1 (0.4)	0
歯牙破折	1 (0.4)	0	2 (0.8)
創傷	0	1 (0.4)	0
手首関節骨折	0	0	1 (0.4)
臨床検査	16 (6.5)	42 (16.8)	53 (21.1)
アラニンアミノトランスフェラーゼ増加	1 (0.4)	7 (2.8)	7 (2.8)
アミラーゼ増加	1 (0.4)	1 (0.4)	0
抗核抗体増加	1 (0.4)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.8)	9 (3.6)	5 (2.0)
血中アルブミン減少	0	1 (0.4)	0
血中アルブミン増加	0	1 (0.4)	1 (0.4)
血中ビリルビン増加	0	2 (0.8)	3 (1.2)
血中カルシウム増加	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
臨床検査 (Cont.)			
血中コレステロール減少	0	1 (0.4)	0
血中コレステロール増加	0	2 (0.8)	6 (2.4)
血中クレアチンホスホキナーゼ増加	5 (2.0)	15 (6.0)	19 (7.6)
血中クレアチニン増加	2 (0.8)	0	4 (1.6)
血中葉酸減少	0	1 (0.4)	0
血中ブドウ糖増加	0	1 (0.4)	1 (0.4)
血中カリウム減少	0	2 (0.8)	0
血中カリウム増加	0	1 (0.4)	0
血中ナトリウム増加	0	1 (0.4)	0
血中トリグリセリド異常	0	1 (0.4)	0
尿中血陽性	0	0	2 (0.8)
体温上昇	0	1 (0.4)	1 (0.4)
γ－グルタミルトランスフェラーゼ増加	1 (0.4)	5 (2.0)	1 (0.4)
糸球体濾過率減少	1 (0.4)	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
臨床検査 (Cont.)			
顆粒球数減少	0	0	1 (0.4)
握力低下	0	1 (0.4)	0
ヘモグロビン減少	1 (0.4)	2 (0.8)	1 (0.4)
尿中ヘモグロビン陽性	0	0	1 (0.4)
肝酵素上昇	0	1 (0.4)	1 (0.4)
Ｂ型肝炎ＤＮＡ測定陽性	0	0	1 (0.4)
高比重リポ蛋白増加	0	3 (1.2)	1 (0.4)
リパーゼ増加	0	1 (0.4)	0
肝機能検査値上昇	0	0	1 (0.4)
低比重リポ蛋白減少	0	1 (0.4)	0
低比重リポ蛋白増加	0	1 (0.4)	5 (2.0)
リンパ球数減少	2 (0.8)	5 (2.0)	4 (1.6)
リンパ球数増加	1 (0.4)	1 (0.4)	2 (0.8)
リンパ球百分率減少	0	1 (0.4)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
臨床検査 (Cont.)			
リンパ球百分率増加	0	1 (0.4)	0
単球数増加	0	1 (0.4)	0
好中球数減少	2 (0.8)	5 (2.0)	8 (3.2)
好中球数増加	2 (0.8)	2 (0.8)	2 (0.8)
好中球百分率増加	0	0	1 (0.4)
血小板数減少	1 (0.4)	0	0
血小板数増加	0	0	2 (0.8)
プレアルブミン減少	0	1 (0.4)	0
総蛋白減少	0	1 (0.4)	0
総蛋白増加	0	0	1 (0.4)
尿中蛋白陽性	1 (0.4)	1 (0.4)	1 (0.4)
赤血球数減少	0	1 (0.4)	2 (0.8)
血沈亢進	0	1 (0.4)	0
ブドウ球菌検査陽性	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
臨床検査 (Cont.)			
尿検査異常	0	1 (0.4)	0
ビタミンD減少	0	1 (0.4)	0
体重増加	0	1 (0.4)	2 (0.8)
白血球数減少	2 (0.8)	4 (1.6)	6 (2.4)
白血球数増加	0	1 (0.4)	1 (0.4)
尿中白血球陽性	0	1 (0.4)	0
代謝および栄養障害	16 (6.5)	16 (6.4)	15 (6.0)
食欲減退	1 (0.4)	0	0
脂質異常症	0	4 (1.6)	1 (0.4)
葉酸欠乏	0	0	1 (0.4)
耐糖能障害	1 (0.4)	0	0
痛風	0	1 (0.4)	0
高カルシウム血症	0	0	1 (0.4)
高コレステロール血症	2 (0.8)	4 (1.6)	4 (1.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
代謝および栄養障害 (Cont.)			
高血糖	1 (0.4)	2 (0.8)	0
高リパーゼ血症	1 (0.4)	0	0
高脂血症	0	1 (0.4)	2 (0.8)
高尿酸血症	0	0	1 (0.4)
低カリウム血症	3 (1.2)	1 (0.4)	0
低ナトリウム血症	2 (0.8)	0	1 (0.4)
低リン酸血症	1 (0.4)	0	0
鉄欠乏	1 (0.4)	0	1 (0.4)
代謝症候群	0	0	1 (0.4)
２型糖尿病	1 (0.4)	0	0
ビタミンD欠乏	2 (0.8)	3 (1.2)	2 (0.8)
筋骨格系および結合組織障害	51 (20.8)	36 (14.4)	27 (10.8)
強直性脊椎炎	1 (0.4)	0	0
関節痛	25 (10.2)	14 (5.6)	7 (2.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
筋骨格系および結合組織障害 (Cont.)			
関節炎	0	1 (0.4)	0
腸炎性関節炎	1 (0.4)	0	0
関節障害	7 (2.9)	1 (0.4)	3 (1.2)
背部痛	10 (4.1)	7 (2.8)	1 (0.4)
骨痛	0	0	1 (0.4)
滑液包炎	0	0	1 (0.4)
頚部脊柱管狭窄症	0	0	1 (0.4)
軟骨軟化症	0	0	1 (0.4)
尾骨痛	1 (0.4)	0	0
肋軟骨炎	1 (0.4)	0	1 (0.4)
線維筋痛	0	1 (0.4)	0
側腹部痛	1 (0.4)	0	1 (0.4)
出血性関節症	1 (0.4)	0	0
椎間板変性症	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
筋骨格系および結合組織障害 (Cont.)			
関節硬直	0	1 (0.4)	0
関節腫脹	0	2 (0.8)	1 (0.4)
腰部脊柱管狭窄症	0	0	1 (0.4)
筋力低下	1 (0.4)	0	0
筋骨格系胸痛	2 (0.8)	1 (0.4)	0
筋骨格痛	3 (1.2)	2 (0.8)	1 (0.4)
筋骨格硬直	1 (0.4)	0	0
筋肉痛	2 (0.8)	2 (0.8)	1 (0.4)
筋炎	1 (0.4)	1 (0.4)	0
頚部痛	1 (0.4)	2 (0.8)	2 (0.8)
骨炎	0	0	1 (0.4)
変形性関節症	2 (0.8)	0	0
骨壊死	0	1 (0.4)	0
骨減少症	0	1 (0.4)	2 (0.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
筋骨格系および結合組織障害 (Cont.)			
骨粗鬆症	1 (0.4)	1 (0.4)	1 (0.4)
四肢痛	4 (1.6)	1 (0.4)	3 (1.2)
関節周囲炎	0	0	2 (0.8)
足底筋膜炎	0	0	1 (0.4)
肩回旋筋腱板症候群	2 (0.8)	2 (0.8)	0
変形性脊椎症	1 (0.4)	0	0
脊椎関節障害	1 (0.4)	1 (0.4)	0
腱痛	1 (0.4)	0	0
腱炎	1 (0.4)	0	0
腱鞘炎	1 (0.4)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (1.2)	5 (2.0)	8 (3.2)
結腸腺癌	0	0	1 (0.4)
基底細胞癌	0	0	3 (1.2)
良性脾腫瘍	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
大腸腺腫	1 (0.4)	0	0
線維性組織球腫	0	0	1 (0.4)
皮膚血管腫	0	1 (0.4)	0
浸潤性乳癌	1 (0.4)	1 (0.4)	0
メラノサイト性母斑	0	1 (0.4)	0
卵巣胚細胞良性奇形腫	0	1 (0.4)	0
脂漏性角化症	1 (0.4)	1 (0.4)	0
皮膚乳頭腫	0	0	1 (0.4)
小細胞癌	0	0	1 (0.4)
神経系障害	22 (9.0)	18 (7.2)	20 (8.0)
手根管症候群	1 (0.4)	1 (0.4)	2 (0.8)
頚髄神経根障害	1 (0.4)	0	0
浮動性めまい	3 (1.2)	2 (0.8)	2 (0.8)
味覚不全	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
神経系障害 (Cont.)			
てんかん	1 (0.4)	0	0
本態性振戦	1 (0.4)	0	0
頭痛	11 (4.5)	8 (3.2)	9 (3.6)
知覚過敏	1 (0.4)	0	0
感覚鈍麻	1 (0.4)	4 (1.6)	1 (0.4)
腰仙部神経根障害	0	1 (0.4)	0
片頭痛	3 (1.2)	1 (0.4)	3 (1.2)
神経圧迫	0	0	1 (0.4)
末梢性ニューロパチー	1 (0.4)	0	0
錯感覚	2 (0.8)	1 (0.4)	1 (0.4)
坐骨神経痛	0	1 (0.4)	0
脊椎炎性脊髄症	0	0	1 (0.4)
くも膜下出血	0	0	1 (0.4)
硬膜下滲出液	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
神経系障害 (Cont.)			
失神	1 (0.4)	0	0
精神障害	14 (5.7)	7 (2.8)	13 (5.2)
不安	6 (2.4)	1 (0.4)	2 (0.8)
不安障害	0	1 (0.4)	0
抑うつ気分	0	0	1 (0.4)
うつ病	2 (0.8)	1 (0.4)	4 (1.6)
不眠症	7 (2.9)	2 (0.8)	8 (3.2)
易刺激性	1 (0.4)	0	0
精神障害	1 (0.4)	0	0
パニック発作	0	1 (0.4)	0
睡眠障害	0	1 (0.4)	0
自殺念慮	1 (0.4)	0	0
腎および尿路障害	7 (2.9)	6 (2.4)	12 (4.8)
急性腎障害	1 (0.4)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
腎および尿路障害 (Cont.)			
排尿困難	1 (0.4)	0	1 (0.4)
糖尿	1 (0.4)	0	0
血尿	1 (0.4)	1 (0.4)	2 (0.8)
水腎症	1 (0.4)	0	0
緊張性膀胱	0	0	1 (0.4)
白血球尿	1 (0.4)	0	0
排尿異常	0	0	1 (0.4)
腎石灰沈着症	1 (0.4)	0	0
腎結石症	2 (0.8)	3 (1.2)	2 (0.8)
頻尿	0	0	1 (0.4)
蛋白尿	1 (0.4)	0	0
腎仙痛	0	0	4 (1.6)
腎機能障害	0	1 (0.4)	0
尿管結石症	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
腎および尿路障害 (Cont.)			
尿閉	0	1 (0.4)	0
生殖系および乳房障害	8 (3.3)	10 (4.0)	7 (2.8)
無月経	0	1 (0.4)	1 (0.4)
バルトリン嚢腫	1 (0.4)	0	0
良性前立腺肥大症	0	1 (0.4)	2 (0.8)
乳房嚢胞	1 (0.4)	1 (0.4)	0
乳房痛	0	1 (0.4)	0
子宮頚部上皮異形成	0	0	2 (0.8)
機能不全性子宮出血	1 (0.4)	0	0
月経困難症	0	1 (0.4)	0
閉経期症状	1 (0.4)	0	0
月経過多	0	1 (0.4)	0
不規則月経	1 (0.4)	0	0
不正子宮出血	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
生殖系および乳房障害 (Cont.)			
卵巣静脈血栓症	1 (0.4)	0	0
多嚢胞性卵巣	0	1 (0.4)	0
前立腺腫瘤	0	0	1 (0.4)
前立腺炎	1 (0.4)	1 (0.4)	1 (0.4)
精液変色	0	0	1 (0.4)
腟分泌物	0	1 (0.4)	0
腟出血	1 (0.4)	1 (0.4)	0
外陰腟そう痒症	1 (0.4)	0	0
呼吸器、胸郭および縦隔障害	18 (7.3)	15 (6.0)	20 (8.0)
急性呼吸不全	1 (0.4)	0	1 (0.4)
喘息	0	1 (0.4)	1 (0.4)
気管支拡張症	1 (0.4)	0	0
慢性閉塞性肺疾患	0	1 (0.4)	0
咳嗽	3 (1.2)	3 (1.2)	4 (1.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
呼吸困難	0	1 (0.4)	0
労作性呼吸困難	0	0	1 (0.4)
肺気腫	0	0	1 (0.4)
鼻出血	0	0	1 (0.4)
喀血	1 (0.4)	0	0
しゃっくり	1 (0.4)	0	1 (0.4)
間質性肺疾患	1 (0.4)	0	0
肺過膨脹	0	0	1 (0.4)
肺浸潤	0	0	1 (0.4)
鼻閉	3 (1.2)	0	2 (0.8)
非感染性気管支炎	0	0	1 (0.4)
口腔咽頭痛	5 (2.0)	3 (1.2)	6 (2.4)
湿性咳嗽	1 (0.4)	2 (0.8)	0
肺塞栓症	0	2 (0.8)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
肺出血	1 (0.4)	0	0
アレルギー性鼻炎	2 (0.8)	1 (0.4)	1 (0.4)
鼻漏	0	0	1 (0.4)
副鼻腔うっ血	2 (0.8)	0	1 (0.4)
咽喉刺激感	0	0	1 (0.4)
上気道の炎症	2 (0.8)	1 (0.4)	0
上気道咳症候群	0	0	1 (0.4)
皮膚および皮下組織障害	49 (20.0)	38 (15.2)	50 (19.9)
ざ瘡	8 (3.3)	6 (2.4)	9 (3.6)
脱毛症	0	2 (0.8)	3 (1.2)
皮脂欠乏症	0	0	1 (0.4)
皮膚嚢腫	0	1 (0.4)	1 (0.4)
皮膚炎	3 (1.2)	2 (0.8)	3 (1.2)
アトピー性皮膚炎	2 (0.8)	3 (1.2)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
皮膚および皮下組織障害 (Cont.)			
接触皮膚炎	2 (0.8)	1 (0.4)	1 (0.4)
びまん性脱毛症	0	1 (0.4)	0
皮膚乾燥	5 (2.0)	0	1 (0.4)
異汗性湿疹	2 (0.8)	0	0
斑状出血	1 (0.4)	0	1 (0.4)
湿疹	5 (2.0)	2 (0.8)	5 (2.0)
皮脂欠乏性湿疹	1 (0.4)	0	1 (0.4)
紅斑	2 (0.8)	3 (1.2)	1 (0.4)
結節性紅斑	1 (0.4)	0	1 (0.4)
機械性蕁麻疹	0	0	1 (0.4)
神経皮膚炎	1 (0.4)	0	0
寝汗	1 (0.4)	1 (0.4)	1 (0.4)
爪破損	1 (0.4)	0	1 (0.4)
爪甲剥離症	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
皮膚および皮下組織障害 (Cont.)			
掌蹠膿疱症	0	1 (0.4)	0
脂肪織炎	0	1 (0.4)	0
丘疹	0	0	1 (0.4)
光線性皮膚症	1 (0.4)	0	0
光線過敏性反応	1 (0.4)	0	1 (0.4)
そう痒症	6 (2.4)	2 (0.8)	1 (0.4)
壊疽性膿皮症	1 (0.4)	0	0
発疹	9 (3.7)	8 (3.2)	11 (4.4)
紅斑性皮疹	1 (0.4)	1 (0.4)	0
毛孔性皮疹	0	1 (0.4)	0
斑状皮疹	0	1 (0.4)	1 (0.4)
斑状丘疹状皮疹	1 (0.4)	1 (0.4)	1 (0.4)
丘疹性皮疹	0	1 (0.4)	0
そう痒性皮疹	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
皮膚および皮下組織障害 (Cont.)			
酒さ	1 (0.4)	2 (0.8)	1 (0.4)
脂漏性皮膚炎	7 (2.9)	2 (0.8)	2 (0.8)
皮膚灼熱感	1 (0.4)	0	0
皮膚びらん	1 (0.4)	0	0
皮膚剥脱	1 (0.4)	0	0
皮膚亀裂	1 (0.4)	0	0
皮膚色素過剰	1 (0.4)	0	0
皮膚病変	0	0	2 (0.8)
皮膚腫瘤	0	1 (0.4)	0
皮膚潰瘍	0	0	1 (0.4)
蕁麻疹	2 (0.8)	0	4 (1.6)
外科および内科処置	0	2 (0.8)	0
人工流産	0	2 (0.8)	0
血管障害	4 (1.6)	8 (3.2)	9 (3.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
血管障害 (Cont.)			
大動脈瘤	0	1 (0.4)	0
大動脈硬化症	0	0	1 (0.4)
出血性静脈瘤	0	1 (0.4)	0
深部静脈血栓症	0	0	2 (0.8)
血腫	0	0	1 (0.4)
高血圧	2 (0.8)	6 (2.4)	5 (2.0)
低血圧	1 (0.4)	0	0
末梢動脈閉塞性疾患	0	0	1 (0.4)
静脈血栓症	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

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表4

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STUDY M14-234 SUBSTUDY 3
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TABLE 14.3__1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
Any adverse event	674 (499.4)	626 (313.9)	691 (316.2)
血液およびリンパ系障害	31 (23.0)	29 (14.5)	20 (9.2)
貧血	13 (9.6)	10 (5.0)	8 (3.7)
好酸球増加症	1 (0.7)	0	0
内出血発生の増加傾向	0	0	1 (0.5)
鉄欠乏性貧血	5 (3.7)	0	0
白血球増加症	1 (0.7)	0	0
白血球減少症	3 (2.2)	9 (4.5)	1 (0.5)
リンパ節症	0	0	1 (0.5)
リンパ球増加症	1 (0.7)	0	0
リンパ球減少症	3 (2.2)	3 (1.5)	1 (0.5)
小球性貧血	0	0	1 (0.5)
好中球減少症	3 (2.2)	6 (3.0)	6 (2.7)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
血液およびリンパ系障害 (Cont.)			
脾腫	0	1 (0.5)	0
血小板減少症	1 (0.7)	0	0
血小板増加症	0	0	1 (0.5)
心臓障害	6 (4.4)	4 (2.0)	8 (3.7)
急性心筋梗塞	1 (0.7)	0	0
不整脈	0	1 (0.5)	0
心房細動	1 (0.7)	0	0
二束ブロック	0	0	1 (0.5)
心不全	0	0	1 (0.5)
うっ血性心不全	1 (0.7)	1 (0.5)	0
慢性左室不全	0	0	1 (0.5)
動悸	2 (1.5)	1 (0.5)	0
心膜炎	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
心臓障害 (Cont.)			
洞性徐脈	0	1 (0.5)	1 (0.5)
上室性頻脈	0	0	1 (0.5)
頻脈	1 (0.7)	0	0
心室性期外収縮	0	0	1 (0.5)
ウォルフ・パーキンソン・ホワイト症候群	0	0	1 (0.5)
先天性、家族性および遺伝性障害	0	1 (0.5)	2 (0.9)
皮様嚢腫	0	0	1 (0.5)
胃腸管動静脈奇形	0	0	1 (0.5)
ジルベール症候群	0	1 (0.5)	0
耳および迷路障害	3 (2.2)	4 (2.0)	1 (0.5)
感音性難聴	0	1 (0.5)	0
片耳難聴	0	0	1 (0.5)
耳痛	0	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
耳および迷路障害 (Cont.)			
耳部腫脹	1 (0.7)	0	0
外耳道の外骨腫	1 (0.7)	0	0
中耳滲出液	1 (0.7)	0	0
回転性めまい	0	2 (1.0)	0
内分泌障害	1 (0.7)	1 (0.5)	0
クッシング症候群	1 (0.7)	0	0
甲状腺腫	0	1 (0.5)	0
眼障害	12 (8.9)	10 (5.0)	11 (5.0)
眼瞼炎	1 (0.7)	0	2 (0.9)
白内障	1 (0.7)	3 (1.5)	2 (0.9)
霰粒腫	0	0	3 (1.4)
結膜充血	1 (0.7)	0	0
アレルギー性結膜炎	1 (0.7)	1 (0.5)	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
眼障害 (Cont.)			
角膜混濁	1 (0.7)	0	0
ドライアイ	0	1 (0.5)	1 (0.5)
上強膜炎	1 (0.7)	0	0
眼刺激	0	1 (0.5)	0
眼そう痒症	0	1 (0.5)	0
眼部腫脹	0	1 (0.5)	0
眼瞼障害	1 (0.7)	0	0
眼瞼発疹	1 (0.7)	0	0
角膜炎	1 (0.7)	0	1 (0.5)
流涙増加	0	1 (0.5)	0
眼充血	0	1 (0.5)	1 (0.5)
眼窩周囲腫脹	1 (0.7)	0	0
潰瘍性角膜炎	1 (0.7)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
眼障害 (Cont.)			
ぶどう膜炎	1 (0.7)	0	0
胃腸障害	152 (112.6)	88 (44.1)	88 (40.3)
腹部膨満	1 (0.7)	2 (1.0)	5 (2.3)
腹部腫瘤	1 (0.7)	0	0
腹痛	6 (4.4)	7 (3.5)	4 (1.8)
下腹部痛	4 (3.0)	0	0
上腹部痛	2 (1.5)	4 (2.0)	2 (0.9)
腹部圧痛	0	0	2 (0.9)
異常便	1 (0.7)	0	0
裂肛	1 (0.7)	1 (0.5)	0
痔瘻	0	0	3 (1.4)
肛門の炎症	0	0	1 (0.5)
肛門そう痒症	2 (1.5)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
胃腸障害 (Cont.)			
アフタ性潰瘍	2 (1.5)	1 (0.5)	3 (1.4)
大腸炎	3 (2.2)	2 (1.0)	0
虚血性大腸炎	0	1 (0.5)	0
潰瘍性大腸炎	81 (60.0)	35 (17.5)	20 (9.2)
結腸異形成	0	1 (0.5)	0
便秘	2 (1.5)	4 (2.0)	6 (2.7)
便意切迫	0	0	1 (0.5)
齲歯	1 (0.7)	1 (0.5)	0
歯嚢胞	0	0	1 (0.5)
下痢	2 (1.5)	2 (1.0)	2 (0.9)
口内乾燥	0	0	1 (0.5)
消化不良	3 (2.2)	1 (0.5)	1 (0.5)
嚥下障害	1 (0.7)	1 (0.5)	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
胃腸障害 (Cont.)			
小腸炎	0	1 (0.5)	2 (0.9)
変色便	0	0	1 (0.5)
大腿ヘルニア	1 (0.7)	0	0
鼓腸	3 (2.2)	0	2 (0.9)
胃潰瘍	0	1 (0.5)	0
胃炎	0	3 (1.5)	1 (0.5)
胃食道逆流性疾患	3 (2.2)	1 (0.5)	3 (1.4)
歯肉腫脹	1 (0.7)	0	0
舌痛	1 (0.7)	0	0
血便排泄	1 (0.7)	0	0
痔出血	2 (1.5)	1 (0.5)	0
痔核	1 (0.7)	3 (1.5)	2 (0.9)
血栓性痔核	1 (0.7)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
胃腸障害 (Cont.)			
単径ヘルニア	0	1 (0.5)	0
腸閉塞	0	1 (0.5)	0
過敏性腸症候群	0	0	1 (0.5)
大腸穿孔	1 (0.7)	0	0
大腸ポリープ	2 (1.5)	0	1 (0.5)
口唇腫脹	0	0	1 (0.5)
口腔嚢胞	1 (0.7)	0	0
口腔内潰瘍形成	2 (1.5)	0	1 (0.5)
粘液便	1 (0.7)	0	0
悪心	6 (4.4)	4 (2.0)	5 (2.3)
非感染性歯肉炎	0	0	1 (0.5)
嚥下痛	1 (0.7)	0	0
食道炎	0	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
胃腸障害 (Cont.)			
口腔障害	0	0	1 (0.5)
膵炎	1 (0.7)	0	0
歯周病	1 (0.7)	0	1 (0.5)
肛門周囲痛	0	1 (0.5)	0
直腸炎	1 (0.7)	0	0
直腸分泌物	0	0	1 (0.5)
直腸出血	1 (0.7)	0	2 (0.9)
直腸攣縮	1 (0.7)	0	0
直腸しぶり	1 (0.7)	0	0
口内炎	3 (2.2)	1 (0.5)	4 (1.8)
埋伏歯	0	1 (0.5)	0
歯の脱落	0	0	1 (0.5)
歯痛	0	4 (2.0)	3 (1.4)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
胃腸障害 (Cont.)			
臍ヘルニア	1 (0.7)	0	0
嘔吐	1 (0.7)	1 (0.5)	1 (0.5)
一般・全身障害および投与部位の状態	29 (21.5)	22 (11.0)	38 (17.4)
胸部不快感	0	1 (0.5)	0
胸痛	1 (0.7)	3 (1.5)	2 (0.9)
悪寒	2 (1.5)	2 (1.0)	0
医療機器に対する不耐性	1 (0.7)	0	0
薬効欠如	1 (0.7)	0	0
疲労	5 (3.7)	2 (1.0)	4 (1.8)
全身性浮腫	0	1 (0.5)	0
高体温症	1 (0.7)	0	0
炎症	0	0	1 (0.5)
インフルエンザ様疾患	1 (0.7)	0	2 (0.9)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
一般・全身障害および投与部位の状態 (Cont.)			
注射部位疼痛	0	1 (0.5)	4 (1.8)
倦怠感	1 (0.7)	0	2 (0.9)
腫瘤	0	0	2 (0.9)
粘膜乾燥	1 (0.7)	0	0
小結節	0	0	1 (0.5)
非心臓性胸痛	1 (0.7)	0	0
浮腫	0	1 (0.5)	0
末梢性浮腫	3 (2.2)	1 (0.5)	1 (0.5)
疼痛	1 (0.7)	1 (0.5)	0
末梢腫脹	1 (0.7)	1 (0.5)	1 (0.5)
発熱	8 (5.9)	8 (4.0)	16 (7.3)
異物感	1 (0.7)	0	0
腫脹	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
一般・全身障害および投与部位の状態 (Cont.)			
顔面腫脹	0	0	1 (0.5)
肝胆道系障害	4 (3.0)	7 (3.5)	2 (0.9)
薬物性肝障害	0	1 (0.5)	1 (0.5)
肝機能異常	3 (2.2)	2 (1.0)	0
脂肪肝	0	2 (1.0)	0
高トランスアミナーゼ血症	0	1 (0.5)	0
肝障害	0	0	1 (0.5)
肝損傷	1 (0.7)	1 (0.5)	0
免疫系障害	1 (0.7)	2 (1.0)	1 (0.5)
薬物過敏症	1 (0.7)	0	0
季節性アレルギー	0	2 (1.0)	1 (0.5)
感染症および寄生虫症	126 (93.4)	162 (81.2)	183 (83.8)
腹部膿瘍	1 (0.7)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
ダニ皮膚炎	0	2 (1.0)	0
急性心内膜炎	1 (0.7)	0	0
肛門膿瘍	0	2 (1.0)	0
肛門直腸感染	2 (1.5)	0	0
細菌性関節炎	0	1 (0.5)	0
細菌感染	0	0	1 (0.5)
細菌性膣症	1 (0.7)	0	0
乳房膿瘍	0	1 (0.5)	0
気管支炎	3 (2.2)	6 (3.0)	1 (0.5)
感染性滑液包炎	0	0	1 (0.5)
カンピロバクター感染	0	1 (0.5)	0
カンジダ感染	1 (0.7)	0	0
蜂巣炎	0	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
クロストリジウム・ディフィシレ感染	2 (1.5)	1 (0.5)	2 (0.9)
結膜炎	0	2 (1.0)	1 (0.5)
ＣＯＶＩＤ－１９	8 (5.9)	5 (2.5)	11 (5.0)
ＣＯＶＩＤ－１９肺炎	1 (0.7)	1 (0.5)	2 (0.9)
膀胱炎	0	3 (1.5)	3 (1.4)
サイトメガロウイルス感染	1 (0.7)	1 (0.5)	0
毛嚢虫症	0	3 (1.5)	2 (0.9)
皮膚糸状菌症	1 (0.7)	0	0
憩室炎	0	0	1 (0.5)
耳感染	0	1 (0.5)	2 (0.9)
感染性腸炎	0	0	1 (0.5)
エンテロウイルス感染	0	0	1 (0.5)
大腸菌性尿路感染	0	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
毛包炎	4 (3.0)	4 (2.0)	10 (4.6)
真菌感染	0	0	1 (0.5)
皮膚真菌感染	0	0	2 (0.9)
せつ	0	1 (0.5)	0
胃腸炎	4 (3.0)	5 (2.5)	3 (1.4)
ウイルス性胃腸炎	0	0	2 (0.9)
歯肉膿瘍	0	0	1 (0.5)
歯肉炎	0	1 (0.5)	0
ヘモフィルス感染	1 (0.7)	0	0
ヘルペス性皮膚炎	0	1 (0.5)	0
単純ヘルペス	0	2 (1.0)	1 (0.5)
帯状疱疹	0	11 (5.5)	15 (6.9)
帯状疱疹性髄膜炎	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
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Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
麦粒腫	3 (2.2)	0	2 (0.9)
膿痂疹	1 (0.7)	1 (0.5)	0
感染性皮膚嚢腫	0	1 (0.5)	0
インフルエンザ	3 (2.2)	7 (3.5)	10 (4.6)
大腸感染	0	1 (0.5)	0
喉頭炎	1 (0.7)	0	1 (0.5)
潜伏結核	0	0	2 (0.9)
下気道感染	1 (0.7)	1 (0.5)	0
乳腺炎	0	1 (0.5)	0
伝染性軟属腫	1 (0.7)	0	0
上咽頭炎	21 (15.6)	32 (16.0)	38 (17.4)
食道カンジダ症	0	1 (0.5)	0
爪真菌症	2 (1.5)	1 (0.5)	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
口腔カンジダ症	2 (1.5)	1 (0.5)	1 (0.5)
口腔ヘルペス	4 (3.0)	7 (3.5)	8 (3.7)
外耳炎	1 (0.7)	0	0
乳頭腫ウイルス感染	0	0	1 (0.5)
爪囲炎	0	1 (0.5)	0
歯周炎	1 (0.7)	0	2 (0.9)
咽頭炎	4 (3.0)	2 (1.0)	1 (0.5)
レンサ球菌性咽頭炎	1 (0.7)	2 (1.0)	1 (0.5)
毛巣嚢胞	0	1 (0.5)	0
胸膜感染	0	0	1 (0.5)
ニューモシスチス・イロベチイ肺炎	1 (0.7)	0	0
肺炎	4 (3.0)	1 (0.5)	2 (0.9)
クリプトコッカス性肺炎	0	0	2 (0.9)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
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Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
ウイルス性肺炎	0	0	1 (0.5)
歯髄炎	0	1 (0.5)	1 (0.5)
膿疱	1 (0.7)	0	1 (0.5)
腎盂腎炎	1 (0.7)	1 (0.5)	0
膿皮症	0	0	1 (0.5)
ウイルス性気道感染	1 (0.7)	4 (2.0)	0
鼻炎	3 (2.2)	1 (0.5)	2 (0.9)
セラチア感染	1 (0.7)	0	0
副鼻腔炎	4 (3.0)	2 (1.0)	3 (1.4)
ブドウ球菌感染	1 (0.7)	0	0
白癬感染	2 (1.5)	0	0
足部白癬	2 (1.5)	3 (1.5)	1 (0.5)
癜風	0	1 (0.5)	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
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Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
扁桃炎	1 (0.7)	2 (1.0)	3 (1.4)
歯膿瘍	0	1 (0.5)	1 (0.5)
歯感染	3 (2.2)	0	3 (1.4)
トリコモナス症	1 (0.7)	0	0
上気道感染	9 (6.7)	13 (6.5)	14 (6.4)
尿路感染	7 (5.2)	10 (5.0)	4 (1.8)
水痘帯状疱疹ウイルス感染	0	1 (0.5)	0
ウイルス血症	1 (0.7)	0	0
ウイルス感染	0	1 (0.5)	2 (0.9)
ウイルス性上気道感染	4 (3.0)	1 (0.5)	4 (1.8)
外陰部腟カンジダ症	1 (0.7)	1 (0.5)	2 (0.9)
外陰腟真菌感染	1 (0.7)	1 (0.5)	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
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Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

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傷害、中毒および処置合併症	13 (9.6)	14 (7.0)	12 (5.5)
動物による引っかき傷	1 (0.7)	0	0
骨挫傷	1 (0.7)	0	1 (0.5)
挫傷	0	0	3 (1.4)
毒性物質曝露	0	1 (0.5)	0
眼外傷	0	0	1 (0.5)
熱中症	1 (0.7)	0	0
損傷	1 (0.7)	0	0
関節損傷	0	2 (1.0)	0
靭帯捻挫	1 (0.7)	1 (0.5)	1 (0.5)
四肢損傷	1 (0.7)	1 (0.5)	0
四肢外傷性切断	0	0	1 (0.5)
腰椎骨折	0	0	1 (0.5)
筋断裂	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
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TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

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傷害、中毒および処置合併症 (Cont.)			
肉離れ	1 (0.7)	1 (0.5)	0
外傷後疼痛	0	2 (1.0)	0
肺挫傷	0	1 (0.5)	0
肋骨骨折	1 (0.7)	0	0
交通事故	1 (0.7)	0	0
皮膚裂傷	1 (0.7)	3 (1.5)	0
脊椎圧迫骨折	1 (0.7)	0	0
皮下血腫	1 (0.7)	0	0
胸椎骨折	0	1 (0.5)	0
歯牙破折	1 (0.7)	0	2 (0.9)
創傷	0	1 (0.5)	0
手首関節骨折	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
臨床検査	29 (21.5)	102 (51.1)	104 (47.6)
アラニンアミノトランスフェラーゼ増加	1 (0.7)	9 (4.5)	7 (3.2)
アミラーゼ増加	1 (0.7)	1 (0.5)	0
抗核抗体増加	1 (0.7)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (1.5)	9 (4.5)	5 (2.3)
血中アルブミン減少	0	2 (1.0)	0
血中アルブミン増加	0	1 (0.5)	1 (0.5)
血中ビリルビン増加	0	3 (1.5)	3 (1.4)
血中カルシウム増加	0	1 (0.5)	0
血中コレステロール減少	0	1 (0.5)	0
血中コレステロール増加	0	2 (1.0)	6 (2.7)
血中クレアチンホスホキナーゼ増加	5 (3.7)	16 (8.0)	22 (10.1)
血中クレアチニン増加	2 (1.5)	0	4 (1.8)
血中葉酸減少	0	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
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Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

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臨床検査 (Cont.)			
血中ブドウ糖増加	0	1 (0.5)	1 (0.5)
血中カリウム減少	0	2 (1.0)	0
血中カリウム増加	0	1 (0.5)	0
血中ナトリウム増加	0	1 (0.5)	0
血中トリグリセリド異常	0	1 (0.5)	0
尿中血陽性	0	0	2 (0.9)
体温上昇	0	1 (0.5)	1 (0.5)
γ－グルタミルトランスフェラーゼ増加	1 (0.7)	5 (2.5)	1 (0.5)
糸球体濾過率減少	1 (0.7)	1 (0.5)	0
顆粒球数減少	0	0	1 (0.5)
握力低下	0	1 (0.5)	0
ヘモグロビン減少	1 (0.7)	2 (1.0)	1 (0.5)
尿中ヘモグロビン陽性	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
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Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

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臨床検査 (Cont.)			
肝酵素上昇	0	1 (0.5)	1 (0.5)
Ｂ型肝炎ＤＮＡ測定陽性	0	0	1 (0.5)
高比重リポ蛋白増加	0	3 (1.5)	1 (0.5)
リパーゼ増加	0	1 (0.5)	0
肝機能検査値上昇	0	0	1 (0.5)
低比重リポ蛋白減少	0	1 (0.5)	0
低比重リポ蛋白増加	0	1 (0.5)	6 (2.7)
リンパ球数減少	2 (1.5)	6 (3.0)	5 (2.3)
リンパ球数増加	1 (0.7)	1 (0.5)	2 (0.9)
リンパ球百分率減少	0	1 (0.5)	1 (0.5)
リンパ球百分率増加	0	1 (0.5)	0
単球数増加	0	1 (0.5)	0
好中球数減少	4 (3.0)	5 (2.5)	12 (5.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
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Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

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臨床検査 (Cont.)			
好中球数増加	2 (1.5)	2 (1.0)	2 (0.9)
好中球百分率増加	0	0	1 (0.5)
血小板数減少	1 (0.7)	0	0
血小板数増加	0	0	2 (0.9)
プレアルブミン減少	0	1 (0.5)	0
総蛋白減少	0	1 (0.5)	0
総蛋白増加	0	0	1 (0.5)
尿中蛋白陽性	1 (0.7)	2 (1.0)	1 (0.5)
赤血球数減少	0	1 (0.5)	2 (0.9)
血沈亢進	0	1 (0.5)	0
ブドウ球菌検査陽性	0	1 (0.5)	0
尿検査異常	0	1 (0.5)	0
ビタミンD減少	0	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
臨床検査 (Cont.)			
体重増加	0	1 (0.5)	2 (0.9)
白血球数減少	3 (2.2)	4 (2.0)	6 (2.7)
白血球数増加	0	1 (0.5)	1 (0.5)
尿中白血球陽性	0	1 (0.5)	0
代謝および栄養障害	16 (11.9)	18 (9.0)	15 (6.9)
食欲減退	1 (0.7)	0	0
脂質異常症	0	4 (2.0)	1 (0.5)
葉酸欠乏	0	0	1 (0.5)
耐糖能障害	1 (0.7)	0	0
痛風	0	2 (1.0)	0
高カルシウム血症	0	0	1 (0.5)
高コレステロール血症	2 (1.5)	4 (2.0)	4 (1.8)
高血糖	1 (0.7)	3 (1.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
代謝および栄養障害 (Cont.)			
高リパーゼ血症	1 (0.7)	0	0
高脂血症	0	1 (0.5)	2 (0.9)
高尿酸血症	0	0	1 (0.5)
低カリウム血症	3 (2.2)	1 (0.5)	0
低ナトリウム血症	2 (1.5)	0	1 (0.5)
低リン酸血症	1 (0.7)	0	0
鉄欠乏	1 (0.7)	0	1 (0.5)
代謝症候群	0	0	1 (0.5)
２型糖尿病	1 (0.7)	0	0
ビタミンD欠乏	2 (1.5)	3 (1.5)	2 (0.9)
筋骨格系および結合組織障害	78 (57.8)	42 (21.1)	35 (16.0)
強直性脊椎炎	1 (0.7)	0	0
関節痛	25 (18.5)	14 (7.0)	8 (3.7)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
筋骨格系および結合組織障害 (Cont.)			
関節炎	0	1 (0.5)	0
腸炎性関節炎	3 (2.2)	0	0
関節障害	7 (5.2)	1 (0.5)	3 (1.4)
背部痛	10 (7.4)	7 (3.5)	1 (0.5)
骨痛	0	0	1 (0.5)
滑液包炎	0	0	1 (0.5)
頚部脊柱管狭窄症	0	0	1 (0.5)
軟骨軟化症	0	0	2 (0.9)
尾骨痛	1 (0.7)	0	0
肋軟骨炎	2 (1.5)	0	1 (0.5)
線維筋痛	0	1 (0.5)	0
側腹部痛	1 (0.7)	0	1 (0.5)
出血性関節症	1 (0.7)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
筋骨格系および結合組織障害 (Cont.)			
椎間板変性症	1 (0.7)	0	0
関節硬直	0	1 (0.5)	0
関節腫脹	0	2 (1.0)	1 (0.5)
腰部脊柱管狭窄症	0	0	1 (0.5)
筋力低下	1 (0.7)	0	0
筋骨格系胸痛	3 (2.2)	1 (0.5)	0
筋骨格痛	3 (2.2)	2 (1.0)	1 (0.5)
筋骨格硬直	1 (0.7)	0	0
筋肉痛	2 (1.5)	2 (1.0)	1 (0.5)
筋炎	1 (0.7)	1 (0.5)	0
頚部痛	1 (0.7)	2 (1.0)	2 (0.9)
骨炎	0	0	1 (0.5)
変形性関節症	2 (1.5)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
筋骨格系および結合組織障害 (Cont.)			
骨壊死	0	1 (0.5)	0
骨減少症	0	1 (0.5)	2 (0.9)
骨粗鬆症	1 (0.7)	1 (0.5)	1 (0.5)
四肢痛	4 (3.0)	1 (0.5)	3 (1.4)
関節周囲炎	0	0	2 (0.9)
足底筋膜炎	0	0	1 (0.5)
肩回旋筋腱板症候群	2 (1.5)	2 (1.0)	0
変形性脊椎症	1 (0.7)	0	0
脊椎関節障害	1 (0.7)	1 (0.5)	0
腱痛	1 (0.7)	0	0
腱炎	1 (0.7)	0	0
腱鞘炎	1 (0.7)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (2.2)	5 (2.5)	9 (4.1)
結腸腺癌	0	0	1 (0.5)
基底細胞癌	0	0	3 (1.4)
良性脾腫瘍	0	0	1 (0.5)
大腸腺腫	1 (0.7)	0	0
線維性組織球腫	0	0	1 (0.5)
皮膚血管腫	0	1 (0.5)	0
浸潤性乳癌	1 (0.7)	1 (0.5)	0
メラノサイト性母斑	0	1 (0.5)	0
卵巣胚細胞良性奇形腫	0	1 (0.5)	0
脂漏性角化症	1 (0.7)	1 (0.5)	0
皮膚乳頭腫	0	0	2 (0.9)
小細胞癌	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
神経系障害	29 (21.5)	20 (10.0)	22 (10.1)
手根管症候群	1 (0.7)	1 (0.5)	2 (0.9)
頚髄神経根障害	1 (0.7)	0	0
浮動性めまい	3 (2.2)	2 (1.0)	2 (0.9)
味覚不全	1 (0.7)	0	0
てんかん	1 (0.7)	0	0
本態性振戦	1 (0.7)	0	0
頭痛	11 (8.2)	8 (4.0)	10 (4.6)
知覚過敏	1 (0.7)	0	0
感覚鈍麻	1 (0.7)	4 (2.0)	1 (0.5)
腰仙部神経根障害	0	1 (0.5)	0
片頭痛	4 (3.0)	1 (0.5)	3 (1.4)
神経圧迫	0	0	1 (0.5)
末梢性ニューロパチー	1 (0.7)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
神経系障害 (Cont.)			
錯感覚	2 (1.5)	1 (0.5)	1 (0.5)
坐骨神経痛	0	1 (0.5)	0
脊椎炎性脊髄症	0	0	1 (0.5)
くも膜下出血	0	0	1 (0.5)
硬膜下滲出液	0	1 (0.5)	0
失神	1 (0.7)	0	0
精神障害	18 (13.3)	7 (3.5)	16 (7.3)
不安	6 (4.4)	1 (0.5)	2 (0.9)
不安障害	0	1 (0.5)	0
抑うつ気分	0	0	1 (0.5)
うつ病	2 (1.5)	1 (0.5)	4 (1.8)
不眠症	7 (5.2)	2 (1.0)	9 (4.1)
易刺激性	1 (0.7)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
精神障害 (Cont.)			
精神障害	1 (0.7)	0	0
パニック発作	0	1 (0.5)	0
睡眠障害	0	1 (0.5)	0
自殺念慮	1 (0.7)	0	0
腎および尿路障害	11 (8.2)	6 (3.0)	14 (6.4)
急性腎障害	1 (0.7)	0	1 (0.5)
排尿困難	1 (0.7)	0	1 (0.5)
糖尿	1 (0.7)	0	0
血尿	2 (1.5)	1 (0.5)	2 (0.9)
水腎症	1 (0.7)	0	0
緊張性膀胱	0	0	1 (0.5)
白血球尿	1 (0.7)	0	0
排尿異常	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
腎および尿路障害 (Cont.)			
腎石灰沈着症	1 (0.7)	0	0
腎結石症	2 (1.5)	3 (1.5)	2 (0.9)
頻尿	0	0	1 (0.5)
蛋白尿	1 (0.7)	0	0
腎仙痛	0	0	4 (1.8)
腎機能障害	0	1 (0.5)	0
尿管結石症	0	0	1 (0.5)
尿閉	0	1 (0.5)	0
生殖系および乳房障害	9 (6.7)	11 (5.5)	8 (3.7)
無月経	0	1 (0.5)	1 (0.5)
バルトリン嚢腫	1 (0.7)	0	0
良性前立腺肥大症	0	1 (0.5)	2 (0.9)
乳房嚢胞	1 (0.7)	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
生殖系および乳房障害 (Cont.)			
乳房痛	0	1 (0.5)	0
子宮頚部上皮異形成	0	0	2 (0.9)
機能不全性子宮出血	1 (0.7)	0	0
月経困難症	0	1 (0.5)	0
閉経期症状	1 (0.7)	0	0
月経過多	0	1 (0.5)	0
不規則月経	1 (0.7)	0	0
不正子宮出血	0	1 (0.5)	0
卵巣静脈血栓症	1 (0.7)	0	0
多嚢胞性卵巣	0	1 (0.5)	0
前立腺腫瘤	0	0	1 (0.5)
前立腺炎	1 (0.7)	1 (0.5)	1 (0.5)
精液変色	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
生殖系および乳房障害 (Cont.)			
腟分泌物	0	1 (0.5)	0
腟出血	1 (0.7)	1 (0.5)	0
外陰腟そう痒症	1 (0.7)	0	0
呼吸器、胸郭および縦隔障害	24 (17.8)	15 (7.5)	27 (12.4)
急性呼吸不全	1 (0.7)	0	1 (0.5)
喘息	0	1 (0.5)	1 (0.5)
気管支拡張症	1 (0.7)	0	0
慢性閉塞性肺疾患	0	1 (0.5)	0
咳嗽	3 (2.2)	3 (1.5)	5 (2.3)
呼吸困難	0	1 (0.5)	0
労作性呼吸困難	0	0	1 (0.5)
肺気腫	0	0	1 (0.5)
鼻出血	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
呼吸器、胸郭および縦隔障害 (Cont.)			
喀血	1 (0.7)	0	0
しゃっくり	1 (0.7)	0	1 (0.5)
間質性肺疾患	1 (0.7)	0	0
肺過膨脹	0	0	1 (0.5)
肺浸潤	0	0	1 (0.5)
鼻閉	3 (2.2)	0	2 (0.9)
非感染性気管支炎	0	0	1 (0.5)
口腔咽頭痛	5 (3.7)	3 (1.5)	6 (2.7)
湿性咳嗽	1 (0.7)	2 (1.0)	0
肺塞栓症	0	2 (1.0)	0
肺出血	1 (0.7)	0	0
アレルギー性鼻炎	2 (1.5)	1 (0.5)	1 (0.5)
鼻漏	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
呼吸器、胸郭および縦隔障害 (Cont.)			
副鼻腔うっ血	2 (1.5)	0	1 (0.5)
咽喉刺激感	0	0	1 (0.5)
上気道の炎症	2 (1.5)	1 (0.5)	0
上気道咳症候群	0	0	1 (0.5)
皮膚および皮下組織障害	75 (55.6)	45 (22.6)	64 (29.3)
ざ瘡	8 (5.9)	7 (3.5)	10 (4.6)
脱毛症	0	2 (1.0)	3 (1.4)
皮脂欠乏症	0	0	1 (0.5)
皮膚嚢腫	0	1 (0.5)	1 (0.5)
皮膚炎	3 (2.2)	2 (1.0)	3 (1.4)
アトピー性皮膚炎	3 (2.2)	3 (1.5)	1 (0.5)
接触皮膚炎	2 (1.5)	1 (0.5)	1 (0.5)
びまん性脱毛症	0	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
皮膚乾燥	5 (3.7)	0	1 (0.5)
異汗性湿疹	2 (1.5)	0	0
斑状出血	1 (0.7)	0	1 (0.5)
湿疹	5 (3.7)	2 (1.0)	5 (2.3)
皮脂欠乏性湿疹	1 (0.7)	0	1 (0.5)
紅斑	3 (2.2)	3 (1.5)	1 (0.5)
結節性紅斑	1 (0.7)	0	1 (0.5)
機械性蕁麻疹	0	0	1 (0.5)
神経皮膚炎	1 (0.7)	0	0
寝汗	1 (0.7)	1 (0.5)	1 (0.5)
爪破損	1 (0.7)	0	1 (0.5)
爪甲剥離症	0	0	1 (0.5)
掌蹠膿疱症	0	1 (0.5)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
脂肪織炎	0	1 (0.5)	0
丘疹	0	0	1 (0.5)
光線性皮膚症	1 (0.7)	0	0
光線過敏性反応	1 (0.7)	0	1 (0.5)
そう痒症	8 (5.9)	2 (1.0)	1 (0.5)
壊疽性膿皮症	1 (0.7)	0	0
発疹	9 (6.7)	8 (4.0)	11 (5.0)
紅斑性皮疹	1 (0.7)	1 (0.5)	0
毛孔性皮疹	0	1 (0.5)	0
斑状皮疹	0	1 (0.5)	1 (0.5)
斑状丘疹状皮疹	1 (0.7)	1 (0.5)	4 (1.8)
丘疹性皮疹	0	1 (0.5)	0
そう痒性皮疹	0	0	1 (0.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
酒さ	1 (0.7)	2 (1.0)	1 (0.5)
脂漏性皮膚炎	7 (5.2)	2 (1.0)	2 (0.9)
皮膚灼熱感	1 (0.7)	0	0
皮膚びらん	1 (0.7)	0	0
皮膚剥脱	1 (0.7)	0	0
皮膚亀裂	1 (0.7)	0	0
皮膚色素過剰	1 (0.7)	0	0
皮膚病変	0	0	2 (0.9)
皮膚腫瘤	0	1 (0.5)	0
皮膚潰瘍	0	0	1 (0.5)
蕁麻疹	3 (2.2)	0	4 (1.8)
外科および内科処置	0	2 (1.0)	0
人工流産	0	2 (1.0)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) (PYS=135.0) Events (E/100PY)	UPA 15 mg QD (N=250) (PYS=199.4) Events (E/100PY)	UPA 30 mg QD (N=251) (PYS=218.5) Events (E/100PY)
血管障害	4 (3.0)	9 (4.5)	11 (5.0)
大動脈瘤	0	1 (0.5)	0
大動脈硬化症	0	0	1 (0.5)
出血性静脈瘤	0	1 (0.5)	0
深部静脈血栓症	0	0	2 (0.9)
血腫	0	0	1 (0.5)
高血圧	2 (1.5)	7 (3.5)	6 (2.7)
低血圧	1 (0.7)	0	0
末梢動脈閉塞性疾患	0	0	1 (0.5)
静脈血栓症	1 (0.7)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表5

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STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
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TABLE 14.3__1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
Any adverse event	84 (34.3)	87 (34.8)	96 (38.2)
血液およびリンパ系障害	14 (5.7)	6 (2.4)	9 (3.6)
貧血	6 (2.4)	1 (0.4)	4 (1.6)
好酸球増加症	1 (0.4)	0	0
白血球減少症	3 (1.2)	3 (1.2)	1 (0.4)
リンパ球増加症	1 (0.4)	0	0
リンパ球減少症	2 (0.8)	1 (0.4)	1 (0.4)
好中球減少症	3 (1.2)	2 (0.8)	5 (2.0)
血小板減少症	1 (0.4)	0	0
心臓障害	0	0	1 (0.4)
洞性徐脈	0	0	1 (0.4)
耳および迷路障害	1 (0.4)	0	0
耳部腫脹	1 (0.4)	0	0
眼障害	2 (0.8)	2 (0.8)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
眼障害 (Cont.)			
眼部腫脹	0	1 (0.4)	0
眼瞼障害	1 (0.4)	0	0
眼充血	0	1 (0.4)	0
眼窩周囲腫脹	1 (0.4)	0	0
胃腸障害	30 (12.2)	10 (4.0)	13 (5.2)
腹部膨満	1 (0.4)	0	2 (0.8)
腹痛	0	0	1 (0.4)
上腹部痛	1 (0.4)	0	0
肛門の炎症	0	0	1 (0.4)
アフタ性潰瘍	0	0	1 (0.4)
大腸炎	1 (0.4)	1 (0.4)	0
潰瘍性大腸炎	23 (9.4)	6 (2.4)	3 (1.2)
結腸異形成	0	1 (0.4)	0
便秘	1 (0.4)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
胃腸障害 (Cont.)			
消化不良	1 (0.4)	1 (0.4)	1 (0.4)
鼓腸	0	0	2 (0.8)
胃食道逆流性疾患	0	1 (0.4)	0
悪心	2 (0.8)	0	3 (1.2)
非感染性歯肉炎	0	0	1 (0.4)
口腔障害	0	0	1 (0.4)
膵炎	1 (0.4)	0	0
直腸分泌物	0	0	1 (0.4)
直腸出血	1 (0.4)	0	0
口内炎	1 (0.4)	0	1 (0.4)
一般・全身障害および投与部位の状態	6 (2.4)	2 (0.8)	8 (3.2)
薬効欠如	1 (0.4)	0	0
疲労	2 (0.8)	2 (0.8)	0
インフルエンザ様疾患	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
倦怠感	0	0	1 (0.4)
腫瘤	0	0	1 (0.4)
小結節	0	0	1 (0.4)
末梢腫脹	0	0	1 (0.4)
発熱	2 (0.8)	0	2 (0.8)
異物感	1 (0.4)	0	0
腫脹	0	0	1 (0.4)
肝胆道系障害	2 (0.8)	3 (1.2)	2 (0.8)
薬物性肝障害	0	1 (0.4)	1 (0.4)
肝機能異常	2 (0.8)	0	0
高トランスアミナーゼ血症	0	1 (0.4)	0
肝障害	0	0	1 (0.4)
肝損傷	0	1 (0.4)	0
感染症および寄生虫症	29 (11.8)	34 (13.6)	40 (15.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
細菌性関節炎	0	1 (0.4)	0
細菌性膣症	1 (0.4)	0	0
気管支炎	1 (0.4)	2 (0.8)	0
感染性滑液包炎	0	0	1 (0.4)
クロストリジウム・ディフィシレ感染	1 (0.4)	0	1 (0.4)
結膜炎	0	0	1 (0.4)
ＣＯＶＩＤ－１９	2 (0.8)	0	1 (0.4)
ＣＯＶＩＤ－１９肺炎	0	0	1 (0.4)
毛嚢虫症	0	3 (1.2)	2 (0.8)
皮膚糸状菌症	1 (0.4)	0	0
耳感染	0	1 (0.4)	0
毛包炎	1 (0.4)	0	4 (1.6)
皮膚真菌感染	0	0	1 (0.4)
せつ	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
胃腸炎	1 (0.4)	0	0
ヘモフィルス感染	1 (0.4)	0	0
ヘルペス性皮膚炎	0	1 (0.4)	0
帯状疱疹	0	9 (3.6)	12 (4.8)
帯状疱疹性髄膜炎	0	0	1 (0.4)
感染性皮膚嚢腫	0	1 (0.4)	0
インフルエンザ	0	2 (0.8)	2 (0.8)
潜伏結核	0	0	1 (0.4)
上咽頭炎	5 (2.0)	9 (3.6)	4 (1.6)
爪真菌症	1 (0.4)	1 (0.4)	1 (0.4)
口腔カンジダ症	1 (0.4)	0	0
口腔ヘルペス	1 (0.4)	0	2 (0.8)
咽頭炎	0	2 (0.8)	1 (0.4)
レンサ球菌性咽頭炎	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
胸膜感染	0	0	1 (0.4)
ニューモシスチス・イロベチイ肺炎	1 (0.4)	0	0
肺炎	2 (0.8)	0	0
クリプトコッカス性肺炎	0	0	2 (0.8)
歯髄炎	0	0	1 (0.4)
腎盂腎炎	1 (0.4)	1 (0.4)	0
ウイルス性気道感染	1 (0.4)	0	0
鼻炎	0	0	1 (0.4)
セラチア感染	1 (0.4)	0	0
副鼻腔炎	1 (0.4)	1 (0.4)	1 (0.4)
ブドウ球菌感染	1 (0.4)	0	0
白癬感染	1 (0.4)	0	0
足部白癬	1 (0.4)	0	0
癜風	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
扁桃炎	0	1 (0.4)	1 (0.4)
歯膿瘍	0	1 (0.4)	0
歯感染	0	0	2 (0.8)
上気道感染	4 (1.6)	1 (0.4)	4 (1.6)
尿路感染	3 (1.2)	2 (0.8)	1 (0.4)
水痘帯状疱疹ウイルス感染	0	1 (0.4)	0
ウイルス感染	0	0	2 (0.8)
ウイルス性上気道感染	1 (0.4)	0	1 (0.4)
外陰部腟カンジダ症	0	1 (0.4)	0
傷害、中毒および処置合併症	1 (0.4)	0	1 (0.4)
挫傷	0	0	1 (0.4)
肋骨骨折	1 (0.4)	0	0
臨床検査	12 (4.9)	29 (11.6)	38 (15.1)
アラニンアミノトランスフェラーゼ増加	1 (0.4)	6 (2.4)	5 (2.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
臨床検査 (Cont.)			
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.8)	7 (2.8)	3 (1.2)
血中アルブミン増加	0	1 (0.4)	1 (0.4)
血中ビリルビン増加	0	2 (0.8)	2 (0.8)
血中カルシウム増加	0	1 (0.4)	0
血中コレステロール減少	0	1 (0.4)	0
血中コレステロール増加	0	2 (0.8)	3 (1.2)
血中クレアチンホスホキナーゼ増加	4 (1.6)	10 (4.0)	13 (5.2)
血中クレアチニン増加	0	0	3 (1.2)
血中カリウム減少	0	1 (0.4)	0
血中トリグリセリド異常	0	1 (0.4)	0
尿中血陽性	0	0	1 (0.4)
γーグルタミルトランスフェラーゼ増加	1 (0.4)	2 (0.8)	0
糸球体濾過率減少	1 (0.4)	1 (0.4)	0
顆粒球数減少	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
臨床検査 (Cont.)			
握力低下	0	1 (0.4)	0
ヘモグロビン減少	1 (0.4)	0	1 (0.4)
肝酵素上昇	0	1 (0.4)	1 (0.4)
Ｂ型肝炎ＤＮＡ測定陽性	0	0	1 (0.4)
高比重リポ蛋白増加	0	2 (0.8)	1 (0.4)
肝機能検査値上昇	0	0	1 (0.4)
低比重リポ蛋白減少	0	1 (0.4)	0
低比重リポ蛋白増加	0	1 (0.4)	4 (1.6)
リンパ球数減少	2 (0.8)	5 (2.0)	2 (0.8)
リンパ球数増加	1 (0.4)	1 (0.4)	2 (0.8)
リンパ球百分率減少	0	1 (0.4)	0
単球数増加	0	1 (0.4)	0
好中球数減少	2 (0.8)	4 (1.6)	7 (2.8)
好中球数増加	2 (0.8)	1 (0.4)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
臨床検査 (Cont.)			
血小板数減少	1 (0.4)	0	0
血小板数増加	0	0	2 (0.8)
総蛋白増加	0	0	1 (0.4)
尿中蛋白陽性	1 (0.4)	1 (0.4)	1 (0.4)
赤血球数減少	0	1 (0.4)	2 (0.8)
体重増加	0	0	1 (0.4)
白血球数減少	1 (0.4)	3 (1.2)	5 (2.0)
白血球数増加	0	1 (0.4)	0
代謝および栄養障害	1 (0.4)	7 (2.8)	5 (2.0)
脂質異常症	0	1 (0.4)	1 (0.4)
高コレステロール血症	0	3 (1.2)	2 (0.8)
高血糖	0	2 (0.8)	0
高リパーゼ血症	1 (0.4)	0	0
高脂血症	0	1 (0.4)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
代謝および栄養障害 (Cont.)			
高尿酸血症	0	0	1 (0.4)
筋骨格系および結合組織障害	9 (3.7)	1 (0.4)	5 (2.0)
関節痛	3 (1.2)	0	3 (1.2)
関節障害	3 (1.2)	0	1 (0.4)
背部痛	2 (0.8)	0	0
骨痛	0	0	1 (0.4)
筋骨格系胸痛	1 (0.4)	0	0
筋骨格痛	1 (0.4)	1 (0.4)	0
筋肉痛	2 (0.8)	0	0
四肢痛	0	0	1 (0.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4)	0	3 (1.2)
基底細胞癌	0	0	2 (0.8)
線維性組織球腫	0	0	1 (0.4)
浸潤性乳癌	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
神経系障害	6 (2.4)	3 (1.2)	2 (0.8)
浮動性めまい	1 (0.4)	1 (0.4)	1 (0.4)
頭痛	6 (2.4)	1 (0.4)	1 (0.4)
感覚鈍麻	0	1 (0.4)	0
精神障害	0	0	4 (1.6)
うつ病	0	0	1 (0.4)
不眠症	0	0	3 (1.2)
腎および尿路障害	1 (0.4)	2 (0.8)	2 (0.8)
急性腎障害	0	0	1 (0.4)
血尿	0	1 (0.4)	0
水腎症	1 (0.4)	0	0
蛋白尿	1 (0.4)	0	0
腎仙痛	0	0	1 (0.4)
腎機能障害	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
生殖系および乳房障害	2 (0.8)	1 (0.4)	2 (0.8)
バルトリン嚢腫	1 (0.4)	0	0
良性前立腺肥大症	0	0	1 (0.4)
前立腺腫瘤	0	0	1 (0.4)
精液変色	0	0	1 (0.4)
腟分泌物	0	1 (0.4)	0
外陰腟そう痒症	1 (0.4)	0	0
呼吸器、胸郭および縦隔障害	6 (2.4)	2 (0.8)	7 (2.8)
気管支拡張症	1 (0.4)	0	0
咳嗽	0	0	1 (0.4)
労作性呼吸困難	0	0	1 (0.4)
間質性肺疾患	1 (0.4)	0	0
鼻閉	1 (0.4)	0	1 (0.4)
非感染性気管支炎	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
口腔咽頭痛	3 (1.2)	0	2 (0.8)
湿性咳嗽	0	1 (0.4)	0
肺塞栓症	0	1 (0.4)	0
上気道の炎症	1 (0.4)	0	0
上気道咳症候群	0	0	1 (0.4)
皮膚および皮下組織障害	20 (8.2)	19 (7.6)	18 (7.2)
ざ瘡	2 (0.8)	3 (1.2)	3 (1.2)
脱毛症	0	2 (0.8)	1 (0.4)
皮膚炎	1 (0.4)	0	0
アトピー性皮膚炎	1 (0.4)	0	0
接触皮膚炎	0	1 (0.4)	0
皮膚乾燥	2 (0.8)	0	0
異汗性湿疹	1 (0.4)	0	0
斑状出血	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
皮膚および皮下組織障害 (Cont.)			
湿疹	2 (0.8)	0	0
紅斑	2 (0.8)	2 (0.8)	1 (0.4)
結節性紅斑	1 (0.4)	0	0
神経皮膚炎	1 (0.4)	0	0
寝汗	0	1 (0.4)	0
爪破損	1 (0.4)	0	1 (0.4)
脂肪織炎	0	1 (0.4)	0
丘疹	0	0	1 (0.4)
光線性皮膚症	1 (0.4)	0	0
そう痒症	4 (1.6)	1 (0.4)	1 (0.4)
発疹	3 (1.2)	4 (1.6)	10 (4.0)
紅斑性皮疹	0	1 (0.4)	0
斑状皮疹	0	1 (0.4)	0
斑状丘疹状皮疹	1 (0.4)	1 (0.4)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
皮膚および皮下組織障害 (Cont.)			
酒さ	0	2 (0.8)	0
脂漏性皮膚炎	0	0	1 (0.4)
皮膚びらん	1 (0.4)	0	0
皮膚剥脱	1 (0.4)	0	0
皮膚潰瘍	0	0	1 (0.4)
蕁麻疹	1 (0.4)	0	0
血管障害	2 (0.8)	1 (0.4)	1 (0.4)
高血圧	1 (0.4)	1 (0.4)	1 (0.4)
静脈血栓症	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表6

TABLE 14.3__1.3.3.3

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
Any adverse event	23 (9.4)	14 (5.6)	20 (8.0)
血液およびリンパ系障害	2 (0.8)	0	2 (0.8)
貧血	0	0	1 (0.4)
鉄欠乏性貧血	1 (0.4)	0	0
好中球減少症	1 (0.4)	0	1 (0.4)
心臓障害	1 (0.4)	0	2 (0.8)
急性心筋梗塞	1 (0.4)	0	0
慢性左室不全	0	0	1 (0.4)
上室性頻脈	0	0	1 (0.4)
眼障害	0	1 (0.4)	0
白内障	0	1 (0.4)	0
胃腸障害	11 (4.5)	1 (0.4)	2 (0.8)
腹部腫瘤	1 (0.4)	0	0
痔瘻	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3.3

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
胃腸障害 (Cont.)			
潰瘍性大腸炎	9 (3.7)	1 (0.4)	1 (0.4)
大腸穿孔	1 (0.4)	0	0
膵炎	1 (0.4)	0	0
一般・全身障害および投与部位の状態	1 (0.4)	0	0
発熱	1 (0.4)	0	0
肝胆道系障害	0	0	1 (0.4)
肝障害	0	0	1 (0.4)
感染症および寄生虫症	4 (1.6)	7 (2.8)	7 (2.8)
腹部膿瘍	1 (0.4)	0	0
急性心内膜炎	1 (0.4)	0	0
肛門膿瘍	0	1 (0.4)	0
乳房膿瘍	0	1 (0.4)	0
感染性滑液包炎	0	0	1 (0.4)
クロストリジウム・ディフィシレ感染	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3.3

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
ＣＯＶＩＤ－１９肺炎	0	0	2 (0.8)
単純ヘルペス	0	1 (0.4)	0
帯状疱疹	0	1 (0.4)	0
帯状疱疹性髄膜炎	0	0	1 (0.4)
インフルエンザ	0	1 (0.4)	0
大腸感染	0	1 (0.4)	0
レンサ球菌性咽頭炎	0	0	1 (0.4)
ニューモシスチス・イロベチイ肺炎	1 (0.4)	0	0
肺炎	1 (0.4)	0	0
クリプトコッカス性肺炎	0	0	2 (0.8)
傷害、中毒および処置合併症	0	1 (0.4)	0
肺挫傷	0	1 (0.4)	0
胸椎骨折	0	1 (0.4)	0
臨床検査	1 (0.4)	1 (0.4)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3.3

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
臨床検査 (Cont.)			
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (0.4)
血中クレアチンホスホキナーゼ増加	0	0	1 (0.4)
リンパ球数減少	0	1 (0.4)	0
リンパ球百分率減少	0	1 (0.4)	0
好中球数減少	1 (0.4)	0	0
筋骨格系および結合組織障害	0	1 (0.4)	0
関節炎	0	1 (0.4)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4)	1 (0.4)	2 (0.8)
結腸腺癌	0	0	1 (0.4)
浸潤性乳癌	1 (0.4)	1 (0.4)	0
小細胞癌	0	0	1 (0.4)
神経系障害	1 (0.4)	0	1 (0.4)
頭痛	1 (0.4)	0	0
片頭痛	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3.3

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
神経系障害 (Cont.)			
くも膜下出血	0	0	1 (0.4)
精神障害	1 (0.4)	0	1 (0.4)
不安	1 (0.4)	0	1 (0.4)
うつ病	1 (0.4)	0	1 (0.4)
精神障害	1 (0.4)	0	0
自殺念慮	1 (0.4)	0	0
生殖系および乳房障害	0	0	1 (0.4)
子宮頚部上皮異形成	0	0	1 (0.4)
呼吸器、胸郭および縦隔障害	0	1 (0.4)	1 (0.4)
急性呼吸不全	0	0	1 (0.4)
肺塞栓症	0	1 (0.4)	0
皮膚および皮下組織障害	1 (0.4)	0	0
結節性紅斑	1 (0.4)	0	0
外科および内科処置	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3.3

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
外科および内科処置 (Cont.)			
人工流産	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表7

[redacted]20[redacted] 11:17 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.3.1.3

Subjects with Treatment-Emergent Adverse Events Leading to Death
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
Any adverse event	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表8

[redacted]20[redacted] 11:17 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL

TABLE 14.3__2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
Any adverse event	23 (9.4)	21 (8.4)	21 (8.4)
血液およびリンパ系障害	1 (0.4)	0	1 (0.4)
貧血	0	0	1 (0.4)
鉄欠乏性貧血	1 (0.4)	0	0
心臓障害	2 (0.8)	0	0
急性心筋梗塞	1 (0.4)	0	0
心房細動	1 (0.4)	0	0
眼障害	0	1 (0.4)	0
白内障	0	1 (0.4)	0
胃腸障害	7 (2.9)	1 (0.4)	3 (1.2)
痔瘻	0	0	1 (0.4)
大腸炎	1 (0.4)	0	0
潰瘍性大腸炎	5 (2.0)	1 (0.4)	2 (0.8)
膵炎	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
一般・全身障害および投与部位の状態	2 (0.8)	0	0
医療機器に対する不耐性	1 (0.4)	0	0
発熱	1 (0.4)	0	0
肝胆道系障害	0	0	1 (0.4)
肝障害	0	0	1 (0.4)
感染症および寄生虫症	8 (3.3)	9 (3.6)	7 (2.8)
腹部膿瘍	1 (0.4)	0	0
急性心内膜炎	1 (0.4)	0	0
肛門膿瘍	0	1 (0.4)	0
細菌性関節炎	0	1 (0.4)	0
乳房膿瘍	0	1 (0.4)	0
気管支炎	0	1 (0.4)	0
感染性滑液包炎	0	0	1 (0.4)
クロストリジウム・ディフィシレ感染	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
ＣＯＶＩＤ－１９	0	0	1 (0.4)
ＣＯＶＩＤ－１９肺炎	1 (0.4)	1 (0.4)	2 (0.8)
帯状疱疹	0	1 (0.4)	0
帯状疱疹性髄膜炎	0	0	1 (0.4)
インフルエンザ	0	1 (0.4)	0
大腸感染	0	1 (0.4)	0
乳腺炎	0	1 (0.4)	0
ニューモシスチス・イロベチイ肺炎	1 (0.4)	0	0
肺炎	3 (1.2)	0	0
クリプトコッカス性肺炎	0	0	2 (0.8)
扁桃炎	1 (0.4)	0	0
傷害、中毒および処置合併症	0	2 (0.8)	0
肺挫傷	0	1 (0.4)	0
皮膚裂傷	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
傷害、中毒および処置合併症 (Cont.)			
胸椎骨折	0	1 (0.4)	0
筋骨格系および結合組織障害	0	1 (0.4)	1 (0.4)
関節炎	0	1 (0.4)	0
軟骨軟化症	0	0	1 (0.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4)	1 (0.4)	2 (0.8)
結腸腺癌	0	0	1 (0.4)
浸潤性乳癌	1 (0.4)	1 (0.4)	0
小細胞癌	0	0	1 (0.4)
神経系障害	0	0	1 (0.4)
くも膜下出血	0	0	1 (0.4)
精神障害	1 (0.4)	0	1 (0.4)
不安	1 (0.4)	0	1 (0.4)
うつ病	1 (0.4)	0	1 (0.4)
精神障害	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
精神障害 (Cont.)			
自殺念慮	1 (0.4)	0	0
腎および尿路障害	0	1 (0.4)	0
尿閉	0	1 (0.4)	0
生殖系および乳房障害	0	0	2 (0.8)
子宮頚部上皮異形成	0	0	2 (0.8)
呼吸器、胸郭および縦隔障害	1 (0.4)	3 (1.2)	2 (0.8)
急性呼吸不全	1 (0.4)	0	1 (0.4)
慢性閉塞性肺疾患	0	1 (0.4)	0
間質性肺疾患	1 (0.4)	0	0
非感染性気管支炎	0	0	1 (0.4)
肺塞栓症	0	2 (0.8)	0
皮膚および皮下組織障害	1 (0.4)	1 (0.4)	0
結節性紅斑	1 (0.4)	0	0
脂肪織炎	0	1 (0.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1.3

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
外科および内科処置	0	2 (0.8)	0
人工流産	0	2 (0.8)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表9

[redacted]20[redacted] 11:17 <[redacted] >
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 4

TABLE 14.3__2.2.1.3

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
Any adverse event	25 (10.2)	10 (4.0)	18 (7.2)
心臓障害	1 (0.4)	0	0
急性心筋梗塞	1 (0.4)	0	0
胃腸障害	15 (6.1)	6 (2.4)	3 (1.2)
潰瘍性大腸炎	13 (5.3)	5 (2.0)	3 (1.2)
腸閉塞	0	1 (0.4)	0
大腸穿孔	1 (0.4)	0	0
膵炎	1 (0.4)	0	0
一般・全身障害および投与部位の状態	1 (0.4)	0	0
発熱	1 (0.4)	0	0
肝胆道系障害	0	0	1 (0.4)
薬物性肝障害	0	0	1 (0.4)
感染症および寄生虫症	3 (1.2)	1 (0.4)	5 (2.0)
腹部膿瘍	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.2.1.3

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
感染症および寄生虫症 (Cont.)			
急性心内膜炎	1 (0.4)	0	0
細菌性関節炎	0	1 (0.4)	0
ＣＯＶＩＤ－１９肺炎	0	0	1 (0.4)
帯状疱疹	0	0	2 (0.8)
帯状疱疹性髄膜炎	0	0	1 (0.4)
肺炎	1 (0.4)	0	0
クリプトコッカス性肺炎	0	0	2 (0.8)
臨床検査	0	0	4 (1.6)
血中クレアチンホスホキナーゼ増加	0	0	1 (0.4)
ヘモグロビン減少	0	0	1 (0.4)
Ｂ型肝炎ＤＮＡ測定陽性	0	0	1 (0.4)
好中球数減少	0	0	1 (0.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.4)	1 (0.4)	2 (0.8)
結腸腺癌	0	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.2.1.3

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
浸潤性乳癌	1 (0.4)	1 (0.4)	0
小細胞癌	0	0	1 (0.4)
腎および尿路障害	0	1 (0.4)	0
腎機能障害	0	1 (0.4)	0
呼吸器、胸郭および縦隔障害	1 (0.4)	0	1 (0.4)
間質性肺疾患	1 (0.4)	0	0
肺浸潤	0	0	1 (0.4)
皮膚および皮下組織障害	2 (0.8)	2 (0.8)	1 (0.4)
紅斑	0	1 (0.4)	0
結節性紅斑	1 (0.4)	0	0
脂肪織炎	0	1 (0.4)	0
そう痒症	1 (0.4)	0	0
脂漏性皮膚炎	0	0	1 (0.4)
血管障害	2 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.2.1.3

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=245) n (%)	UPA 15 mg QD (N=250) n (%)	UPA 30 mg QD (N=251) n (%)
血管障害 (Cont.)			
深部静脈血栓症	0	0	1 (0.4)
高血圧	1 (0.4)	0	0
静脈血栓症	1 (0.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表10

[redacted]20[redacted] 11:57 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__1.1.1.3_J

Overview of Treatment-Emergent Adverse Events and All Deaths
(SA_C Population - Japan Analysis Set)

	Placebo (N=41) n (%) [SSA%]	UPA 15 mg QD (N=45) n (%) [SSA%]	UPA 30 mg QD (N=45) n (%) [SSA%]	- Treatment Comparison (95% CI) [A] - UPA 15 mg QD - Placebo	UPA 30 mg QD - Placebo
Subjects with:					
Any adverse event (AE)	35 (85.4) [85.1]	34 (75.6) [75.7]	41 (91.1) [91.2]	-9.4 (-26.3, 7.6)	6.2 (-8.2, 20.5)
Any AE with reasonable possibility of being related to study drug$	13 (31.7) [31.5]	16 (35.6) [36.4]	22 (48.9) [48.9]	4.9 (-14.9, 24.6)	17.3 (-2.9, 37.5)
Any severe AE	6 (14.6) [14.6]	2 (4.4) [4.6]	3 (6.7) [6.7]	-10.0 (-23.4, 3.3)	-7.9 (-21.7, 5.9)
Any serious AE	5 (12.2) [12.1]	3 (6.7) [7.0]	3 (6.7) [6.7]	-5.0 (-18.4, 8.4)	-5.4 (-18.6, 7.8)
Any AE leading to discontinuation of study drug	4 (9.8) [9.7]	1 (2.2) [2.5]	5 (11.1) [10.9]	-7.3 (-18.8, 4.3)	1.2 (-12.5, 14.8)
Any AE leading to death	0	0	0	0.0	0.0
Deaths#	0	0	0	0.0	0.0
Occurring <= 30 days after last dose	0	0	0	0.0	0.0
Occurring > 30 days after last dose	0	0	0	0.0	0.0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.

Program Source Code: [redacted]

表11

[redacted]20[redacted] 11:57 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.2.3_J

Overview of Treatment-Emergent Adverse Events and All Deaths per 100 Patient-Years (PYS)
(SA_C Population - Japan Analysis Set)

	Placebo (N=41) (PYS=23.2) Events (E/100PY) [SSA E/100PY]	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY) [SSA E/100PY]	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY) [SSA E/100PY]	-- Treatment Comparison (95% CI) [A] -- UPA 15 mg QD - Placebo	UPA 30 mg QD - Placebo
Any treatment-emergent:					
Any adverse event (AE)	122 (525.5) [520.8]	118 (285.8) [288.3]	145 (359.7) [360.9]	-232.5 (-339.1, -126.0)	-159.9 (-269.8, -50.0)
Any AE with reasonable possibility of being related to study drug$	28 (120.6) [115.9]	31 (75.1) [79.5]	52 (129.0) [127.6]	-36.4 (-87.8, 15.0)	11.7 (-43.6, 67.1)
Any severe AE	6 (25.8) [25.3]	3 (7.3) [7.3]	3 (7.4) [7.5]	-18.0 (-39.9, 3.9)	-17.7 (-39.7, 4.3)
Any serious AE	5 (21.5) [20.7]	5 (12.1) [12.8]	3 (7.4) [7.5]	-7.9 (-29.3, 13.5)	-13.2 (-33.3, 6.9)
Any AE leading to discontinuation of study drug	4 (17.2) [16.8]	2 (4.8) [5.5]	6 (14.9) [14.8]	-11.3 (-29.6, 6.9)	-2.0 (-22.4, 18.3)
Any AE leading to death	0	0	0	0.0	0.0
Deaths#	0	0	0	0.0	0.0
Occurring <= 30 days after last dose	0	0	0	0.0	0.0
Occurring > 30 days after last dose	0	0	0	0.0	0.0

Note: PYS is defined as the sum of the study drug exposure of all subjects, normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.
$ As assessed by investigator.
# Includes non treatment emergent deaths.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.

Program Source Code: [redacted]

表12

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 14

TABLE 14.3__1.2.1.1.3_J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
Any adverse event	35 (85.4)	34 (75.6)	41 (91.1)
血液およびリンパ系障害	7 (17.1)	1 (2.2)	7 (15.6)
貧血	2 (4.9)	1 (2.2)	2 (4.4)
鉄欠乏性貧血	3 (7.3)	0	0
白血球減少症	1 (2.4)	0	0
リンパ球減少症	1 (2.4)	0	0
小球性貧血	0	0	1 (2.2)
好中球減少症	1 (2.4)	0	4 (8.9)
血小板減少症	1 (2.4)	0	0
心臓障害	0	1 (2.2)	0
不整脈	0	1 (2.2)	0
耳および迷路障害	0	2 (4.4)	1 (2.2)
感音性難聴	0	1 (2.2)	0
片耳難聴	0	0	1 (2.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
耳および迷路障害 (Cont.)			
回転性めまい	0	1 (2.2)	0
眼障害	3 (7.3)	2 (4.4)	3 (6.7)
眼瞼炎	1 (2.4)	0	0
白内障	0	1 (2.2)	0
霰粒腫	0	0	1 (2.2)
アレルギー性結膜炎	1 (2.4)	1 (2.2)	1 (2.2)
ドライアイ	0	0	1 (2.2)
角膜炎	0	0	1 (2.2)
潰瘍性角膜炎	1 (2.4)	0	0
胃腸障害	21 (51.2)	9 (20.0)	7 (15.6)
腹部膨満	1 (2.4)	0	0
腹痛	0	1 (2.2)	0
上腹部痛	1 (2.4)	1 (2.2)	0
裂肛	0	1 (2.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
胃腸障害 (Cont.)			
肛門そう痒症	1 (2.4)	0	0
アフタ性潰瘍	1 (2.4)	0	0
虚血性大腸炎	0	1 (2.2)	0
潰瘍性大腸炎	13 (31.7)	1 (2.2)	0
便秘	0	1 (2.2)	3 (6.7)
齲歯	0	1 (2.2)	0
歯嚢胞	0	0	1 (2.2)
胃食道逆流性疾患	1 (2.4)	0	0
歯肉腫脹	1 (2.4)	0	0
舌痛	1 (2.4)	0	0
痔出血	1 (2.4)	0	0
痔核	1 (2.4)	1 (2.2)	0
血栓性痔核	1 (2.4)	0	0
鼡径ヘルニア	0	1 (2.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
胃腸障害 (Cont.)			
口腔嚢胞	1 (2.4)	0	0
悪心	1 (2.4)	0	0
膵炎	1 (2.4)	0	0
歯周病	1 (2.4)	0	1 (2.2)
直腸炎	1 (2.4)	0	0
口内炎	2 (4.9)	1 (2.2)	2 (4.4)
歯の脱落	0	0	1 (2.2)
一般・全身障害および投与部位の状態	3 (7.3)	2 (4.4)	9 (20.0)
胸痛	0	0	1 (2.2)
疲労	0	0	1 (2.2)
炎症	0	0	1 (2.2)
注射部位疼痛	0	0	1 (2.2)
倦怠感	1 (2.4)	0	0
非心臓性胸痛	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
末梢性浮腫	1 (2.4)	0	1 (2.2)
発熱	1 (2.4)	2 (4.4)	7 (15.6)
肝胆道系障害	2 (4.9)	1 (2.2)	0
肝機能異常	1 (2.4)	0	0
脂肪肝	0	1 (2.2)	0
肝損傷	1 (2.4)	0	0
免疫系障害	0	1 (2.2)	1 (2.2)
季節性アレルギー	0	1 (2.2)	1 (2.2)
感染症および寄生虫症	16 (39.0)	22 (48.9)	26 (57.8)
ダニ皮膚炎	0	2 (4.4)	0
細菌性関節炎	0	1 (2.2)	0
細菌性膣症	1 (2.4)	0	0
蜂巣炎	0	1 (2.2)	0
結膜炎	0	1 (2.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
感染症および寄生虫症 (Cont.)			
膀胱炎	0	1 (2.2)	2 (4.4)
感染性腸炎	0	0	1 (2.2)
毛包炎	1 (2.4)	1 (2.2)	3 (6.7)
胃腸炎	1 (2.4)	2 (4.4)	0
歯肉炎	0	1 (2.2)	0
ヘルペス性皮膚炎	0	1 (2.2)	0
帯状疱疹	0	4 (8.9)	5 (11.1)
帯状疱疹性髄膜炎	0	0	1 (2.2)
麦粒腫	2 (4.9)	0	1 (2.2)
インフルエンザ	0	1 (2.2)	2 (4.4)
大腸感染	0	1 (2.2)	0
潜伏結核	0	0	1 (2.2)
伝染性軟属腫	1 (2.4)	0	0
上咽頭炎	5 (12.2)	8 (17.8)	11 (24.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
感染症および寄生虫症 (Cont.)			
口腔カンジダ症	1 (2.4)	0	0
口腔ヘルペス	0	2 (4.4)	4 (8.9)
外耳炎	1 (2.4)	0	0
歯周炎	1 (2.4)	0	1 (2.2)
咽頭炎	0	1 (2.2)	0
胸膜感染	0	0	1 (2.2)
ニューモシスチス・イロベチイ肺炎	1 (2.4)	0	0
肺炎	1 (2.4)	0	0
白癬感染	1 (2.4)	0	0
足部白癬	1 (2.4)	1 (2.2)	0
扁桃炎	0	0	1 (2.2)
上気道感染	0	3 (6.7)	1 (2.2)
傷害、中毒および処置合併症	3 (7.3)	2 (4.4)	1 (2.2)
骨挫傷	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
傷害、中毒および処置合併症 (Cont.)			
挫傷	0	0	1 (2.2)
熱中症	1 (2.4)	0	0
関節損傷	0	1 (2.2)	0
肺挫傷	0	1 (2.2)	0
肋骨骨折	1 (2.4)	0	0
皮下血腫	1 (2.4)	0	0
胸椎骨折	0	1 (2.2)	0
臨床検査	4 (9.8)	12 (26.7)	16 (35.6)
アラニンアミノトランスフェラーゼ増加	0	1 (2.2)	4 (8.9)
アミラーゼ増加	1 (2.4)	1 (2.2)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (4.4)	3 (6.7)
血中コレステロール増加	0	0	1 (2.2)
血中クレアチンホスホキナーゼ増加	1 (2.4)	5 (11.1)	6 (13.3)
血中クレアチニン増加	1 (2.4)	0	1 (2.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
臨床検査 (Cont.)			
γ-グルタミルトランスフェラーゼ増加	0	3 (6.7)	0
高比重リポ蛋白増加	0	2 (4.4)	0
リパーゼ増加	0	1 (2.2)	0
リンパ球数減少	0	1 (2.2)	2 (4.4)
リンパ球数増加	1 (2.4)	0	0
リンパ球百分率増加	0	1 (2.2)	0
好中球数減少	1 (2.4)	1 (2.2)	4 (8.9)
好中球数増加	0	0	1 (2.2)
体重増加	0	1 (2.2)	0
白血球数減少	1 (2.4)	1 (2.2)	1 (2.2)
代謝および栄養障害	2 (4.9)	4 (8.9)	1 (2.2)
脂質異常症	0	3 (6.7)	0
高コレステロール血症	0	1 (2.2)	1 (2.2)
高リパーゼ血症	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
代謝および栄養障害 (Cont.)			
低ナトリウム血症	1 (2.4)	0	0
筋骨格系および結合組織障害	9 (22.0)	7 (15.6)	3 (6.7)
関節痛	4 (9.8)	2 (4.4)	1 (2.2)
関節障害	1 (2.4)	0	0
背部痛	3 (7.3)	3 (6.7)	0
腰部脊柱管狭窄症	0	0	1 (2.2)
筋骨格系胸痛	1 (2.4)	0	0
筋骨格痛	0	1 (2.2)	0
筋肉痛	0	1 (2.2)	0
変形性関節症	1 (2.4)	0	0
骨壊死	0	1 (2.2)	0
四肢痛	1 (2.4)	0	0
関節周囲炎	0	0	1 (2.2)
肩回旋筋腱板症候群	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
筋骨格系および結合組織障害 (Cont.)			
腱鞘炎	1 (2.4)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (2.4)	0	1 (2.2)
結腸腺癌	0	0	1 (2.2)
大腸腺腫	1 (2.4)	0	0
神経系障害	2 (4.9)	2 (4.4)	5 (11.1)
浮動性めまい	0	0	1 (2.2)
てんかん	1 (2.4)	0	0
頭痛	0	2 (4.4)	2 (4.4)
感覚鈍麻	0	1 (2.2)	1 (2.2)
片頭痛	1 (2.4)	0	0
末梢性ニューロパチー	1 (2.4)	0	0
くも膜下出血	0	0	1 (2.2)
精神障害	3 (7.3)	1 (2.2)	2 (4.4)
不安障害	0	1 (2.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
精神障害 (Cont.)			
抑うつ気分	0	0	1 (2.2)
不眠症	3 (7.3)	0	2 (4.4)
腎および尿路障害	0	0	2 (4.4)
急性腎障害	0	0	1 (2.2)
尿管結石症	0	0	1 (2.2)
生殖系および乳房障害	2 (4.9)	2 (4.4)	0
機能不全性子宮出血	1 (2.4)	0	0
月経困難症	0	1 (2.2)	0
不規則月経	1 (2.4)	0	0
前立腺炎	0	1 (2.2)	0
呼吸器、胸郭および縦隔障害	3 (7.3)	3 (6.7)	3 (6.7)
咳嗽	0	1 (2.2)	0
しゃっくり	1 (2.4)	0	1 (2.2)
口腔咽頭痛	0	0	2 (4.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
アレルギー性鼻炎	0	1 (2.2)	0
上気道の炎症	2 (4.9)	1 (2.2)	0
皮膚および皮下組織障害	13 (31.7)	10 (22.2)	13 (28.9)
ざ瘡	3 (7.3)	1 (2.2)	3 (6.7)
皮脂欠乏症	0	0	1 (2.2)
皮膚炎	0	1 (2.2)	0
アトピー性皮膚炎	0	2 (4.4)	0
接触皮膚炎	1 (2.4)	0	0
湿疹	1 (2.4)	2 (4.4)	2 (4.4)
皮脂欠乏性湿疹	1 (2.4)	0	1 (2.2)
掌蹠膿疱症	0	1 (2.2)	0
脂肪織炎	0	1 (2.2)	0
光線過敏性反応	1 (2.4)	0	1 (2.2)
そう痒症	0	1 (2.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.1.3 J

Subjects with Treatment-Emergent Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
皮膚および皮下組織障害 (Cont.)			
壊疽性膿皮症	1 (2.4)	0	0
発疹	2 (4.9)	1 (2.2)	1 (2.2)
紅斑性皮疹	1 (2.4)	0	0
斑状丘疹状皮疹	0	0	1 (2.2)
脂漏性皮膚炎	4 (9.8)	2 (4.4)	1 (2.2)
蕁麻疹	0	0	4 (8.9)
血管障害	1 (2.4)	1 (2.2)	2 (4.4)
大動脈瘤	0	1 (2.2)	0
血腫	0	0	1 (2.2)
高血圧	0	0	1 (2.2)
静脈血栓症	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表13

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UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL

TABLE 14.3__1.2.1.2.3_J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
Any adverse event	122 (525.5)	118 (285.8)	145 (359.7)
血液およびリンパ系障害	10 (43.1)	1 (2.4)	7 (17.4)
貧血	3 (12.9)	1 (2.4)	2 (5.0)
鉄欠乏性貧血	3 (12.9)	0	0
白血球減少症	1 (4.3)	0	0
リンパ球減少症	1 (4.3)	0	0
小球性貧血	0	0	1 (2.5)
好中球減少症	1 (4.3)	0	4 (9.9)
血小板減少症	1 (4.3)	0	0
心臓障害	0	1 (2.4)	0
不整脈	0	1 (2.4)	0
耳および迷路障害	0	2 (4.8)	1 (2.5)
感音性難聴	0	1 (2.4)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
耳および迷路障害 (Cont.)			
片耳難聴	0	0	1 (2.5)
回転性めまい	0	1 (2.4)	0
眼障害	3 (12.9)	2 (4.8)	4 (9.9)
眼瞼炎	1 (4.3)	0	0
白内障	0	1 (2.4)	0
霰粒腫	0	0	1 (2.5)
アレルギー性結膜炎	1 (4.3)	1 (2.4)	1 (2.5)
ドライアイ	0	0	1 (2.5)
角膜炎	0	0	1 (2.5)
潰瘍性角膜炎	1 (4.3)	0	0
胃腸障害	30 (129.2)	11 (26.6)	10 (24.8)
腹部膨満	1 (4.3)	0	0
腹痛	0	1 (2.4)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
胃腸障害 (Cont.)			
上腹部痛	1 (4.3)	1 (2.4)	0
裂肛	0	1 (2.4)	0
肛門そう痒症	1 (4.3)	0	0
アフタ性潰瘍	1 (4.3)	0	0
虚血性大腸炎	0	1 (2.4)	0
潰瘍性大腸炎	13 (56.0)	1 (2.4)	0
便秘	0	1 (2.4)	3 (7.4)
齲歯	0	1 (2.4)	0
歯嚢胞	0	0	1 (2.5)
胃食道逆流性疾患	1 (4.3)	0	0
歯肉腫脹	1 (4.3)	0	0
舌痛	1 (4.3)	0	0
痔出血	1 (4.3)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
胃腸障害 (Cont.)			
痔核	1 (4.3)	2 (4.8)	0
血栓性痔核	1 (4.3)	0	0
鼠径ヘルニア	0	1 (2.4)	0
口腔嚢胞	1 (4.3)	0	0
悪心	1 (4.3)	0	0
膵炎	1 (4.3)	0	0
歯周病	1 (4.3)	0	1 (2.5)
直腸炎	1 (4.3)	0	0
口内炎	2 (8.6)	1 (2.4)	4 (9.9)
歯の脱落	0	0	1 (2.5)
一般・全身障害および投与部位の状態	4 (17.2)	2 (4.8)	13 (32.2)
胸痛	0	0	1 (2.5)
疲労	0	0	1 (2.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
一般・全身障害および投与部位の状態 (Cont.)			
炎症	0	0	1 (2.5)
注射部位疼痛	0	0	2 (5.0)
倦怠感	1 (4.3)	0	0
非心臓性胸痛	1 (4.3)	0	0
末梢性浮腫	1 (4.3)	0	1 (2.5)
発熱	1 (4.3)	2 (4.8)	7 (17.4)
肝胆道系障害	2 (8.6)	1 (2.4)	0
肝機能異常	1 (4.3)	0	0
脂肪肝	0	1 (2.4)	0
肝損傷	1 (4.3)	0	0
免疫系障害	0	1 (2.4)	1 (2.5)
季節性アレルギー	0	1 (2.4)	1 (2.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
感染症および寄生虫症	18 (77.5)	40 (96.9)	40 (99.2)
ダニ皮膚炎	0	2 (4.8)	0
細菌性関節炎	0	1 (2.4)	0
細菌性膣症	1 (4.3)	0	0
蜂巣炎	0	1 (2.4)	0
結膜炎	0	1 (2.4)	0
膀胱炎	0	1 (2.4)	3 (7.4)
感染性腸炎	0	0	1 (2.5)
毛包炎	1 (4.3)	1 (2.4)	3 (7.4)
胃腸炎	1 (4.3)	2 (4.8)	0
歯肉炎	0	1 (2.4)	0
ヘルペス性皮膚炎	0	1 (2.4)	0
帯状疱疹	0	4 (9.7)	5 (12.4)
帯状疱疹性髄膜炎	0	0	1 (2.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
麦粒腫	2 (8.6)	0	1 (2.5)
インフルエンザ	0	1 (2.4)	2 (5.0)
大腸感染	0	1 (2.4)	0
潜伏結核	0	0	1 (2.5)
伝染性軟属腫	1 (4.3)	0	0
上咽頭炎	5 (21.5)	14 (33.9)	15 (37.2)
口腔カンジダ症	1 (4.3)	0	0
口腔ヘルペス	0	4 (9.7)	4 (9.9)
外耳炎	1 (4.3)	0	0
歯周炎	1 (4.3)	0	1 (2.5)
咽頭炎	0	1 (2.4)	0
胸膜感染	0	0	1 (2.5)
ニューモシスチス・イロベチイ肺炎	1 (4.3)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
感染症および寄生虫症 (Cont.)			
肺炎	1 (4.3)	0	0
白癬感染	1 (4.3)	0	0
足部白癬	1 (4.3)	1 (2.4)	0
扁桃炎	0	0	1 (2.5)
上気道感染	0	3 (7.3)	1 (2.5)
傷害、中毒および処置合併症	4 (17.2)	3 (7.3)	1 (2.5)
骨挫傷	1 (4.3)	0	0
挫傷	0	0	1 (2.5)
熱中症	1 (4.3)	0	0
関節損傷	0	1 (2.4)	0
肺挫傷	0	1 (2.4)	0
肋骨骨折	1 (4.3)	0	0
皮下血腫	1 (4.3)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
傷害、中毒および処置合併症 (Cont.)			
胸椎骨折	0	1 (2.4)	0
臨床検査	7 (30.2)	20 (48.4)	29 (71.9)
アラニンアミノトランスフェラーゼ増加	0	1 (2.4)	4 (9.9)
アミラーゼ増加	1 (4.3)	1 (2.4)	0
アスパラギン酸アミノトランスフェラーゼ増加	0	2 (4.8)	3 (7.4)
血中コレステロール増加	0	0	1 (2.5)
血中クレアチンホスホキナーゼ増加	1 (4.3)	5 (12.1)	8 (19.8)
血中クレアチニン増加	1 (4.3)	0	1 (2.5)
γ-グルタミルトランスフェラーゼ増加	0	3 (7.3)	0
高比重リポ蛋白増加	0	2 (4.8)	0
リパーゼ増加	0	1 (2.4)	0
リンパ球数減少	0	1 (2.4)	2 (5.0)
リンパ球数増加	1 (4.3)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
臨床検査 (Cont.)			
リンパ球百分率増加	0	1 (2.4)	0
好中球数減少	2 (8.6)	1 (2.4)	8 (19.8)
好中球数増加	0	0	1 (2.5)
体重増加	0	1 (2.4)	0
白血球数減少	1 (4.3)	1 (2.4)	1 (2.5)
代謝および栄養障害	2 (8.6)	4 (9.7)	1 (2.5)
脂質異常症	0	3 (7.3)	0
高コレステロール血症	0	1 (2.4)	1 (2.5)
高リパーゼ血症	1 (4.3)	0	0
低ナトリウム血症	1 (4.3)	0	0
筋骨格系および結合組織障害	14 (60.3)	8 (19.4)	3 (7.4)
関節痛	4 (17.2)	2 (4.8)	1 (2.5)
関節障害	1 (4.3)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
筋骨格系および結合組織障害 (Cont.)			
背部痛	3 (12.9)	3 (7.3)	0
腰部脊柱管狭窄症	0	0	1 (2.5)
筋骨格系胸痛	2 (8.6)	0	0
筋骨格痛	0	1 (2.4)	0
筋肉痛	0	1 (2.4)	0
変形性関節症	1 (4.3)	0	0
骨壊死	0	1 (2.4)	0
四肢痛	1 (4.3)	0	0
関節周囲炎	0	0	1 (2.5)
肩回旋筋腱板症候群	1 (4.3)	0	0
腱鞘炎	1 (4.3)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (4.3)	0	1 (2.5)
結腸腺癌	0	0	1 (2.5)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
大腸腺腫	1 (4.3)	0	0
神経系障害	3 (12.9)	3 (7.3)	5 (12.4)
浮動性めまい	0	0	1 (2.5)
てんかん	1 (4.3)	0	0
頭痛	0	2 (4.8)	2 (5.0)
感覚鈍麻	0	1 (2.4)	1 (2.5)
片頭痛	1 (4.3)	0	0
末梢性ニューロパチー	1 (4.3)	0	0
くも膜下出血	0	0	1 (2.5)
精神障害	3 (12.9)	1 (2.4)	3 (7.4)
不安障害	0	1 (2.4)	0
抑うつ気分	0	0	1 (2.5)
不眠症	3 (12.9)	0	2 (5.0)

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
腎および尿路障害	0	0	2 (5.0)
急性腎障害	0	0	1 (2.5)
尿管結石症	0	0	1 (2.5)
生殖系および乳房障害	2 (8.6)	2 (4.8)	0
機能不全性子宮出血	1 (4.3)	0	0
月経困難症	0	1 (2.4)	0
不規則月経	1 (4.3)	0	0
前立腺炎	0	1 (2.4)	0
呼吸器、胸郭および縦隔障害	3 (12.9)	3 (7.3)	3 (7.4)
咳嗽	0	1 (2.4)	0
しゃっくり	1 (4.3)	0	1 (2.5)
口腔咽頭痛	0	0	2 (5.0)
アレルギー性鼻炎	0	1 (2.4)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
呼吸器、胸郭および縦隔障害 (Cont.)			
上気道の炎症	2 (8.6)	1 (2.4)	0
皮膚および皮下組織障害	15 (64.6)	12 (29.1)	19 (47.1)
ざ瘡	3 (12.9)	1 (2.4)	4 (9.9)
皮脂欠乏症	0	0	1 (2.5)
皮膚炎	0	1 (2.4)	0
アトピー性皮膚炎	0	2 (4.8)	0
接触皮膚炎	1 (4.3)	0	0
湿疹	1 (4.3)	2 (4.8)	2 (5.0)
皮脂欠乏性湿疹	1 (4.3)	0	1 (2.5)
掌蹠膿疱症	0	1 (2.4)	0
脂肪織炎	0	1 (2.4)	0
光線過敏性反応	1 (4.3)	0	1 (2.5)
そう痒症	0	1 (2.4)	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.2.1.2.3 J

Treatment-Emergent Adverse Events per 100 Patient-Years (PYS) by System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) (PYS=23.2) Events (E/100PY)	UPA 15 mg QD (N=45) (PYS=41.3) Events (E/100PY)	UPA 30 mg QD (N=45) (PYS=40.3) Events (E/100PY)
皮膚および皮下組織障害 (Cont.)			
壊疽性膿皮症	1 (4.3)	0	0
発疹	2 (8.6)	1 (2.4)	1 (2.5)
紅斑性皮疹	1 (4.3)	0	0
斑状丘疹状皮疹	0	0	4 (9.9)
脂漏性皮膚炎	4 (17.2)	2 (4.8)	1 (2.5)
蕁麻疹	0	0	4 (9.9)
血管障害	1 (4.3)	1 (2.4)	2 (5.0)
大動脈瘤	0	1 (2.4)	0
血腫	0	0	1 (2.5)
高血圧	0	0	1 (2.5)
静脈血栓症	1 (4.3)	0	0

Note: PYS is defined as the sum of the study drug duration of all subjects normalized by 365.25, and rounded to one decimal place.
E/100PY = Events per 100 patient-years.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表14

TABLE 14.3__1.3.1.1.3_J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
Any adverse event	13 (31.7)	16 (35.6)	22 (48.9)
血液およびリンパ系障害	4 (9.8)	1 (2.2)	5 (11.1)
貧血	1 (2.4)	1 (2.2)	2 (4.4)
白血球減少症	1 (2.4)	0	0
リンパ球減少症	1 (2.4)	0	0
好中球減少症	1 (2.4)	0	3 (6.7)
血小板減少症	1 (2.4)	0	0
胃腸障害	4 (9.8)	0	2 (4.4)
腹部膨満	1 (2.4)	0	0
潰瘍性大腸炎	3 (7.3)	0	0
便秘	0	0	1 (2.2)
膵炎	1 (2.4)	0	0
口内炎	0	0	1 (2.2)
一般・全身障害および投与部位の状態	0	0	1 (2.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
一般・全身障害および投与部位の状態 (Cont.)			
発熱	0	0	1 (2.2)
肝胆道系障害	1 (2.4)	0	0
肝機能異常	1 (2.4)	0	0
感染症および寄生虫症	3 (7.3)	10 (22.2)	8 (17.8)
細菌性関節炎	0	1 (2.2)	0
細菌性膣症	1 (2.4)	0	0
毛包炎	0	0	1 (2.2)
ヘルペス性皮膚炎	0	1 (2.2)	0
帯状疱疹	0	4 (8.9)	5 (11.1)
帯状疱疹性髄膜炎	0	0	1 (2.2)
インフルエンザ	0	1 (2.2)	1 (2.2)
潜伏結核	0	0	1 (2.2)
上咽頭炎	0	3 (6.7)	0
口腔カンジダ症	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
感染症および寄生虫症 (Cont.)			
口腔ヘルペス	0	0	1 (2.2)
咽頭炎	0	1 (2.2)	0
胸膜感染	0	0	1 (2.2)
ニューモシスチス・イロベチイ肺炎	1 (2.4)	0	0
肺炎	1 (2.4)	0	0
上気道感染	0	0	1 (2.2)
傷害、中毒および処置合併症	1 (2.4)	0	0
肋骨骨折	1 (2.4)	0	0
臨床検査	2 (4.9)	7 (15.6)	14 (31.1)
アラニンアミノトランスフェラーゼ増加	0	1 (2.2)	3 (6.7)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (2.2)	2 (4.4)
血中クレアチンホスホキナーゼ増加	1 (2.4)	2 (4.4)	5 (11.1)
血中クレアチニン増加	0	0	1 (2.2)
γ-グルタミルトランスフェラーゼ増加	0	2 (4.4)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
臨床検査 (Cont.)			
高比重リポ蛋白増加	0	2 (4.4)	0
リンパ球数減少	0	1 (2.2)	2 (4.4)
リンパ球数増加	1 (2.4)	0	0
好中球数減少	1 (2.4)	1 (2.2)	4 (8.9)
好中球数増加	0	0	1 (2.2)
白血球数減少	0	1 (2.2)	1 (2.2)
代謝および栄養障害	1 (2.4)	1 (2.2)	1 (2.2)
脂質異常症	0	1 (2.2)	0
高コレステロール血症	0	0	1 (2.2)
高リパーゼ血症	1 (2.4)	0	0
筋骨格系および結合組織障害	1 (2.4)	0	0
関節障害	1 (2.4)	0	0
背部痛	1 (2.4)	0	0
筋骨格系胸痛	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.1.1.3 J

Subjects with Treatment-Emergent Adverse Events with a Reasonable Possibility of Being Related to Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
腎および尿路障害	0	0	1 (2.2)
急性腎障害	0	0	1 (2.2)
呼吸器、胸郭および縦隔障害	1 (2.4)	0	0
上気道の炎症	1 (2.4)	0	0
皮膚および皮下組織障害	1 (2.4)	2 (4.4)	3 (6.7)
ざ瘡	1 (2.4)	0	1 (2.2)
脂肪織炎	0	1 (2.2)	0
そう痒症	0	1 (2.2)	0
発疹	0	0	1 (2.2)
斑状丘疹状皮疹	0	0	1 (2.2)
血管障害	1 (2.4)	0	0
静脈血栓症	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表15

[redacted]20[redacted] 11:58 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__1.3.3.3_J

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
Any adverse event	6 (14.6)	2 (4.4)	3 (6.7)
血液およびリンパ系障害	1 (2.4)	0	0
好中球減少症	1 (2.4)	0	0
胃腸障害	2 (4.9)	0	0
潰瘍性大腸炎	1 (2.4)	0	0
膵炎	1 (2.4)	0	0
感染症および寄生虫症	2 (4.9)	1 (2.2)	1 (2.2)
帯状疱疹性髄膜炎	0	0	1 (2.2)
大腸感染	0	1 (2.2)	0
ニューモシスチス・イロベチイ肺炎	1 (2.4)	0	0
肺炎	1 (2.4)	0	0
傷害、中毒および処置合併症	0	1 (2.2)	0
肺挫傷	0	1 (2.2)	0
胸椎骨折	0	1 (2.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 1.3.3.3 J

Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
臨床検査	1 (2.4)	0	0
好中球数減少	1 (2.4)	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1 (2.2)
結腸腺癌	0	0	1 (2.2)
神経系障害	0	0	1 (2.2)
くも膜下出血	0	0	1 (2.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表16

[redacted]20[redacted] 11:58 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.3__2.3.1.3_J

Subjects with Treatment-Emergent Adverse Events Leading to Death
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
Any adverse event	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表17

[redacted]20[redacted] 11:58 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__2.1.1.3_J

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
Any adverse event	5 (12.2)	3 (6.7)	3 (6.7)
胃腸障害	3 (7.3)	0	0
潰瘍性大腸炎	2 (4.9)	0	0
膵炎	1 (2.4)	0	0
感染症および寄生虫症	2 (4.9)	2 (4.4)	1 (2.2)
細菌性関節炎	0	1 (2.2)	0
帯状疱疹性髄膜炎	0	0	1 (2.2)
大腸感染	0	1 (2.2)	0
ニューモシスチス・イロベチイ肺炎	1 (2.4)	0	0
肺炎	1 (2.4)	0	0
傷害、中毒および処置合併症	0	1 (2.2)	0
肺挫傷	0	1 (2.2)	0
胸椎骨折	0	1 (2.2)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1 (2.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.1.1.3 J

Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
結腸腺癌	0	0	1 (2.2)
神経系障害	0	0	1 (2.2)
くも膜下出血	0	0	1 (2.2)
皮膚および皮下組織障害	0	1 (2.2)	0
脂肪織炎	0	1 (2.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

表18

[redacted]20[redacted] 11:58 <[redacted]>
UPADACITINIB (ULCERATIVE COLITIS)
STUDY M14-234 SUBSTUDY 3
R&D/21/1542 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 2

TABLE 14.3__2.2.1.3_J

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
Any adverse event	4 (9.8)	1 (2.2)	5 (11.1)
胃腸障害	3 (7.3)	0	0
潰瘍性大腸炎	2 (4.9)	0	0
膵炎	1 (2.4)	0	0
感染症および寄生虫症	0	1 (2.2)	2 (4.4)
細菌性関節炎	0	1 (2.2)	0
帯状疱疹	0	0	2 (4.4)
帯状疱疹性髄膜炎	0	0	1 (2.2)
臨床検査	0	0	2 (4.4)
血中クレアチンホスホキナーゼ増加	0	0	1 (2.2)
好中球数減少	0	0	1 (2.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	1 (2.2)
結腸腺癌	0	0	1 (2.2)
皮膚および皮下組織障害	0	1 (2.2)	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

TABLE 14.3 2.2.1.3 J

Subjects with Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug
by Primary MedDRA System Organ Class and Preferred Term
(SA_C Population - Japan Analysis Set)

MedDRA 23.0 System Organ Class Preferred Term	Placebo (N=41) n (%)	UPA 15 mg QD (N=45) n (%)	UPA 30 mg QD (N=45) n (%)
皮膚および皮下組織障害 (Cont.)			
脂肪織炎	0	1 (2.2)	0
血管障害	1 (2.4)	0	0
静脈血栓症	1 (2.4)	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Treatment-emergent AEs (TEAEs) are defined as events that begin either on or after the first dose of the study drug in the Maintenance Study and within 30 days after the last dose administration of the study drug for subjects who do not participate in the long-term extension Study M14-533 or until first dose of study drug in the Study M14-533 if the subject is enrolled into Study M14-533.

Program Source Code: [redacted]

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
結節性紅斑	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-234 SS3 Placebo (MAIN)	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 28	28

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	50 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	400.000 mg	Q6W	Y-M: 20[redacted] / -284
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	SACHETS X2 15.5G EACH g	PRN	Y-M: 20[redacted] / -72
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	SACHETS X 2 15.5 G EACH g	PRN	Y-M: 20[redacted] / -2

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
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	SACHETS X 2 15.5 G EACH g	PRN	Y-M: 20[redacted] / -2	Y-M: 20[redacted] / -2
AMOXICILLIN	500 mg	TID	Y-M: 20[redacted] / 18	Y-M: 20[redacted] / 26
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 28	ONGOING
SODIUM CHLORIDE	1000 mL	PRN	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 28
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 30
HYDROCORTISONE	100 mg	QID	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 30
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 30

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

Event Description	UNCLEAR AETIOL ERYTHEMA NODOSUM
Preferred term	結節性紅斑
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 85
Age at AE Onset	2[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 28): Albumin: 26 [32 - 47] G/L; NPTST165-CRP: 210 [0 - 5] MG/L; NPTST247-GGT: 26 [32 - 35] U/L	
Microbiology	
[redacted]20[redacted] (RX DAY 59): SPUTUM NPTST481-SPUTUM CULTURE: NEGATIVE	
AE Stopped Initial 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, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はオーストラリアの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，病因不明の結節性紅斑を発現した。関連する病歴は，潰瘍性大腸炎，現飲酒者（1 日 2 杯未満）及び非喫煙者であった。

Event 1 の臨床経過：

投与85日後＊，被験者は病因不明の結節性紅斑を発現した。

投与から約2ヵ月後＊ の本事象発現前，被験者は咳嗽，発熱及び胸膜炎性胸痛を発現した。症状は持続し，毎晩汗をかいた。被験者は上気道感染（非重篤）と診断された。被験者は黄色がかった痰を出しており，アモキシシリンによる 1 コースの治療を受けた。被験者は改善した。過去 2 週間にわたって，被験者は複数の赤い小結節及び関節痛を伴う進行性の下腿の痛み及び腫脹を認め

た。

投与85日後＊　　，被験者は結節性紅斑があり入院したところ，体温は摂氏 39°C であり，上気道感染（非重篤）の可能性が高いと判断された。被験者は疲れていると報告したが，それほど具合が悪いわけではなかった。入院中の CRP 値は 188 mg/L であり，投与90日後＊　　に CRP 値 56 mg/L で退院した。

この被験者の治験は中止された。

投与された薬剤は，ヒドロコルチゾン及び paracetamol であった。

The patient's past medications include:

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

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

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

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

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

AMOXICILLIN for UPPER RESPIRATORY TRACT INFECTION ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　Erythema nodosum (10015226)　(Erythema nodosum (10015226))　[v.23.0]　[10015226]

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)

Event of UNCLEAR AETIOL ERYTHEMA NODOSUM

- Investigator: Not applicable

- AbbVie: Event more likely related to pre-existing ulcerative colitis. Additional risk factor is use of amoxicillin (previous upper respiratory tract infection)

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 26 G/L (normal 32 to 47)

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

[redacted] **20[redacted] BODY TEMPERATURE:** 39.1 Degrees C

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

[redacted] **20[redacted] CRP:** 210 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 56 MG/L (normal 0 to 5)

20[redacted] CRP (DURING HOSPITALIZATION): 188 MG/L (normal 0 to 5)

[redacted] **20[redacted] GGT:** 26 U/L (normal 32 to 35)

20[redacted] SEPTIC SCREEN (DURING HOSPITALIZATION): 0 organism

[redacted] **20[redacted] SPUTUM 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
人工流産	X			

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

Medical History	Onset Year
HERNIA INGUINALIS	19[redacted]
LEFT SIDED UC	20[redacted]
SICK HEADACHE	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]

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

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 197	197

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METAMIZOLE	500 mg	PRN	Y-M: 20[redacted] / -74
MESALAZINE	3000 mg	QD	Y: 20[redacted]
PREDNISOLONE	75 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
METAMIZOLE	500 mg	PRN	Y-M: 20[redacted] / -74	ONGOING
MESALAZINE	3000 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	ELECTIVE ABORTION
Preferred term	人工流産
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 259 (7 DAYS AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	259 (7 DAYS AFTER LAST TREATMENT)
Duration of AE	1 DAY
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PREGNANCY.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はオーストリアの 3[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，人工妊娠中絶及び妊娠時の母体の曝露（非重篤）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 1 の臨床経過：

被験者は妊娠時の母体の曝露を経験した（日付不明）。投与259日後＊ ，被験者は人工妊娠中絶を経験した。

投与253日後＊ ，被験者は妊娠を確認した（確認方法は不明）。最終月経は 投与208日後＊であった。避妊方法はパートナーの精管切除であった。胎児は，妊娠確認前に母体が使用した盲検化された治験薬に子宮内で曝された。出産予定日は 投与488日後＊ であった。投与252日後＊，妊娠により治験薬の投与が完全に中止された。

投与259日後＊ ，被験者は妊娠の終了を選択した。外来で処置（内容は不明）が行われ，その後被験者の健康状態は良好であった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Elective abortion (10082264) (Abortion induced (10000220)) [v.23.1] [10082264]

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

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

Dechallenge: Not Applicable

2) Maternal exposure during pregnancy (10071408) (Maternal exposure during pregnancy (10071408)) [v.23.1] [10071408]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of ELECTIVE ABORTION

- Investigator: Pregnancy

- AbbVie: Event is more likely related to the subject's choice to terminate the pregnancy.

Event of MATERNAL EXPOSURE DURING PREGNANCY

- Investigator: Not reported

- AbbVie: Special situation of maternal use of active pharmaceutical ingredient.

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
急性精神病	X			

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

Medical History	Onset Year
ACUTE PSYCHOTIC EPISODE	20[redacted]
ACUTE PSYCHOTIC EPISODE	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]

Prior Procedures	Procedure Year
SAE SUPPLEMENTAL PROCEDURE: PSYCHIATRIC EXAMINATION	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 PACK	3	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 356	356

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	25 mg	QD	Y-M: 20[redacted]
GOLIMUMAB	200.000 mg	EOW	Y-M: 20[redacted]
OLANZAPINE	2.5 mg	QD	Y-M: 20[redacted] / -33
ETHINYLESTRADIOL;ETONOGESTREL	1 OTHER: VAGINAL RING	OTHER: FOR THREE WEEKS, THEN ONE WEEK PAUSE	Y-M: 20[redacted] / -47
PARACETAMOL	500 mg	PRN	Y: 20[redacted]
MEBEVERINE	200 mg	BID	Y: 20[redacted]
METAMIZOLE	20 gtt	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
OLANZAPINE	2.5 mg	QD	Y-M: 20[redacted] / -33	Y-M: 20[redacted] / 1
ETHINYLESTRADIOL;ETONOGESTREL	1 OTHER: VAGINAL RING	OTHER: FOR THREE WEEKS, THEN ONE WEEK PAUSE	Y-M: 20[redacted] / -47	ONGOING
RISPERIDONE	1 mg	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 28
SERTRALINE	50 mg	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 42
BUPROPION	150 mg	QD	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 64
PARACETAMOL	500 mg	PRN	Y: 20[redacted]	ONGOING
MEBEVERINE	200 mg	BID	Y: 20[redacted]	Y-M: 20[redacted] / 42
METAMIZOLE	20 gtt	PRN	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	ACUTE PSYCHOTIC EPISODE
Preferred term	急性精神病
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 4
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	119
Duration of AE	116 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	POTENTIALLY DUE TO HORMONAL CONTRACEPTIVE PATCH
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-675

治験責任医師からの報告。本被験者はオーストリアの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，急性精神病性エピソードの事象を発現した。関連する病歴は，元喫煙者（1 日 1 本を 3 年間），急性精神病性エピソード，現飲酒者（1 日 2 杯未満）及び精神病性統合失調症の家族歴（叔母）であった。

Event 1 の臨床経過：

投与4日後＊　，被験者は急性精神病性エピソードを発現した。投与119日後＊　，急性精神病性エピソードは消失した。

本事象発現前，被験者は 投与30ヵ月前＊（本治験への登録前）に急性精神病性エピソードを経験していた。投与4日後＊　，被験者は急性不安を経験した。被験者には妄想症，精神病及び激越の徴候及び症状があった。被験者は 投与15日後＊　に精神科医を受診する予定があった。

投与16日後＊　　，被験者は急性不安が悪化し，妄想状態に陥ることがあった。同日に被験者は入院した。入院後，被験者は不安及び妄想を増大させていた。被験者は助けてほしいと訴え，精神病棟に入院した。被験者はオランザピンの投与を受け，症状は臨床的に改善した。被験者は 投与19日後＊　　に退院した。投与55日後＊　　，被験者は本導入試験の治験薬投与を完了した。治験責任医師によると，危険因子はホルモン避妊薬の使用であった。

投与された薬剤は，セルトラリン，wellbutrin，リスパダール，オランザピン及びジプレキサであった。

The patient's past medications include:

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

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

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

Causality for UPADACITINIB (Blinded)

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1)　Acute psychosis (10001022)　(Acute psychosis (10001022))　[v.23.1]　[10001022]

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 PSYCHOTIC EPISODE

- Investigator: Potentially due to hormonal contraceptive patch.

- AbbVie: Risk factors include prior psychotic episode in 20[redacted] and recent use of evra prior to event.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BUN:** 7.6 mg/dL (normal 6.0 to 20.0)

[redacted] **20[redacted] COVID TEST:** Nasopharyngeal swab- Negative

[redacted] **20[redacted] COVID TEST:** Nasopharyngeal swab- Negative

[redacted] **20[redacted] CREATININE:** 0.77 mg/dL (normal 0.5 to 0.9)

[redacted] **20[redacted] PSYCHIATRIC EXAMINATION:** Acute psychotic episode

[redacted] **20[redacted] URINE DRUG SCREENING:** Opiate-Negative 6-MAM-Negative Methadone-Negative EDDP-Negative Cocaine-Negative Amphetamine-Negative Barbiturate-Negative Benzodiazepine-Negative Cannabinoid-Negative Buprenorphine-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			
卵巣静脈血栓症				X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	4[redacted]	FEMALE	WHITE

Medical History	Onset Year
DRUG ALLERGIES/REACTIONS: ALLERGY IMURAN	20[redacted]
DRUG ALLERGIES/REACTIONS: REMICADE ALLERGIC REACTION	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ANXIETY DISORDER	NOT REPORTED
OTHER: ARTHRALGIA	NOT REPORTED
OTHER: CHRONIC SINUSITIS	20[redacted]
OTHER: CRAMPS	NOT REPORTED
OTHER: FIBROMYALGIA	20[redacted]
OTHER: HARD STOOL	20[redacted]
OTHER: RESECTION ENDO-ANAL POLYP (APO: TROMBOSED HEMORRHOID)	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): FLEXIBLE SIGMOIDOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: CESARIAN SECTION	19[redacted]
SURGERY: FISTULA RESECTION	20[redacted]
SURGERY: HAEMORRHOIDECETOMY	20[redacted]
SURGERY: SINUS 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	1 PACK	25	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 50	50
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 41	41

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	250 mg	BID	Y-M: 20[redacted]
MESALAZINE	1 DF	QD	Y-M: 20[redacted]
MESALAZINE	500 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	TID	Y-M: 20[redacted]
BECLOMETASONE	5 mg	BID	Y-M: 20[redacted]
BUDESONIDE	2 mg	OTHER: 3 TIMES A WEEK	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	325.000 mg	WEEK 0 AND WEEK 2	Y-M: 20[redacted]
ADALIMUMAB	160.000 mg	ONCE	Y-M: 20[redacted]
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted]
MESALAZINE	500 mg	QD	Y-M: 20[redacted] / -326
BECLOMETASONE	3 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -295
BUDESONIDE	2 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -295
VEDOLIZUMAB	300.000 mg	WEEK 0, 2, 6	Y-M: 20[redacted] / -275
BECLOMETASONE	5 mg	BID	Y-M: 20[redacted] / -281
METHYLPREDNISOLONE	48 mg	QD	Y-M: 20[redacted] / -200
BECLOMETASONE	1 DF	QD	Y-M: 20[redacted] / -165
BUDESONIDE	2 mg	QD	Y-M: 20[redacted] / -165
MAGNESIUM SULFATE	450 mg	QD	Y-M: 20[redacted] / -160
METHYLPREDNISOLONE	8 mg	OTHER: EVERY OTHER DAY	Y-M: 20[redacted] / -121
INFLIXIMAB	375.000 mg	ONCE	Y-M: 20[redacted] / -128
ANTIDEPRESSANTS IN COMBINATION WITH PSYCHOLEPTICS	1 DF	QD	Y-M: 20[redacted] / -130
ASCORBIC ACID;CALCIUM CARBONATE;COLECALCIFEROL;ERGOCALCIFEROL	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -130
METHYLPREDNISOLONE	6 mg	QD	Y-M: 20[redacted] / -77
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -50
PROPOFOL	2 mg/kg	QD	Y-M: 20[redacted] / -58
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -59

LOPERAMIDE	2 mg	PRN	Y-M: 20[redacted] / -65
LIDOCAINE;TRIAMCINOLONE	1 OTHER: FINGERTIP	PRN	Y-M: 20[redacted] / -69
MACROGOL 4000	2 OTHER: SACHET	PRN	Y-M: 20[redacted] / -69
MACROGOL 4000	1 OTHER: SACHET	PRN	Y-M: 20[redacted] / -11
LIDOCAINE;TRIAMCINOLONE	1 OTHER: FINGERTIP	PRN	Y-M: 20[redacted] / -18
CYSTEINE;DL-METHIONINE;HESPERIDIN;MINERALS NOS;PHOSPHORUS;VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -21
GLYCERYL TRINITRATE	1 OTHER: FINGERTIP	PRN	Y-M: 20[redacted] / -21
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -36
MACROGOL 4000	2 OTHER: SACHET	QD	Y-M: 20[redacted] / -5
ETHINYLESTRADIOL;LEVONORGESTREL	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	
MAGNESIUM SULFATE	450 mg	QD	Y-M: 20[redacted] / -160	ONGOING
ANTIDEPRESSANTS IN COMBINATION WITH PSYCHOLEPTICS	1 DF	QD	Y-M: 20[redacted] / -130	ONGOING
ASCORBIC ACID;CALCIUM CARBONATE;COLECALCIFEROL; ERGOCALCIFEROL	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -130	Y-M: 20[redacted] / 54
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -50	ONGOING
CYSTEINE;DL-METHIONINE;HESPERIDIN;MINERALS NOS;PHOSPHORUS;VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -21	ONGOING
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -36	ONGOING
MACROGOL 4000	2 OTHER: SACHET	QD	Y-M: 20[redacted] / -5	Y-M: 20[redacted] / 54
METHYLPREDNISOLONE	2 mg	QD	Y-M: 20[redacted] / 8	Y-M: 20[redacted] / 14
MOMETASONE	1 DF	BID	Y-M: 20[redacted] / 24	ONGOING
ALUMINIUM HYDROXIDE-MAGNESIUM CARBONATE GEL;DIOSMECTITE	1 OTHER: SACHET	PRN	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 42
CODEINE;PARACETAMOL	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 42
HYALURONIC ACID	1 DF	OTHER: ONCE	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 35
RACECADOTRIL	100 mg	PRN	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 42
AMOXICILLIN;CLAVULANIC ACID	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 40	ONGOING
DIHYDROCODEINE	10 mg	TID	Y-M: 20[redacted] / 40	ONGOING
HEPATITIS A VACCINE;HEPATITIS B VACCINE	1 DF	OTHER: ONCE	Y-M: 20[redacted] / 40	Y-M: 20[redacted] / 40
ALIZAPRIDE	50 mg	BID	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 43
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: SACHET	OTHER: ONCE	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 42
DICLOFENAC	75 mg	BID	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 43
ENOXAPARIN	100 mg	QD	Y-M: 20[redacted] / 42	ONGOING
PARACETAMOL	1 g	BID	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 43
TRAMADOL	100 mg	BID	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 43
ETHINYLESTRADIOL;LEVONORGESTREL	1 OTHER: TABLET	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	FLARE UP OF UC
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 92 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 42): Creatinine: 4314.08104 [5304.198 - 19448.726] UMOL/L; Leukocytes: 11.76 [4.2 - 9.8] 10^9/L; NPTST165-CRP: 170 [0 - 7] MG/L; NPTST353-MRSA SCREENING: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 8.49 [1.7 - 7.5] 10^9/L; [redacted]20[redacted] (RX DAY 43): NPTST165-CRP: 180 [0 - 7] MG/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NORMAL COURSE OF DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Adjudicated Other Venous thrombosis Event

Event Description	THROMBOSIS OF THE LEFT OVARIC VEIN
Preferred term	卵巣静脈血栓症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 92 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

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

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はベルギーの 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，宿便を伴う潰瘍性大腸炎の再燃を発現した。関連する病歴は，線維筋痛，元喫煙者（1 日 1 箱を 25 年間），肛門ポリープ切除（血栓性痔核の分離結紮），痔核切除術，潰瘍性大腸炎，硬便，筋痙攣及び現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与92日後＊，被験者は宿便を伴う潰瘍性大腸炎の再燃を発現した。投与から約4ヵ月後＊，宿便を伴う潰瘍性大腸炎の再燃は消失した。

投与92日後＊　　，被験者は急性腹痛，排便困難（少し）及び左腸骨窩の痛みで救急科を受診した。被験者は入院し検査を受けたが，外科的介入は行われなかった。CT スキャン検査を受けたところ穿孔及び膿瘍は除外され，副次的に S 状結腸炎後の所見及び左卵巣静脈の血栓症（非重篤）が発見された。結腸内視鏡検査では Mayo スコアでグレード 3 の活動性の潰瘍性大腸炎を認めた。腹部超音波検査では，中毒性巨大結腸は認められなかった。腹部 X 線検査では，宿便を認めた。被験者は鎮痛薬及び点滴による水分補給で治療された。投与93日後＊　　，被験者は退院した。

投与された薬剤は，paracetamol fresenius，ジクロフェナク，contramal，litican，モビプレップ及びクレキサンであった。

The patient's past medications include:

COLITOFALK SUPPO for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CLAVERSAL FOAM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

BUDENOFALK FOAM for ULCERATIVE COLITIS ([redacted])

MEDROL for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

BECLOMETHASON SUPPO for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

REMSIMA for ULCERATIVE COLITIS ([redacted])

TRI-ANAL RECTAL SALVE for ULCERATIVE COLITIS - FISSURE and ULCERATIVE COLITIS - FISSURE ([redacted])

IMODIUM INSTANT for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Blinded)

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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: Not Applicable

2) Fecal impaction (10016294) (Faecaloma (10056325)) [v.21.1] [10016294]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of FLARE UP OF UC COMPLICATED WITH FECAL IMPACTION

- Investigator:

- AbbVie:

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** No free liquid, no toxic megacolon, rectosigmoiditis with fecal impaction

[redacted] **20[redacted] CRP:** 170 MG/L (normal 0.0 to 7.0)

[redacted] **20[redacted] CT ABDOMEN:** SUBOBSTRUCTING RECTOSIGMOÏDITIS. NO EVIDENCE FOR PERFORATION OR ABCEDATION. THROMBOSIS OF LEFT OVARIC VEIN.

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** Inflamation seen up to 35cm of the anal verge, but too painful to visualize more

[redacted] **20[redacted] MRSA SCREENING:** Negative

[redacted] **20[redacted] NEUTROPHILS:** 8.49 X10**3/MM**3 (normal 1.70 to 7.50)

[redacted] **20[redacted] CRP:** 180 MG/L (normal 0.0 to 7.0)

[redacted] **20[redacted] SCREENING COLONOSCOPY:** a clear demarcation was seen between the normal and inflamed colonic mucosa, distance of demarcation from the anal verge: 50cm Central reader endoscopy subscore: 3

[redacted] **20[redacted] URINE CREATININE:** 488 MG/L (normal 600 to 2200)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.76 X10**3/MM**3 (normal 4.20 to 9.80)

[redacted] **20[redacted] X-RAY ABDOMEN:** NOT OBSTRUCTIVE INTESTINAL GAS PATTERN, SCATTERED FAECAL RESIDUES

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
Placebo	6[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA	20[redacted]
ARM FRACTURE	20[redacted]
ARTERIAL HYPERTENSION	20[redacted]
COSTAL FRACTURE	20[redacted]
FIBROSIS HEPATIS OF UNKNOWN ORIGIN	20[redacted]
HEMORRHOIDS	20[redacted]
LEFT SIDED UC	20[redacted]
ORAL APHTOUS ULCERS	20[redacted]
PELVIC INJURY	20[redacted]
PERIFERAL ARTHROPATHY	20[redacted]
PRIMARY SCLEROSATING CHOLANGITIS	20[redacted]
STROKE	20[redacted]
SUBDURAL HEMATOMA	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: EVACUATION OF SUBDURAL HEMATHOMA	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	20	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 190	190

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CALCIUM CARBONATE;COLECALCIFEROL	500+400 mg	BID	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
MESALAZINE	500 mg	QD	Y-M: 20[redacted]
PREDNISONE	20 mg	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	TID	Y-M: 20[redacted]
PREDNISONE	25 mg	BID	Y-M: 20[redacted]
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
PREDNISONE	50 mg	BID	Y-M: 20[redacted] / -293
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -256
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted] / -257
LOPERAMIDE	2 mg	TID	Y-M: 20[redacted] / -257
LOPERAMIDE	2.000 mg	TID	Y-M: 20[redacted] / -257
POTASSIUM	0.75 g	QD	Y-M: 20[redacted] / -75
SODIUM BICARBONATE	2.5 g	QD	Y-M: 20[redacted] / -75
SODIUM CHLORIDE	6.5 g	QD	Y-M: 20[redacted] / -75
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -91
LOPERAMIDE	2 mg	BID	Y-M: 20[redacted] / -40
IRON	100 mg	BID	Y-M: 20[redacted] / -42
CALCIUM;CALCIUM CARBONATE;COLECALCIFEROL	500 mg	QD	Y-M: 20[redacted] / -56
COLECALCIFEROL;MENAQUINONE	75 ug	QD	Y-M: 20[redacted] / -56
MAGNESIUM;MAGNESIUM OXIDE	300 mg	QD	Y-M: 20[redacted] / -56
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / -11
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / -14
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / -18
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / -21
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / -32
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / -8
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / -1
POTASSIUM	0.75 g	QD	Y-M: 20[redacted] / -1
SODIUM BICARBONATE	2.5 g	QD	Y-M: 20[redacted] / -1
SODIUM CHLORIDE	6.5 g	QD	Y-M: 20[redacted] / -1
LOPERAMIDE	2 mg	QD	Y-M: 20[redacted] / -4
BCG Vaccine	NOT REPORTED	NOT REPORTED	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 / Stop Year-Month / RX Day	
LISINOPRIL	10 mg	QD	Y-M: 20[redacted]	ONGOING
LOPERAMIDE	2.000 mg	TID	Y-M: 20[redacted] / -257	Not reported
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -91	Y-M: 20[redacted] / 108
CALCIUM;CALCIUM CARBONATE;COLECALCIFEROL	500 mg	QD	Y-M: 20[redacted] / -56	Y-M: 20[redacted] / 108
COLECALCIFEROL;MENAQUINONE	75 ug	QD	Y-M: 20[redacted] / -56	Y-M: 20[redacted] / 109
MAGNESIUM;MAGNESIUM OXIDE	300 mg	QD	Y-M: 20[redacted] / -56	Y-M: 20[redacted] / 109
DIOSMIN;HESPERIDIN	500 mg	BID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 116
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 113
CALCIUM;CALCIUM CARBONATE;COLECALCIFEROL	500 mg	BID	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 116
IRON	100 mg	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 113
LOPERAMIDE	2 mg	TID	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 121
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / 109	ONGOING
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 115
VITAMINS, OTHER COMBINATIONS	150+150+6+9+8+10+3.6 mg	QD	Y-M: 20[redacted] / 109	Y-M: 20[redacted] / 116
COPPER;IRON;MANGANESE	5 MG, 0.133 MG, 0.07 MG/ML mg	BID	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 116
ENOXAPARIN	40 mg	QD	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 132
GENTAMICIN	80 mg	QD	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 132
GLUCOSE	500 mL	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 121
IRON	100 mg	QD	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 120
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 121
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 130
NIFUROXAZIDE	200 mg	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 118
PROBIOTICS NOS	3.0 OTHER: MILLION OF ORGANISMS	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 133
SULFAMETHOXAZOLE;TRIMETHOPRIM	960 mg	BID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 137
ALBUMIN HUMAN	20 g	QD	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 132
MESALAZINE	500 mg	QD	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 149
NIFUROXAZIDE	200 mg	QID	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 126
HYDROCORTISONE	100 ug	QID	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 128

CALCIUM GLUCONATE	90 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 132
MESALAZINE	1000 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 154
POTASSIUM	500 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 128
VANCOMYCIN	500 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 133
HYDROCORTISONE	100 mg	TID	Y-M: 20[redacted] / 129	Y-M: 20[redacted] / 130
POTASSIUM	500 mg	TID	Y-M: 20[redacted] / 129	Y-M: 20[redacted] / 132
HYDROCORTISONE	100 mg	BID	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 132
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 132
IRON	100 mg	BID	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 163
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 139
PREDNISONE	40 mg	BID	Y-M: 20[redacted] / 133	Y-M: 20[redacted] / 139
PROBIOTICS NOS	2.5 OTHER: 2.5 BILIONS OF MICROORGANISM PER CAPSULE	QD	Y-M: 20[redacted] / 133	ONGOING

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	[redacted]20[redacted] / 173
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 117): Alanine Aminotransferase: 16 [13 - 40] U/L; Albumin: 23 [32 - 46] G/L; Aspartate Aminotransferase: 9 [19 - 48] U/L; Basophils: 0.02 [0 - 0.06] 10^9/L; Basophils/Leukocytes: 0.1 [0 - 3] %; Blood Urea Nitrogen: 4.8 [3 - 9.2] MMOL/L; Calcium: 1.97 [2.2 - 2.55] MMOL/L; Creatine Kinase: 12 [0 - 177] U/L; Creatine Kinase MB: 19 [0 - 25] U/L; Creatinine: 52 [71 - 115] UMOL/L; Eosinophils: 0 [0 - 0.43] 10^9/L; Eosinophils/Leukocytes: 0.1 [0 - 7] %; Erythrocytes: 4.76 [4.35 - 5.72] 10^12/L; Glucose: 5.4 [4.6 - 6.4] MMOL/L; Hematocrit: 0.297 [0.415 - 0.572] FRACTION OF 1; Hemoglobin: 83 [138 - 175] G/L; Leukocytes: 4.41 [3.4 - 9.7] 10^9/L; Lymphocytes: 0.4 [1.19 - 3.35] 10^9/L; Lymphocytes/Leukocytes: 9 [20 - 46] %; Monocytes: 0.1 [0.12 - 0.84] 10^9/L; Monocytes/Leukocytes: 2.4 [2 - 12] %; NPTST165-CRP: 56.6 [0 - 5] MG/L; NPTST287-HSTROPONIN I: 1.50 [0 - 34.2] PG/ML; NPTST318-LDI: 100 [110 - 210] U/L; NPTST331-MCH: 17.5 [27.4 - 33.9] PG; NPTST332-MCHC: 280 [320 - 345] G/L; NPTST334-MCV: 62.5 [83 - 97.2] FL; NPTST350-MIOGLOBIN: 9.5 [19 - 92] UG/L; NPTST352-MPV: 3.9 [6.8 - 10.4] FL; NPTST397-PCT: 0.015 [0.016 - 0.038] RATIO; NPTST441-RDW-CV: 18.1 [9 - 15] %; Neutrophils: 3.9 [2.06 - 6.49] 10^9/L; Neutrophils/Leukocytes: 88.2 [44 - 72] %; Platelets: 377 [158 - 424] 10^9/L; Potassium: 4 [3.5 - 5.1] MMOL/L; Protein: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Protein: 54 [62 - 81] G/L; Sodium: 138 [136 - 145] MMOL/L; Specific Gravity: 1.022 [1.002 - 1.03] UNIT NOT REPORTED; Urobilinogen: NEGATIVE [0 - 16] umol/L; pH: 6 [5 - 9] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 119): Cholesterol: 2.4 [1.04 - 5.2] MMOL/L; HDL Cholesterol: 1.29 [1.04 - 1.55] MMOL/L; LDL Cholesterol: 0.75 [0 - 3.3] MMOL/L; NPTST226-FERITIN: 220.00 [22 - 322] UG/L; NPTST308-IRON: 3.3 [11.6 - 31.3] UMOL/L; NPTST506-TIBC: 38.8 [49 - 72] UMOL/L; NPTST530-UIBC: 35.5 [12.4 - 43] UMOL/L; Triglycerides: 1.15 [0 - 1.17] MMOL/L; [redacted]20[redacted] (RX DAY 120): Erythrocytes: 4.84 [4.34 - 5.72] 10^12/L; Hematocrit: 0.308 [0.415 - 0.53] FRACTION OF 1; Hemoglobin: 88 [138 - 175] G/L; Leukocytes: 7.13 [3.4 - 9.7] 10^9/L; NPTST165-CRP: 26.7 [0 - 5] MG/L; NPTST334-MCV: 63.6 [83 - 97.2] FL; Neutrophils/Leukocytes: 61,6 [44 - 72] %; Platelets: 373 [158 - 424] 10^9/L; [redacted]20[redacted] (RX DAY 122): Albumin: 27 [32 - 46] G/L; Calcium: 2.05 [2.2 - 2.55] MMOL/L; Erythrocytes: 4.95 [4.34 - 5.72] 10^12/L; Hematocrit: 0.34 [0.415 - 0.53] FRACTION OF 1; Hemoglobin: 99 [138 - 175] G/L; Leukocytes: 3.97 [3.4 - 9.7] 10^9/L; NPTST165-CRP: 43 [0 - 5] MG/L; NPTST330-MAGNESIUM: 0.88 [0.66 - 0.99] MMOL/L; NPTST334-MCV: 68.6 [83 - 97.2] FL; Platelets: 307 [158 - 424] 10^9/L; Potassium: 4.4 [3.5 - 5.1] MMOL/L; Protein: 56 [62 - 81] G/L; Sodium: 142 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 126): Albumin: 27 [32 - 46] G/L; Calcium: 2 [2.2 - 2.55] MMOL/L; Erythrocytes: 4.85 [4.34 - 5.72] 10^12/L; Hematocrit: 0.344 [0.415 - 0.53] FRACTION OF 1; Hemoglobin: 97 [138 - 175] G/L; Leukocytes: 8.9 [3.4 - 9.7] 10^9/L; NPTST165-CRP: 2.7 [0 - 5] MG/L; Platelets: 209 [158 - 424] 10^9/L; Sodium: 138 [136 - 145] MMOL/L; Sodium: 2.9 [3.5 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 129): Albumin: 28 [32 - 46] G/L; Calcium: 2.23 [2.2 - 2.55] MMOL/L; Erythrocytes: 4.89 [4.34 - 5.72] 10^12/L; Hematocrit: 0.343 [0.415 - 0.53] FRACTION OF 1; Leukocytes: 5.43 [3.4 - 9.7] 10^9/L; NPTST165-CRP: 3.8 [0 - 5] MG/L; NPTST331-MCH: 20.5 [27.4 - 33.9] PG; NPTST332-MCHC: 292 [320 - 345] G/L; NPTST334-MCV: 70.2 [83 - 97.2] FL; NPTST352-MPV: 4.8 [6.8 - 10.4] FL; NPTST397-PCT: 0.009 [0.016 - 0.038] RATIO; NPTST438-RDV-CV: 25.7 [9 - 15] %; Platelets: 187 [158 - 424] 10^9/L; Potassium: 3.1 [3.5 - 5.1] MMOL/L; Sodium: 135 [136 - 145] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 117): STOOL NPTST010-ADENOVIRUS PCR IDENTIFICATION: NEGATIVE; STOOL NPTST133-CLOSTRIDIUM DIFFICILE TOXIN A/B: NEGATIVE; STOOL NPTST384-PARASITES IDENTIFICATION: NEGATIVE; OTHER NASOPHARYNX SMEAR NPTST395-PCR TO SARS-COV-2 (COVID-19): NEGATIVE; STOOL NPTST452-ROTA VIRUS PCR IDENTIFICATION: NEGATIVE; STOOL NPTST459-SALMONELLA AND SHIGELLA IDENTIF: NEGATIVE; [redacted]20[redacted] (RX DAY 121): URINE NPTST028-ANALYSIS OF PRESENCE OF BACTERI: NEGATIVE; STOOL NPTST133-CLOSTRIDIUM DIFFICILE TOXIN A/B: NEGATIVE; [redacted]20[redacted] (RX DAY 122): STOOL NPTST133-CLOSTRIDIUM DIFFICILE TOXIN A/B: NEGATIVE; [redacted]20[redacted] (RX DAY 123): OTHER BIOPSY OF COLON NPTST282-HISTOPATOLOGY ANALYSIS: POSITIVE-CHRONIC ULCERATIVE COLITIS; [redacted]20[redacted] (RX DAY 126): STOOL NPTST394-PCR TO CLOSTRIDIUM DIFFICILE: NEGATIVE

AE Stopped Initial Rx Day	189
Duration of AE	17 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]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はボスニア・ヘルツェゴビナの 6[redacted] 歳男性であり，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，潰瘍性大腸炎の悪化を発現した。関連する病歴は，非喫煙者（1 日 1 箱を 20 年間），動脈性高血圧，痔核，貧血，原因不明の肝繊維化，潰瘍性大腸炎，原発性硬化性胆管炎，口腔内アフタ性潰瘍及び非飲酒者であった。

Event 1 の臨床経過：

投与173日後＊ ，被験者は潰瘍性大腸炎の悪化を発現した。投与189日後＊ ，潰瘍性大腸炎の悪化は消失した。

投与173日後＊ ，被験者は血性下痢（1 日 15–20 回）があり入院した。身体検査では，骨筋構造が貧弱で，皮膚が青白く栄養状態が悪かった。腹部は柔らかかったが，右鼠径部，腰部及び左腎部を深く触ると痛みがあった。両側の下肢は腫れていた。左足はより腫れていたが，両側の末梢血管は触知可能であった。当初の計画では，悪化の原因が，クロストリジウム・ディフィシレ腸炎，COVID-19 感染症，細菌性の肛門直腸感染症又は潰瘍性大腸炎の悪化のいずれかで

あるかを判断することとした。複数の検査が行われた。COVID-19 の PCR 検査（鼻咽頭ぬぐい液）は陰性であり，繰り返し行われたクロストリジウム・ディフィシレ検査も同様に陰性であった。内視鏡検査では，ベースライン状態の悪化が示された。腹部 CT 検査では，投与265日前＊の CT スキャン検査と比べて悪化が示された。コルチコステロイド及び抗生物質による治療を開始後，被験者の徴候及び症状は改善し，投与189日後＊に退院した。

投与された薬剤は，enterofuryl，nobel probiotic optima，nbl probiotic gold，glukoza，garamycin，アルブミン，hydrocortizon，バンコマイシン，グルコン酸カルシウム，塩化カリウム，metrozol，urbason，bactrim，nizon，silymarin，seldiar，calcium sandoz 及び iron dextran であった。

The patient's past medications include:

CALCIMONTA 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])

Causality for UPADACITINIB (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.0] [10009901]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Not applicable.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT SCAN WITH CONTRAST:** Descendant, sigmoid colon and rectum thickened, edematous wall up to 8 mm, pronounced PKPD mucosa, irregular outer contour that appears spiculous most pronounced at the transition of the sigmoid to the descending colon, with propagation of banded irregular hyperdensities into the surrounding adipose tissue, pronounced vascularization is seen and lymph nodes up to 8 mm, all as part of chronic inflammatory bowel disease — described changes compared to CT with the findings from [redacted] 20[redacted], they are progressing today. Increased adipose tissue with lamellar form fluid presacral.

[redacted] **20[redacted] ABDOMINAL X-RAY:** In the shown parts of the domen, the intestinal loops are mostly distributed in the left hemiabdomen, moderately distended, raising the left side of diaphragm, filled with air, with occasional smaller aerohydric level. X-ray signs perforation of the intraabdominal portion of the gastrointestinal tract is not seen.

[redacted] **20[redacted] ADENOVIRUS PCR IDENTIFICATION:** Negative

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 16 U/L (normal 13 to 40)

[redacted] **20[redacted] ALBUMIN:** 23 G/L (normal 32 to 46)

[redacted] **20[redacted] ALBUMIN:** 27 G/L (normal 32 to 46)

[redacted] **20[redacted] ALBUMIN:** 28 G/L (normal 32 to 46)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 9 U/L (normal 19 to 48)

[redacted] **20[redacted] BASOPHILS %:** 0.1 % (normal 0 to 3)

[redacted] **20[redacted] BASOPHILS ABS:** 0.02 X10**9/L (normal 0.00 to 0.06)

[redacted] **20[redacted] BIOPSY OF COLON:** histopatology analysis: Positive - CHRONIC ULCERATIVE COLITIS

[redacted] **20[redacted] BLOOD UREA NITROGEN**: 4.8 MMOL/L (normal 3.0 to 9.2)

[redacted] **20[redacted] CALCIUM:** 2.05 MMOL/L (normal 2.20 to 2.55)

[redacted] **20[redacted] CALCIUM:** 2.23 MMOL/L (normal 2.20 to 2.55)

[redacted] **20[redacted] CHOLESTEROL:** 2.4 MMOL/L (normal 1.04 to 5.2)

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE TOXIN A/B:** Negative

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE TOXIN A/B:** Negative

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE TOXIN A/B:** Negative

[redacted] 20[redacted] **COLONOSCOPY:** Ulcerative colitis.

[redacted] 20[redacted] **CREATINE KINASE:** 12 U/L (normal 0 to 177)

[redacted] 20[redacted] **CREATINE KINASE MB:** 19 U/L (normal 0 to 25)

[redacted] 20[redacted] **CREATININE:** 52 MCMOL/L (normal 71 to 115)

[redacted] 20[redacted] **CRP:** 56.6 MG/L (normal 0 to 5)

[redacted] 20[redacted] **CRP:** 43 MG/L (normal 0 to 5.0)

[redacted] 20[redacted] **CRP:** 3.8 MG/L (normal 0 to 5.0)

[redacted] 20[redacted] **CT ABDOMEN:** Not reported.

[redacted] 20[redacted] **ENDOSCOPY:** The worsening of baseline condition.

[redacted] 20[redacted] **EOSINOPHILS %:** 0.1 % (normal 0 to 7)

[redacted] 20[redacted] **EOSINOPHILS ABS:** 0.00 (normal 0.00 to 0.43)

[redacted] 20[redacted] **FERRITIN:** 220 UG/L

[redacted] 20[redacted] **GLUCOSE:** 5.4 MMOL/L (normal 4.6 to 6.4)

[redacted] 20[redacted] **HDL CHOLESTEROL:** 1.29 MMOL/L (normal 1.04 to 1.55)

[redacted] 20[redacted] **HEMATOCRIT:** 0.415 % (normal 0.415 to5.72)

[redacted] 20[redacted] **HEMATOCRIT:** 0.340 L/L

[redacted] 20[redacted] **HEMATOCRIT:** 0.343 L/L

[redacted] 20[redacted] **HEMOGLOBIN:** 83 G/L (normal 138 to 175)

[redacted] 20[redacted] **HEMOGLOBIN:** 99 G/L (normal 138 to 175)

[redacted] 20[redacted] **HEMOGLOBIN:** 97 G/L (normal 138 to 175)

[redacted] 20[redacted] **HS TROPONIN I:** 1.50 PG/ML (normal 0.0 to 34.2)

[redacted] 20[redacted] **IRON:** 3.3 MCMOL/L (normal 11.6 to 31.3)

[redacted] 20[redacted] **LDI:** 100 U/L (normal 110 to 210)

[redacted] 20[redacted] **LDL CHOLESTEROL:** 0.75 MMOL/L (normal 0.00 to 3.3)

[redacted] 20[redacted] **LYMPHOCYTES %:** 9.0 % (normal 20 to 46)

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 0.40 X10**9/L (normal 1.19 to 3.35)

[redacted] 20[redacted] **MAGNESIUM:** 0.88 MMOL/L (normal 0.66 to 0.99)

[redacted] 20[redacted] **MCH:** 17.5 PG (normal 27.4 to 33.9)

[redacted] 20[redacted] **MCH:** 20.5 PG (normal 27.4 to 33.9)

[redacted] 20[redacted] **MCHC:** 280 G/L (normal 320 to 345)

[redacted] 20[redacted] **MCHC:** 292 G/L (normal 320 to 345)

[redacted] 20[redacted] **MCV:** 62.5 FL (normal 83.0 to 97.2)

[redacted] 20[redacted] **MCV:** 68.6 FL (normal 83.0 to 97.2)

[redacted] 20[redacted] **MCV:** 70.2 FL (normal 83.0 to 97.2)

[redacted] 20[redacted] **MIOGLOBIN:** 9.5 N/UL

[redacted] 20[redacted] **MONOCYTES %:** 2.4 % (normal 2 to 12)

[redacted] 20[redacted] **MONOCYTES ABS:** 0.10 X10**9/L (normal 0.12 to 0.84)

[redacted] 20[redacted] **MPV:** 3.9 FL (normal 6.8 to 10.4)

[redacted] 20[redacted] **MPV:** 4.8 FL (normal 6.8 to 10.4)

[redacted] 20[redacted] **NEUTROPHILS %:** 88.2 % (normal 44 to 72)

[redacted] 20[redacted] **NEUTROPHILS %:** 61,6 % (normal 44 to 72)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 3.9 X10**9/L (normal 2.06 to 6.49)

[redacted] 20[redacted] **PARASITES IDENTIFICATION:** Negative

[redacted] 20[redacted] **PCR TO CLOSTRIDIUM DIFFICILE:** Negative

[redacted] 20[redacted] **PCR TO SARS-COV-2 (COVID-19):** Nasopharynx smear: Negative

[redacted] 20[redacted] **PCT:** 0.015 L/L

[redacted] 20[redacted] **PCT:** 0.009 L/L

[redacted] 20[redacted] **PLATELET COUNT:** 377 X10**9/L (normal 158 to 424)

[redacted] 20[redacted] **PLATELET COUNT:** 307 X10**9/L (normal 158 to 424)

[redacted] 20[redacted] **PLATELET COUNT:** 187 X10**9/L (normal 158 to 424)

[redacted] 20[redacted] **POTASSIUM:** 4.0 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **POTASSIUM:** 4.4 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **POTASSIUM:** 3.1 MMOL/L (normal 3.5 to 5.1)

[redacted] 20[redacted] **PROTEIN:** 54 G/L (normal 62 to 81)

[redacted] 20[redacted] **PROTEIN:** 56 G/L (normal 62 to 81)

[redacted] 20[redacted] **RDV-CV:** 25.7 % (normal 9.0 to 15.0)

[redacted] 20[redacted] **RDW-CV:** 18.1 % (normal 9.0 to 15.0)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.76 X10**12/L (normal 4.35 to 5.72)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.95 X10**12/L (normal 4.34 to 5.72)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.89 X10**12/L (normal 4.34 to 5.72)

[redacted] 20[redacted] **ROTA VIRUS PCR IDENTIFICATION:** Negative

[redacted] 20[redacted] **SALMONELLA IDENTIFICATION:** Negative

[redacted] 20[redacted] **SHIGELLA IDENTIFICATION:** Negative

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

[redacted] 20[redacted] **SODIUM:** 142 MMOL/L (normal 136 to 145)

[redacted] 20[redacted] **SODIUM:** 2.9 MMOL/L (normal 3.5 to 5.1)

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

[redacted] 20[redacted] **SPECIFIC GRAVITY:** 1.022 kg/L (normal 1.002 to 1.030)

[redacted] 20[redacted] **TIBC:** 38.8 MCMOL/L (normal 49 to 72)

[redacted] 20[redacted] **TRANSTHORACAL ULTRASOUND:** An abnormal attachment of the chord from the lateral palpillary muscle to the middle third of the septum is registered. In disturbance myocardial function. Contractility preserved EF 56%. Valves normal, ducts normal. Pericardium normal.

[redacted] 20[redacted] **TRIGLYCERIDES:** 1.15 MMOL/L (normal 0.00 to 1.17)

[redacted] 20[redacted] **UIBC:** 35.5 umol/L

[redacted] 20[redacted] **URINE BACTERIA ANALYSIS:** Negative

[redacted] 20[redacted] **URINE PH:** 6 GMOL/LITER (normal 5.0 to 9.0)

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

[redacted] 20[redacted] **URINE UROBILINOGEN:** Negative (Normal 0-16 mcmol/L)

[redacted] 20[redacted] **URINE UROBILINOGEN:** 1.97 MMOL/L (normal 2.20 to 2.55)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 4.41 X10**9/L (normal 3.40 to 9.70)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 3.97 X10**9/L (normal 3.40 to 9.70)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 5.43 X10**9/L (normal 3.40 to 9.70)

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
好中球減少症				X
非感染性気管支炎	X			

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

Medical History	Onset Year
CYSTICERCOSIS	20[redacted]
DIABETES	20[redacted]
EXTENSIVE UC/PANCOLITIS	19[redacted]
HYPERECPLEXY	20[redacted]
HYPERTENSION	20[redacted]
INSOMNIA	20[redacted]
MIGRANEA	20[redacted]
OBSTRUCTIVE SLEEP APNEA SYNDROME	20[redacted]
TREMOR OF INTENTION	20[redacted]
TREMOR OF REST	20[redacted]
ULCERATIVE COLITIS	19[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: VASECTOMY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 PACK	15	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 367	367

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 19[redacted]
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	4 g	QD	Y-M: 20[redacted]
ATENOLOL	50 mg	QD	Y-M: 20[redacted]
HYDROCHLOROTHIAZIDE	25 mg	QD	Y-M: 20[redacted]
PROPRANOLOL	40 mg	QD	Y-M: 20[redacted]
GLIBENCLAMIDE	5 mg	QD	Y-M: 20[redacted]
METFORMIN	850 mg	BID	Y-M: 20[redacted]
LAMOTRIGINE	100 mg	QID	Y-M: 20[redacted]
PRAMIPEXOLE	1 g	QD	Y-M: 20[redacted]
MESALAZINE	800 mg	OTHER: 5 TIMES PER DAY	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
MELATONIN	3 mg	QD	Y-M: 20[redacted] / -262
MANNITOL	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -69
BISACODYL	10 mg	QD	Y-M: 20[redacted] / -70
CARVEDILOL	12.5 mg	BID	Y-M: 20[redacted] / -27
CLONIDINE	150 ug	BID	Y-M: 20[redacted] / -27
DOXAZOSIN	2 mg	QD	Y-M: 20[redacted] / -27
HYDRALAZINE	50 mg	BID	Y-M: 20[redacted] / -27
CAPTOPRIL	25 mg	QD	Y-M: 20[redacted] / -41
FENTANYL	0,005 mg	QD	Y-M: 20[redacted] / -3
MANNITOL	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -3
PROPOFOL	150 mg	QD	Y-M: 20[redacted] / -3
BISACODYL	5 mg	BID	Y-M: 20[redacted] / -4

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	25 mg	QD	Y-M: 20[redacted]	ONGOING
LAMOTRIGINE	100 mg	QID	Y-M: 20[redacted]	ONGOING
PRAMIPEXOLE	1 g	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	800 mg	OTHER: 5 TIMES PER DAY	Y-M: 20[redacted]	Y-M: 20[redacted] / 67
CARVEDILOL	12.5 mg	BID	Y-M: 20[redacted] / -27	ONGOING
CLONIDINE	150 ug	BID	Y-M: 20[redacted] / -27	ONGOING
DOXAZOSIN	2 mg	QD	Y-M: 20[redacted] / -27	ONGOING
HYDRALAZINE	50 mg	BID	Y-M: 20[redacted] / -27	ONGOING
CALCITRIOL	0.25 mg	OTHER: EVERY WEEK	Y-M: 20[redacted] / 16	ONGOING
GLICLAZIDE	30 mg	BID	Y-M: 20[redacted] / 16	ONGOING
LINAGLIPTIN	5 mg	QD	Y-M: 20[redacted] / 16	ONGOING
CYANOCOBALAMIN;FOLIC ACID	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 142
KETOCONAZOLE	20 mg	BID	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 114
BETAMETHASONE;KETOCONAZOLE	20 mg	QD	Y-M: 20[redacted] / 200	Y-M: 20[redacted] / 214
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 242
METAMIZOLE	1 g	QD	Y-M: 20[redacted] / 239	Y-M: 20[redacted] / 239
PARACETAMOL	750 mg	QD	Y-M: 20[redacted] / 239	Y-M: 20[redacted] / 239
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 242	Y-M: 20[redacted] / 244
DEXAMETHASONE	6 mg	BID	Y-M: 20[redacted] / 242	Y-M: 20[redacted] / 243
HEPARIN	5000 IU	BID	Y-M: 20[redacted] / 242	Y-M: 20[redacted] / 243
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 242	Y-M: 20[redacted] / 243
FORMOTEROL	12 ug	BID	Y-M: 20[redacted] / 277	ONGOING
IRON	5 mL	TID	Y-M: 20[redacted] / 281	Y-M: 20[redacted] / 315
AMOXICILLIN	500 mg	TID	Y-M: 20[redacted] / 302	Y-M: 20[redacted] / 312
BISACODYL	5 mg	QID	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 365
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: SACHET	BID	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 366
FENTANYL	100 ug	QD	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
PROPOFOL	120 mg	QD	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366

Event #1: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 127
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
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 - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 137
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
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 Description	INFLAMMATORY BRONCHOPATHY
Preferred term	非感染性気管支炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 291
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 238): Hematocrit: 0.301 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 108 [140 - 180] G/L;
20[redacted] (RX DAY 242): NPTST087-C-REACTIVE PROTEIN: 14.2 [0 - 8] MG/L; NPTST184-DENGUE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

AE Stopped Initial 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	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はブラジルの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，炎症性気管支疾患の事象を発現した。関連する病歴は，喫煙者（1 日 1 箱を 15 年間），潰瘍性大腸炎，高血圧，糖尿病，閉塞性睡眠時無呼吸症候群及び元飲酒者であった。

Event 3 の臨床経過：

投与291日後＊，被験者は炎症性気管支疾患を発現した。

投与297日後＊　，被験者は呼吸窮迫及び発熱を訴え入院した。発熱は薬を使用しても下がらず，発熱の精査のための入院であった。被験者は抗生物質及びコルチコイド療法で治療された。

投与298日後＊，被験者は退院し，自宅で治療を続けた。

投与された薬剤は，アジスロマイシン，デカドロン，dipirone，オメプラゾール，ヘパリン，paracetamol 及び rocefin であった。

The patient's past medications include:

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

SULFASALAZINE 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) Noninfective bronchitis (10062644) (Noninfective bronchitis (10062644)) [v.24.0] [10062644]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of INFLAMMATORY BRONCHOPATHY

- Investigator: Not Applicable

- AbbVie: Event triggers include airway bronchospasm, inhalation of air pollutants and chemical exposures.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY TEMPERATURE:** 38.5 Degrees C

[redacted] **20[redacted] CRP:** 14.7 MG/L (normal 0.0 to 8.0)

[redacted] **20[redacted] CT SCAN:** Inflammatory Bronchopathy

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

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

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Neutropenia: Study drug interrupted.
Anaemia: 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
クロストリジウム・ディフィシレ感染	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	2[redacted]	FEMALE	WHITE

Medical History	Onset Year
ALLERGIC RHINITIS	20[redacted]
CONJUNCTIVITIS	20[redacted]
DYSPEPSIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 369	369

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
MESALAZINE	800 mg	TID	Y-M: 20[redacted]
MESALAZINE	3 g	QD	Y-M: 20[redacted]
CODEINE	30 mg	PRN	Y-M: 20[redacted] / -311
HYOSCINE	10 mg	PRN	Y-M: 20[redacted] / -311
MESALAZINE	2 g	BID	Y-M: 20[redacted] / -311
PREDNISONE	20 mg	BID	Y-M: 20[redacted] / -311
DOMPERIDONE	10 mg	PRN	Y-M: 20[redacted] / -219
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -79
DESOGESTREL;ETHINYLESTRADIOL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -91
FLUTICASONE	2 OTHER: PUFFS	BID	Y-M: 20[redacted] / -56
CARMELLOSE;GLYCEROL	1 OTHER: DROP	QID	Y-M: 20[redacted] / -62
ALFENTANIL	5 mL	QD	Y-M: 20[redacted] / -64
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: SACHET	BID	Y-M: 20[redacted] / -64
DIMENHYDRINATE	50 mg	PRN	Y-M: 20[redacted] / -64
HYOSCINE	1 OTHER: AMPOULE	QD	Y-M: 20[redacted] / -64
LIDOCAINE	1 OTHER: AMPOULE	QD	Y-M: 20[redacted] / -64
PROPOFOL	3 OTHER: AMPOULE	QD	Y-M: 20[redacted] / -64
ALFENTANIL	5 mL	QD	Y-M: 20[redacted] / -8
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: SACHET	BID	Y-M: 20[redacted] / -8
DIMENHYDRINATE	50 mg	PRN	Y-M: 20[redacted] / -8
LIDOCAINE	1 OTHER: AMPOULE	QD	Y-M: 20[redacted] / -8
LIDOCAINE	1 OTHER: VIAL	QD	Y-M: 20[redacted] / -8
PROPOFOL	3 OTHER: AMPOULE	QD	Y-M: 20[redacted] / -8
SIMETICONE	50 OTHER: DROPS	QD	Y-M: 20[redacted] / -8

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
CODEINE	30 mg	PRN	Y-M: 20[redacted] / -311	ONGOING
HYOSCINE	10 mg	PRN	Y-M: 20[redacted] / -311	ONGOING
MESALAZINE	2 g	BID	Y-M: 20[redacted] / -311	ONGOING
DOMPERIDONE	10 mg	PRN	Y-M: 20[redacted] / -219	ONGOING
DESOGESTREL;ETHINYLESTRADIOL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -91	ONGOING
FLUTICASONE	2 OTHER: PUFFS	BID	Y-M: 20[redacted] / -56	ONGOING
CARMELLOSE;GLYCEROL	1 OTHER: DROP	QID	Y-M: 20[redacted] / -62	ONGOING
SUMATRIPTAN	25 mg	PRN	Y-M: 20[redacted] / 14	ONGOING
METAMIZOLE	1 g	PRN	Y-M: 20[redacted] / 51	ONGOING
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 204
PANTOPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 180	Y-M: 20[redacted] / 271
PREDNISONE	25 mg	QD	Y-M: 20[redacted] / 205	Y-M: 20[redacted] / 211
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 212	Y-M: 20[redacted] / 218
PREDNISONE	15 mg	QD	Y-M: 20[redacted] / 219	Y-M: 20[redacted] / 225
PREDNISONE	10 mg	QD	Y-M: 20[redacted] / 226	Y-M: 20[redacted] / 229
BROMOPRIDE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 228
METAMIZOLE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 228
TRAMADOL	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted] / 228	Y-M: 20[redacted] / 228
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 232
HYDROCORTISONE	100 mg	QID	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 232
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 229	Y-M: 20[redacted] / 232
VANCOMYCIN	125 mg	QID	Y-M: 20[redacted] / 232	Y-M: 20[redacted] / 246

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

Event Description	CLOSTRIDIUM 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	[redacted]20[redacted] / 285
Age at AE Onset	2[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 229): Leukocytes: 7.48 [4500 - 11000] 10^9/L; [redacted]20[redacted] (RX DAY 230): Leukocytes: 13.5 [4500 - 11000] 10^9/L; [redacted]20[redacted] (RX DAY 231): Leukocytes: 13.7 [4500 - 11000] 10^9/L
Microbiology	[redacted]20[redacted] (RX DAY 229): STOOL NPTST129-CLOSTRIDIUM DIFFICILE RT-PCR: POSITIVE-TOXINE B (TCDB) POSITIVE; STOOL NPTST132-CLOSTRIDIUM DIFFICILE TOXIN AN: POSITIVE-TOXIN A / TOXIN B FOR CLOSTRIDIUM DIFFICILE AND GDH POSITIVE; [redacted]20[redacted] (RX DAY 230): OTHER INTESTINAL BIOPSY NPTST119-CITOMEGALOVIRUS RT-PCR: NEGATIVE; OTHER INTESTINA BIOPSY NPTST278-HERPES VIRUS RT-PCR: NEGATIVE
AE Stopped Initial Rx Day	288
Duration of AE	4 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]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験ブラジルの 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，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，消化不良，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与285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288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196日後＊，被験者は潰瘍性大腸炎の悪化（非重篤）を発現した。

投与285日後＊　　，被験者は腹痛の悪化及び下痢を訴え入院した。被験者はまた，夜間を含めて 1 日平均 20 回の液状の便通（主に粘液，時には血液を含み，時には腹部膨満，頭痛及び全身倦怠感を伴うこともある）を訴えた。被験者はまた別に最高で摂氏 38°C の発熱も訴えた。被験者は大腸炎による腸管の炎症が悪化している可能性が高いと評価された。

診断検査の結果，胸膜基底部には病変がなく，クロストリジウム・ディフィシレ感染が確認された。肝臓の大きさ，輪郭及び形態は保たれており，局所的な実質病変は認められなかった。また，小さくまばらな胆管嚢胞及び VS/VIII 移行部に約 4 mm の血腫が認められた。その他の検査項目は，正常又は臨床的に重要でない変化を示した。被験者は隔離され，抗生物質の投与により被験者の状態は改善した。投与227日後＊，被験者は退院した。

治験責任医師によると，この被験者における危険因子は病院内で仕事をしていることであった。

投与された薬剤は，ceftriaxone，ヒドロコルチゾン，vancomicina，ドンペリドン，ブスコパン，メサラジン，コデイン，bromopride，メトロニダゾール，トラマール及び dipyrone であった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Clostridium difficile infection (10054236)　(Clostridium difficile infection (10054236))　[v.24.0] [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 UPADACITINIB (Blinded)

Event of CLOSTRIDIUM DIFFICILE INFECTION

- Investigator: The worsening of Ulcerative Colitis was related to admission to the Hospital.

- AbbVie: The event is more likely related to pre-existing Ulcerative colitis. Patients with inflammatory bowel disease, including ulcerative colitis, are at an increased risk of developing Clostridium difficile infection, with higher rates of asymptomatic carriage of C. difficile (9.4% in patients with ulcerative colitis, versus 1% in healthy volunteers).

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE RT-PCR:** POSITIVE-TOXINE B (TCDB) POSITIVE

[redacted] 20[redacted] CT SCAN: Discreet mucosal enhancement of the walls of the colonic and rectal segments associated with the presenceof lymph nodes in greater numbers than usual, measuring up to 9 mm. Reaction aspect, suggestive for infectious inflammatory process.

[redacted] **20[redacted] INTESTINAL BIOPSY:** HERPES VIRUS RT-PCR - NEGATIVE

[redacted] **20[redacted] INTESTINAL BIOPSY:** CYTOMEGALOVIRUS RT-PCR - NEGATIVE

[redacted] **20[redacted] PCR SARS COV-2:** (NASAL MUCOSA FOR FEVER)Not detectable

[redacted] **20[redacted] QUALITATIVE CYTOMEGALOVIRUS RESEARCH:** Not detectable

[redacted] **20[redacted] SIGMOIDOSCOPY:** Active colitis- Mayo endoscopic score 2

[redacted] **20[redacted] TOXIN CLOSTRIDOIDES DIFFICILE IN THE FECES:** POSITIVE-TOXIN A / TOXIN B FOR CLOSTRIDIUM DIFFICILE AND GDH 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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	4[redacted]	MALE	WHITE

Medical History	Onset Year
AXIAL ARTHROPATHY	20[redacted]
DIARRHEA	20[redacted]
ENVIRONMENTAL ALLERGIES	19[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
PENICILLIN ALLERGY	20[redacted]
RECTAL BLEEDING	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	FORMER			
CIGARETTES	FORMER	0.5 PACK	6	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		ORAL	QD	[redacted] / 1	[redacted] / 55	55
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 1	[redacted] / 61	61

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PROBIOTICS NOS	NOT REPORTED	QD	Y-M: [redacted]
MESALAZINE	4800 mg	QD	Y-M: [redacted] / -303
CORTICOSTEROIDS	10.000 %	QD	Y-M: [redacted] / -219
BETAMETHASONE	1 OTHER: BOTTLE	QD	Y-M: [redacted] / -94
MESALAZINE	4 OTHER: GM	QD	Y-M: [redacted] / -94
MESALAZINE	4 g	QD	Y-M: [redacted] / -94
CALCIUM CARBONATE	2500 mg	QD	Y-M: [redacted] / -55
FENTANYL	100 ug	OTHER: ONCE	Y-M: [redacted] / -62
MIDAZOLAM	5 mg	OTHER: ONCE	Y-M: [redacted] / -62
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	4 L	OTHER: ONCE	Y-M: [redacted] / -63
PREDNISONE	30 mg	QD	Y-M: [redacted] / -69
PREDNISONE	25 mg	QD	Y-M: [redacted] / -70
PREDNISONE	15 mg	QD	Y-M: [redacted] / -73
INFLUENZA VACCINE	60 OTHER: MCQ	OTHER: ONCE	Y-M: [redacted] / -80
CALCIUM CARBONATE	2400 mg	QD	Y-M: [redacted] / -46
FENTANYL	50 ug	OTHER: X 1	Y-M: [redacted] / -7
MIDAZOLAM	5 mg	OTHER: X 1	Y-M: [redacted] / -7
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	4 L	OTHER: X 1	Y-M: [redacted] / -8
CETIRIZINE	10 mg	PRN	Y: [redacted]
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: [redacted]
VITAMIN D NOS	1000 mg	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 / Stop Year-Month / RX Day	
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -303	ONGOING
CALCIUM CARBONATE	2400 mg	QD	Y-M: 20[redacted] / -46	Y-M: 20[redacted] / 56
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / 21	Y-M: 20[redacted] / 25
TOFACITINIB	10 mg	BID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 69
METHYLPREDNISOLONE	30 mg	BID	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 73
FENTANYL	50 ug	OTHER: ONCE	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 70
MIDAZOLAM	3 mg	OTHER: ONCE	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 70
SODIUM PHOSPHATE	2 OTHER: APPLICATIONS	OTHER: TWICE	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 70
TINZAPARIN	4500 IU	QD	Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 74
CALCIUM	500 mg	BID	Y-M: 20[redacted] / 71	ONGOING
DIPHENHYDRAMINE	50 mg	OTHER: X1	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 71
INFLIXIMAB	800 mg	OTHER: Q2WEEKS	Y-M: 20[redacted] / 71	ONGOING
PARACETAMOL	650 mg	OTHER: X1	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 71
CETIRIZINE	10 mg	PRN	Y: 19[redacted]	ONGOING
VITAMIN D NOS	1000 mg	QD	Y: 20[redacted]	ONGOING

Event #1: 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	[redacted]20[redacted] / 110
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	123 (7 DAYS AFTER LAST TREATMENT)
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	YES
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	WORSENING OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 124 (8 DAYS AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
[redacted]20[redacted] (RX DAY 70): STOOL NPTST131-CLOSTRIDIUM DIFFICILE TEST: NEGATIVE	
AE Stopped Initial Rx Day	128 (12 DAYS AFTER LAST TREATMENT)
Duration of AE	5 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	SUBJECT HAD A LOSS OF RESPONSE TO STUDY DRUG. SUBJECT DISCONTINUED STUDY AND NEW MEDICATION STARTED. DESPITE THIS THE SUBJECT WAS HAVING A FLARE AND WAS HOSPITALIZED.
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]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はカナダの 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，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 0.5 箱を 6 年間），潰瘍性大腸炎（左側），下痢，直腸出血，体軸性脊椎関節炎及び元飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与124日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与128日後＊　，潰瘍性大腸炎の悪化は消失した。

投与110日後＊　，被験者は潰瘍性大腸炎の悪化（非重篤）を発現した。被験者は治験薬の効果がみられなくなったため，投与116日後＊　に治験薬の投与が中止され，新しい薬を開始した。投与123日後＊，本事象は消失したと考えられた。

投与124日後＊　，被験者は潰瘍性大腸炎の再燃の疑いで入院した。被験者は 1.5–2 時間ごとに緩い血の混じった粘液状の便通があり，頻度は 1 日 10 回以上であった。被験者は過去 1 週間に，激しい筋痙攣及び食欲不振があった。被験者は以前にもこの症状を経験していた。被験者は入院中，外科的処置は受けなかった。投与128日後＊，被験者は退院した。

投与された薬剤は，ソル・メドロール及び inflectra であった。

The patient's past medications include:

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

Causality for ABT-494 (Blinded)

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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: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of WORSENING OF ULCERATIVE COLITIS

- Investigator: Not reported

- AbbVie: More likely related to pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL X-RAY:** NO ACUTE INTRATHORACIC ABNORMALITY. NO BOWEL OBSTRUCTION

[redacted] **20[redacted] ALBUMIN:** 34 no unit

[redacted] **20[redacted] ANION GAP:** 11 no unit

[redacted] **20[redacted] CHEST X-RAY:** RIGHT BASILAR ATELECTASIS, NO FOCAL CONSOLIDATION. PLEURAL SPACES ARE CLEAR. CARDIOMEDIASTINAL CONTOURS ARE WITHIN NORMAL LIMITS

[redacted] **20[redacted] CL:** 101 no unit

[redacted] **20[redacted] CLOSTRIDIUM DIFFICILE STOOL:** Negative

[redacted] **20[redacted] CO2:** 24 no unit

[redacted] **20[redacted] CREATININE:** 101 no unit

[redacted] **20[redacted] CRP:** 36.1 no unit

[redacted] **20[redacted] FLEXIBLE SIGMOIDOSCOPY:** EVERE CONFLUENT INFLAMMATION THROUGHOUT ALL THE MUCOSA WITH ULCERATION AND ABUNDANT MUCOUS, IT WAS FRIABLE AND A NORMAL VASCULAR PATTERN WAS NO WHERE TO BE SEEN.

[redacted] **20[redacted] GFR:** 75 no unit

[redacted] **20[redacted] HCT:** 0.42 no unit

[redacted] **20[redacted] HGB:** 145 no unit

[redacted] **20[redacted] INR:** 1.2 no unit

[redacted] **20[redacted] K:** 4.6 no unit

[redacted] **20[redacted] MCHC:** 349 no unit

[redacted] **20[redacted] MCV:** 88 no unit

[redacted] **20[redacted] NA:** 136 no unit

[redacted] **20[redacted] PLT:** 440 no unit

[redacted] **20[redacted] RBC:** 4.74 no unit

[redacted] **20[redacted] RDW:** 12.5 no unit

[redacted] **20[redacted] UREA:** 3.4 no unit

[redacted] **20[redacted] WBC:** 9.9 no unit

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
潰瘍性大腸炎	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	6[redacted]	MALE	WHITE

Medical History	Onset Year
ANEMIA: ANEMIA	20[redacted]
COGNITIVE OR PSYCHIATRIC DISORDER: ANXIETY	20[redacted]
DIABETES MELLITUS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HYPERTENSION	NOT REPORTED
OTHER: INSOMNIA	20[redacted]
OTHER: LOW ALBUMIN	20[redacted]
OTHER: LOW HEMATOCRIT	20[redacted]
OTHER: LOWER LIMBS MYALGIA	20[redacted]
OTHER: LOWER LIMBS WEAKNESS	20[redacted]
OTHER: NUMBNESS OF FEET INTERMITTENTLY	20[redacted]
OTHER: VISUAL BLURRING	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: ANAL FISSURE 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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 62	62
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 154	154

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METFORMIN;SITAGLIPTIN	50-500 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	5.000 mg/kg	Q 2 WEEKS	Y-M: 20[redacted] / -259
METHYLPREDNISOLONE	30 mg	OTHER: Q 8 HOURS	Y-M: 20[redacted] / -266
PREDNISONE	60 mg	QD	Y-M: 20[redacted] / -270
CALCIUM	500 mg	BID	Y-M: 20[redacted] / -180
COLECALCIFEROL	1000 OTHER: UI	QD	Y-M: 20[redacted] / -180
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted] / -182
HYDROCORTISONE	100 mg	OTHER: Q 8 HOURS	Y-M: 20[redacted] / -145
MIRTAZAPINE	7.5 mg	QD	Y-M: 20[redacted] / -115
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -117
GLICLAZIDE	120 mg	QD	Y-M: 20[redacted] / -119
MIRTAZAPINE	15 mg	QD	Y-M: 20[redacted] / -77
INSULIN HUMAN	4-10 OTHER: U	QD	Y-M: 20[redacted] / -82
FENTANYL	100 mg	QD	Y-M: 20[redacted] / -83
MIDAZOLAM	3 mg	QD	Y-M: 20[redacted] / -83
CLONAZEPAM	0.25 mg	QD	Y-M: 20[redacted] / -85
ZOPICLONE	7.5 mg	OTHER: HS	Y-M: 20[redacted] / -89
OXAZEPAM	30 mg	QD	Y-M: 20[redacted] / -62
CLONAZEPAM	0.5 mg	QD	Y-M: 20[redacted] / -13
MIRTAZAPINE	15 mg	QD	Y-M: 20[redacted] / -13
PAROXETINE	10 mg	QD	Y-M: 20[redacted] / -13
MIRTAZAPINE	30 mg	QD	Y-M: 20[redacted] / -33
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -3
PAROXETINE	20 mg	QD	Y-M: 20[redacted] / -5
FENTANYL	100 mg	QD	Y-M: 20[redacted] / -6
MIDAZOLAM	3 mg	QD	Y-M: 20[redacted] / -6

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	
METFORMIN;SITAGLIPTIN	50-500 mg	BID	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	1000 OTHER: UI	QD	Y-M: 20[redacted] / -180	ONGOING
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted] / -182	ONGOING
OXAZEPAM	30 mg	QD	Y-M: 20[redacted] / -62	Y-M: 20[redacted] / 119
MIRTAZAPINE	15 mg	QD	Y-M: 20[redacted] / -13	Y-M: 20[redacted] / 92
PAROXETINE	10 mg	QD	Y-M: 20[redacted] / 9	ONGOING
GLICLAZIDE	60 mg	QD	Y-M: 20[redacted] / 38	ONGOING
IRON	300 mg	BID	Y-M: 20[redacted] / 88	ONGOING
MIRTAZAPINE	7.5 mg	QD	Y-M: 20[redacted] / 93	ONGOING
OXAZEPAM	20 mg	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 126
OXAZEPAM	15 mg	QD	Y-M: 20[redacted] / 127	ONGOING
PARACETAMOL	325 mg	PRN	Y-M: 20[redacted] / 155	ONGOING

Event #1: Event of Interest - Anemia

Event Description	WORSENING OF ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 150
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	217 (1 DAY AFTER LAST TREATMENT)
Duration of AE	68 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

Event Description	ULCERATIVE COLITIS EXACERBATION
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 217 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 128): Creatinine: 87 [60 - 105] UMOL/L; Sodium: 137 [135 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 156): Hemoglobin: 80 [135 - 175] G/L; NPTST087-C-REACTIVE PROTEIN: 245.9 [0 - 5] MG/L; Platelets: 594 [140 - 450] 10^9/L; Potassium: 3.6 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 157): Potassium: 3.5 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 161): NPTST087-C-REACTIVE PROTEIN: 202.2 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 162): Hemoglobin: 80 [135 - 175] G/L; Platelets: 704 [140 - 450] 10^9/L

Microbiology

NOT REPORTED

AE Stopped Initial 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]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はカナダの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，潰瘍性大腸炎の悪化を発現した。関連する病歴は，裂肛手術，糖尿病，貧血，不安，断続的な足のしびれ感，潰瘍性大腸炎，下肢の筋肉痛，下肢の脱力，高血圧，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 2 の臨床経過：

投与217日後＊，被験者は潰瘍性大腸炎の悪化を発現した。

投与217日後＊　，被験者は潰瘍性大腸炎の悪化があり入院した。被験者は直腸出血，並びにその他の腸管外症状として末梢性関節症，右眼の上強膜炎（非重篤），結節性脛骨前紅斑（非重篤），口腔内アフタ性潰瘍（非重篤），貧血の悪化（非重篤）及び発熱（非重篤）を呈した。投与227日後＊，被験者は退院した。

投与218日後＊，本事象によりこの被験者の治験は完全に中止された。

投与された薬剤は，salazopyrine，メトロニダゾール，ciprofloxacine，アセトアミノフェン及びprednisone であった。

The patient's past medications include:

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

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

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

Causality for ABT-494 (Blinded)

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

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

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

Dechallenge: No

Alternative Etiology for ABT-494 (Blinded)

Event of ULCERATIVE COLITIS EXACERBATION

- Investigator: Not applicable.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 245.9 MG/L (normal 0 to 5)

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 202.2 MG/L (normal 0 to 5)

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

[redacted] 20[redacted] **COLONOSCOPY:** Mayo score 3

[redacted] 20[redacted] **HEMOGLOBIN:** 80 G/DL (normal 135 to 175)

[redacted] 20[redacted] **HEMOGLOBIN:** 80 G/DL (normal 135 to 175)

[redacted] 20[redacted] **PLATELET COUNT:** 594 X10**9/L (normal 140 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 704 X10**9/L (normal 140 to 450)

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
肝酵素上昇				X
肝炎	X	X		X
肺炎球菌性肺炎	X			X

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

Medical History	Onset Year
ANEMIA: ANEMIA	20[redacted]
LEFT SIDED UC	20[redacted]
OTHER: ARTICULAR PAIN	20[redacted]
OTHER: BUCCAL HERPES	19[redacted]
OTHER: DISCREET SPONDYLOSIS DORSAL MULTI-STAGE	20[redacted]
OTHER: DYSLIPIDEMIA	20[redacted]
OTHER: ECZEMA	20[redacted]
OTHER: EXERTIONAL PAINFUL LEGS	19[redacted]
OTHER: GLOBUS SENSATION	19[redacted]
OTHER: HEMORROIDS	20[redacted]
OTHER: INSOMNIA	20[redacted]
OTHER: INTERSTITIAL CYSTITIS	20[redacted]
OTHER: NIGHT SWEATS	20[redacted]
OTHER: OCCASIONAL DIZZINESS FOLLOWING SUDDEN MOVEMENTS	20[redacted]
OTHER: SEASONAL ALLERGIC RHINITIS	20[redacted]
OTHER: SHORTNESS OF BREATH ON EXERTION	20[redacted]
OTHER: STOMACH SPASMS	20[redacted]
OTHER: TIREDNESS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	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	17	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 283	283

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
FLUTICASONE	55 ug	PRN	Y-M: 20[redacted]
LANSOPRAZOLE	30 mg	BID	Y-M: 20[redacted]
ROSUVASTATIN	20 mg	QD	Y-M: 20[redacted]
CALCIUM	500 mg	BID	Y-M: 20[redacted]
ESTRADIOL	10 OTHER: MCG	OTHER: 2 TIMES A WEEK	Y-M: 20[redacted]
HYDROCORTISONE	0.5 %	PRN	Y-M: 20[redacted]
MOMETASONE	0.1 %	QD	Y-M: 20[redacted]
VITAMIN D NOS	400 IU	BID	Y-M: 20[redacted]
AMITRIPTYLINE	25 mg	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]
PREDNISONE	5 mg	QD	Y-M: 20[redacted] / -346
INFLIXIMAB	5.000 mg/kg	Q 6 WEEKS	Y-M: 20[redacted] / -252
CYANOCOBALAMIN	1200 ug	QD	Y-M: 20[redacted] / -125
ACICLOVIR	50 mg	PRN	Y-M: 20[redacted] / -63
FENTANYL	100 mg	QD	Y-M: 20[redacted] / -70
MIDAZOLAM	3 mg	QD	Y-M: 20[redacted] / -70
IRON	300 mg	TID	Y-M: 20[redacted] / -28
IRON	300 mg	BID	Y-M: 20[redacted] / -14
VITAMIN D NOS	400 IU	BID	Y-M: 20[redacted] / -14

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
FLUTICASONE	55 ug	PRN	Y-M: 20[redacted]	ONGOING
LANSOPRAZOLE	30 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 285
ROSUVASTATIN	20 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 283
CALCIUM	500 mg	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 283
ESTRADIOL	10 OTHER: MCG	OTHER: 2 TIMES A WEEK	Y-M: 20[redacted]	Y-M: 20[redacted] / 283
HYDROCORTISONE	0.5 %	PRN	Y-M: 20[redacted]	ONGOING
MOMETASONE	0.1 %	QD	Y-M: 20[redacted]	ONGOING
AMITRIPTYLINE	25 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 283
MESALAZINE	4.8 g	QD	Y-M: 20[redacted]	ONGOING
CYANOCOBALAMIN	1200 ug	QD	Y-M: 20[redacted] / -125	Y-M: 20[redacted] / 283
VITAMIN D NOS	400 IU	BID	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 283
IRON	300 mg	TID	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 283
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / 88	Y-M: 20[redacted] / 144
DICYCLOVERINE	10 mg	TID	Y-M: 20[redacted] / 148	ONGOING
PERINDOPRIL	4 mg	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 283
ACICLOVIR	500 mg	TID	Y-M: 20[redacted] / 283	Y-M: 20[redacted] / 289
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 283	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 283	Y-M: 20[redacted] / 283
POTASSIUM	20 mEq	QD	Y-M: 20[redacted] / 283	Y-M: 20[redacted] / 283
HEPARIN	5000 OTHER: U	BID	Y-M: 20[redacted] / 284	Y-M: 20[redacted] / 292
MEROPENEM	2 g	TID	Y-M: 20[redacted] / 284	Y-M: 20[redacted] / 284
VANCOMYCIN	750 mg	TID	Y-M: 20[redacted] / 284	Y-M: 20[redacted] / 284
POTASSIUM	40 mEq	BID	Y-M: 20[redacted] / 285	Y-M: 20[redacted] / 285
DEXLANSOPRAZOLE	60 mg	QD	Y-M: 20[redacted] / 286	ONGOING
LORAZEPAM	1 mg	QD	Y-M: 20[redacted] / 286	Y-M: 20[redacted] / 286
MAGNESIUM SULFATE	2 g	QD	Y-M: 20[redacted] / 288	Y-M: 20[redacted] / 288
POTASSIUM	40 mEq	BID	Y-M: 20[redacted] / 288	Y-M: 20[redacted] / 288
FENTANYL	100 mg	QD	Y-M: 20[redacted] / 304	Y-M: 20[redacted] / 304
MIDAZOLAM	3 mg	QD	Y-M: 20[redacted] / 304	Y-M: 20[redacted] / 304

Event #1: Event of Interest - Hepatic Disorder

Event Description	ELEVATED LIVER ENZYMES
Preferred term	肝酵素上昇
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 114
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	144
Duration of AE	31 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 - Hepatic Disorder

Event Description	INCREASED LIVER ENZYMES
Preferred term	肝酵素上昇
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 316
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	339
Duration of AE	24 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, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections, Event of Interest - Hepatic Disorder

Event Description	HEPATITIS INDETERMINATE ETIOLOGY
Preferred term	肝炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 339
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 283): Alanine Aminotransferase: 559 [5 - 35] U/L; Aspartate Aminotransferase: 499 [5 - 35] U/L; Bilirubin: 50 [3 - 21] UMOL/L; Creatinine: 92 [45 - 85] UMOL/L; Erythrocytes: 3.85 [4 - 5.2] 10^12/L; Leukocytes: 33.5 [4.5 - 11.3] 10^9/L; NPTST034-ANTI-HEPATITIS-C: NEGATIF [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST165-CRP: 334.1 [0 - 5] MG/L; Platelets: 764 [140 - 450] 10^9/L; Potassium: 2.8 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 289): Alkaline Phosphatase: 277 [35 - 105] U/L; [redacted]20[redacted] (RX DAY 290): Alanine Aminotransferase: 46 [5 - 35] U/L; Aspartate Aminotransferase: 41 [5 - 35] U/L; Bilirubin: 12 [3 - 21] UMOL/L; Potassium: 3.7 [3.5 - 5] MMOL/L; [redacted]20[redacted] (RX DAY 292): Alanine Aminotransferase: 30 [5 - 35] U/L; Alkaline Phosphatase: 199 [35 - 105] U/L; Aspartate Aminotransferase: 27 [5 - 35] U/L; Bilirubin: 10 [3 - 21] UMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 283): BLOOD NPTST031-ANTI HBS: NEGATIVE; BLOOD NPTST032-ANTI HEPATITIS C: NEGATIVE; BLOOD NPTST075-BLOOD CULTURE: NEGATIVE; BLOOD NPTST134-CMV: NEGATIVE; URINE NPTST170-CULTURE: NEGATIVE; BLOOD NPTST191-EBV VCA IGM: NEGATIVE; BLOOD NPTST270-HEP A IGM: NEGATIVE; BLOOD NPTST305-INFLUENZA: NEGATIVE; URINE NPTST320-LEGIONNELLA: NEGATIVE; BLOOD NPTST351-MONOTEST: NEGATIVE; [redacted]20[redacted] (RX DAY 284): CEREBROSPINAL FLUID NPTST290-HSV1 - HSV2 (HERPES)QUANTITATIV: NEGATIVE; [redacted]20[redacted] (RX DAY 288): BLOOD NPTST284-HIV: NEGATIVE

AE Stopped Initial Rx Day	348 (9 DAYS AFTER LAST TREATMENT)
Duration of AE	10 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #4: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	SEVERE INFECTION: PNEUMOCOCCAL PNEUMONIA
Preferred term	肺炎球菌性肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 339
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 283): Erythrocytes: 3.85 [4 - 5.2] 10^12/L; Leukocytes: 32 [4.5 - 11.3] 10^9/L; NPTST114-CEREBROSPINAL FLUID: NO ABNORMALITIES [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST170-CULTURE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST173-CULTURES: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST320-LEGIONNELLA: ABSENCE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST351-MONOTEST: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST418-PROTEIN C REACTIVE: 334.1 [0 - 5] MG/L; Neutrophils: 21.76 [1.8 - 7] 10^9/L; Platelets: 764 [140 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 284): NPTST170-CULTURE: PRESENCE OF STREPTOC [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 290): NPTST417-PROTEIN C REACTICE: 51.3 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 292): Erythrocytes: 2.8 [4 - 5.2] 10^12/L; Leukocytes: 11.7 [4.5 - 11.3] 10^9/L; Platelets: 915 [140 - 450] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 283): URINE NPTST170-CULTURE: POSITIVE-PRESENCE OF STREPTOCOCCUS PNEUMONIAE ANTIGEN; BLOOD NPTST266-HEMOCULTURES: NEGATIVE

AE Stopped Initial 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

Event #5: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 360 (21 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial 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]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はカナダの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，高度の感染症である肺炎球菌性肺炎及び原因不明の肝炎の事象を発現した。関連する病歴は，頬のヘルペス，元喫煙者（1 日 1 箱を 17 年間），季節性アレルギー性鼻炎，潰瘍性大腸炎，湿疹，間質性膀胱炎，貧血，運動時の息切れ，現飲酒者（1 日 2–4 杯）及び高血圧であった。

Event 3 及び 4 の臨床経過：

投与339日後＊　，被験者は高度の感染症である肺炎球菌性肺炎及び原因不明の肝炎を発現した。投与348日後＊，原因不明の肝炎は消失した。

投与316日後＊，被験者は肝酵素の上昇（非重篤）を経験した。

投与339日後＊　　，被験者は発熱，悪寒，錯乱，精神運動の低下及び著しい細胞溶解があり，救急治療室に入院した。被験者の入院は，肺炎球菌性肺炎及び原因不明の肝炎のためであった。被験者はさらに，食欲不振，疲労，嘔吐，悪心，暗色尿，黄疸，腹痛及び振戦の症状があった。抗生物質の静脈内投与及び抗ウイルス薬の投与を開始した。投与348日後＊　　，被験者の全身状態は改善し，発熱もなく，肝酵素も正常値となった（結果は提供なし）。本事象により治験薬の投与は完全に中止された。被験者は引き続き入院した。

被験者はレクリエーショナルドラッグ，ハーブのサプリメント又はお茶は使用しておらず，国外への旅行もしていなかった。過去に刺鍼法の経験はなく，タトゥーも入れておらず，職業上の毒素曝露もなく，肝臓病の家族歴もなかった。

投与された薬剤は，アシクロビル，バンコマイシン，セフトリアキソン，ヘパリン及びメロペネムであった。

The patient's past medications include:

PREDNISONE for ULCERATIVE COLITIS ([redacted])

INFLECTRA for ULCERATIVE COLITIS ([redacted])

BUDESONIDE for ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Blinded)

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1) Pneumococcal pneumonia (10035647) (Pneumonia pneumococcal (10035728)) [v.21.1] [10035647]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Hepatitis (10019717) (Hepatitis (10019717)) [v.21.1] [10019717]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for ABT-494 (Blinded)

Event of SEVERE INFECTION: PNEUMOCOCCAL PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Event of HEPATITIS INDETERMINATE ETIOLOGY

- Investigator: Infectious versus Drug Side Effect (JAK) suspected.

- AbbVie: Event is more likely related to severe infection: pneumococcal pneumonia and pulmonary abscess.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Liver and bile ducts within the limits of the abnormal, no inflammatory process, no ascites.

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 559 U/L (normal 5 to 35)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 46 U/L (normal 5 to 35)

[redacted] **20[redacted] ALBUMIN:** 4.0 G/DL

[redacted] **20[redacted] ALBUMIN:** 4.6 G/DL

[redacted] **20[redacted] ALBUMIN:** 4.8 G/DL

[redacted] **20[redacted] ALBUMIN:** 4.5 G/DL

[redacted] **20[redacted] ALBUMIN:** 4.7 G/DL

[redacted] **20[redacted] ALBUMIN:** 4.5 G/DL

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 115 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 125 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 108 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 103 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 105 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 114 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 207 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 103 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 98 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 72 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 101 U/L (normal 35 to 105)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 199 U/L (normal 35 to 105)

[redacted] **20[redacted] ALT:** 16 U/L

[redacted] **20[redacted] ALT:** 16 U/L

[redacted] **20[redacted] ALT:** 17 U/L

[redacted] **20[redacted] ALT:** 18 U/L

[redacted] **20[redacted] ALT:** 18 U/L

[redacted] **20[redacted] ALT:** 24 U/L

[redacted] **20[redacted] ALT:** 24 U/L

[redacted] **20[redacted] ALT:** 36 U/L

[redacted] **20[redacted] ALT:** 22 U/L

[redacted] **20[redacted] ALT:** 37 U/L

[redacted] **20[redacted] ALT:** 25 U/L

[redacted] **20[redacted] ALT:** 25 U/L

[redacted] **20[redacted] ALT:** 61 U/L

[redacted] **20[redacted] ALT:** 283 U/L (normal 5 to 35)

[redacted] **20[redacted] ANTI-HEPATITIS C ANTIBODY:** Negative

Unknown date ASMA: negative

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 499 U/L (normal 5 to 35)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 41 U/L (normal 5 to 35)

[redacted] **20[redacted] AST:** 25 U/L

[redacted] **20[redacted] AST:** 21 U/L

[redacted] **20[redacted] AST:** 24 U/L

[redacted] **20[redacted] AST:** 28 U/L

[redacted] **20[redacted] AST:** 37 U/L

[redacted] **20[redacted] AST:** 37 U/L

[redacted] **20[redacted] AST:** 23 U/L

[redacted] **20[redacted] AST:** 32 U/L

[redacted] **20[redacted] AST:** 18 U/L

[redacted] **20[redacted] AST:** 32 U/L

[redacted] **20[redacted] AST:** 48 U/L

[redacted] **20[redacted] BILIRUBIN:** 0.2 mg/dL

[redacted] **20[redacted] BILIRUBIN:** <0.2 mg/dl

[redacted] **20[redacted] BILIRUBIN**: 0.3 mg/dL

[redacted] **20[redacted] BILIRUBIN:** <0.2mg/dl

[redacted] **20[redacted] BILIRUBIN:** <0.2 mg/dl

[redacted] **20[redacted] BILIRUBIN:** 0.3 mg/dL

[redacted] **20[redacted] BILIRUBIN:** 0.3 mg/dL

[redacted] **20[redacted] BILIRUBIN:** 0.4 mg/dL

[redacted] **20[redacted] BILIRUBIN:** 50 umol/L (normal 3 to 21)

[redacted] **20[redacted] BILIRUBIN:** 12 umol/L (normal 3 to 21)

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

[redacted] **20[redacted] BRONCHOSCOPY WITH BRONCHOALVEOLAR LAVAGE:** POLYNUCLEAR PRESENCE EPITHELIAL CELLS BACTERIA ABSENCE.

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 51.3 MG/L (normal 0 to 5.0)

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 334.1 MG/L (normal 0 to 5.0)

[redacted] **20[redacted] CEREBROSPINAL FLUID:** No abnomalities

[redacted] **20[redacted] CERULOPLASMIN:** 0.3 G/L (normal 0.16 to 0.45)

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

Unknown date CMV: Negative

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

[redacted] **20[redacted] CREATININE:** 92 umol/L (normal 45 to 85)

[redacted] **20[redacted] CRP:** 334.1 MG/L (normal 0 to 5)

Unknown date EBV: Negative

Unknown date ERV: Negative

Unknown date HAV: Negative

Unknown date HBV: Negative

Unknown date INFLUENZA TEST: Negative

Unknown date LEGIONELLA: Negative

[redacted] **20[redacted] LEGIONELLA TEST:** Absent

Unknown date LIVER BIOPSY: Not available

Unknown date LKM: negative

[redacted] 20[redacted] **LUMBAR PUNCTURE:** CEPHALO-RACHIDIAN FLUID ANALYSIS: NORMAL

Unknown date LYME DISEASE TEST: Negative

[redacted] 20[redacted] **MONOTEST:** Negative

[redacted] 20[redacted] **MRI CEREBRAL SCANNER:** Normal

[redacted] 20[redacted] **NEUTROPHILS:** 21.76

[redacted] 20[redacted] **PLATELET COUNT:** 764 X10**9/L (normal 140 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 915 X10**9/L (normal 140 to 450)

[redacted] 20[redacted] **POTASSIUM:** 2.8 MMOL/L (normal 3.5 to 5.0)

[redacted] 20[redacted] **POTASSIUM:** 3.7 MMOL/L (normal 3.5 to 5.0)

[redacted] 20[redacted] **RED BLOOD CELLS:** 3.85 X10**12/L (normal 4 to 5.2)

[redacted] 20[redacted] **RED BLOOD CELLS:** 2.8 X10**12/L (normal 4 to 5.2)

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

Unknown date SYPHILLIS: Negative

[redacted] 20[redacted] **THORACIC SCINTIGRAPHY:** STREPTOCOCCAL PNEUMONIA PULMONARY ABSCESS

[redacted] 20[redacted] **URINE CULTURE:** Presence of streptococcus pneumonia antigen-Positive

Unknown date VIH: Negative

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 32 X10**9/L (normal 4.5 to 11.3)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 11.7 X10**9/L (normal 4.5 to 11.3)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Hepatic enzyme increased ([redacted] 20[redacted]): Asymptomatic
Hepatic enzyme increased ([redacted] 20[redacted]): 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
アスパラギン酸アミノトランスフェラーゼ増加				X
血中クレアチンホスホキナーゼ増加				X
肺炎	X	X		X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	4[redacted]	MALE	ASIAN

Medical History	Onset Year
ARTHRALGIA	20[redacted]
BRONCHITIS	20[redacted]
CHRONIC GASTRITIS	20[redacted]
EMPHYSEMA	NOT REPORTED
EXTENSIVE UC/PANCOLITIS	20[redacted]
MILD ANEMIA	20[redacted]
NUMBNESS OF THE HANDS AND FEET	20[redacted]
PULMONARY INFLAMMATION	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: CHEST CT SCAN	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: SPECIFY CT SCAN	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 59	59
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 1	[redacted] / 2	2

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	40 mg	OTHER: QN	Y-M: 20[redacted]
METHYLPREDNISOLONE	50 mg	QD	Y-M: 20[redacted]
THALIDOMIDE	100 mg	OTHER: QN	Y-M: 20[redacted]
MESALAZINE	30 mL	OTHER: QN	Y-M: 20[redacted]
DEXAMETHASONE	2.5 mg	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	QID	Y-M: 20[redacted]
MESALAZINE	60 mL	OTHER: QN	Y-M: 20[redacted]
DEXAMETHASONE	2.5 mg	QD	Y-M: 20[redacted]
THALIDOMIDE	50 mg	OTHER: QN	Y-M: 20[redacted]
MESALAZINE	1000 mg	QID	Y-M: 20[redacted]
MESALAZINE	1000 mg	TID	Y-M: 20[redacted]
MESALAZINE	30 mL	OTHER: QN	Y-M: 20[redacted]
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -351
MESALAZINE	60 mL	OTHER: QN	Y-M: 20[redacted] / -351
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -324
ACETYLCYSTEINE	PRN g	PRN	Y-M: 20[redacted] / -338
MONTELUKAST	PRN mg	PRN	Y-M: 20[redacted] / -338
PROCATEROL	PRN ug	PRN	Y-M: 20[redacted] / -338
TIOTROPIUM	PRN OTHER: PRN	PRN	Y-M: 20[redacted] / -338
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -267
MESALAZINE	60 mL	OTHER: QN	Y-M: 20[redacted] / -241
METHYLPREDNISOLONE	40 mg	OTHER: QN	Y-M: 20[redacted] / -190
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -168
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -185
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	180 g	OTHER: ONCE	Y-M: 20[redacted] / -95
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -95
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / -74
ISONIAZID	0.3 g	QD	Y-M: 20[redacted] / -76
CALCIUM CARBONATE;COLECALCIFEROL	600 mg	QD	Y-M: 20[redacted] / -77
MIDAZOLAM	5 mg	QD	Y-M: 20[redacted] / -78

ALANINE;ARGININE;ASPARTIC ACID;CYSTEINE;GLUTAMIC ACID;GLYCEROL;GLYCINE;GLYCINE MAX;HISTIDINE;ISOLEUCINE;LECITHIN; LEUCINE;LYSINE;METHIONINE;PHENYL ALANINE;PROLINE;SERINE;SODIUM BISULFITE;SORBITOL;THREO	250 mL	QD	Y-M: 20[redacted] / -80
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	1.5 g	TID	Y-M: 20[redacted] / -80
GLUCOSE	100 mL	QD	Y-M: 20[redacted] / -80
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / -80
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	200 g	QD	Y-M: 20[redacted] / -80
MINERALS NOS	40 mL	QD	Y-M: 20[redacted] / -80
POTASSIUM	3 g	QD	Y-M: 20[redacted] / -80
PROPOFOL	APPROPRIATE OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / -80
SODIUM CHLORIDE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / -82
TUBERCULIN	50 IU	QD	Y-M: 20[redacted] / -82
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / -85
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -87
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / -37
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -44
METHYLPREDNISOLONE	6 mg	QD	Y-M: 20[redacted] / -11
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / -15
METHYLPREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -20
METHYLPREDNISOLONE	12 mg	QD	Y-M: 20[redacted] / -25
CAFFEINE;PARACETAMOL	0.5 g	QD	Y-M: 20[redacted] / -3
METHYLPREDNISOLONE	14 mg	QD	Y-M: 20[redacted] / -30
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -7
CALCIUM CARBONATE;COLECALCIFEROL	600 mg	PRN	Y-M: 20[redacted] / -1
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	120 g	OTHER: ONCE	Y-M: 20[redacted] / -1
OSELTAMIVIR	75 mg	BID	Y-M: 20[redacted] / -1
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -2
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -2
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / -2

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
ACETYLCYSTEINE	PRN g	PRN	Y-M: 20[redacted] / -338	ONGOING
MONTELUKAST	PRN mg	PRN	Y-M: 20[redacted] / -338	ONGOING
PROCATEROL	PRN ug	PRN	Y-M: 20[redacted] / -338	ONGOING
TIOTROPIUM	PRN OTHER: PRN	PRN	Y-M: 20[redacted] / -338	ONGOING
METHYLPREDNISOLONE	24 mg	QD	Y-M: 20[redacted] / -74	Y-M: 20[redacted] / -45
CALCIUM CARBONATE;COLECALCIFEROL	600 mg	QD	Y-M: 20[redacted] / -77	Y-M: 20[redacted] / -5
MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -87	Y-M: 20[redacted] / -5
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / -37	Y-M: 20[redacted] / -31
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -44	Y-M: 20[redacted] / -38
METHYLPREDNISOLONE	6 mg	QD	Y-M: 20[redacted] / -11	Y-M: 20[redacted] / -8
METHYLPREDNISOLONE	8 mg	QD	Y-M: 20[redacted] / -15	Y-M: 20[redacted] / -12
METHYLPREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -20	Y-M: 20[redacted] / -16
METHYLPREDNISOLONE	12 mg	QD	Y-M: 20[redacted] / -25	Y-M: 20[redacted] / -21
CAFFEINE;PARACETAMOL	0.5 g	QD	Y-M: 20[redacted] / -3	Y-M: 20[redacted] / -2
METHYLPREDNISOLONE	14 mg	QD	Y-M: 20[redacted] / -30	Y-M: 20[redacted] / -26
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -5
CALCIUM CARBONATE;COLECALCIFEROL	600 mg	PRN	Y-M: 20[redacted] / -1	ONGOING
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	120 g	OTHER: ONCE	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
OSELTAMIVIR	75 mg	BID	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 4

MESALAZINE	1000 mg	QID	Y-M: 20[redacted] / -2	ONGOING
METHYLPREDNISOLONE	4 mg	QD	Y-M: 20[redacted] / -2	Y-M: 20[redacted] / -2
MOXIFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / -2	Y-M: 20[redacted] / 4
PROPOFOL	APPROPRIATE OTHER: UNKNOWN	OTHER: ONCE	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	500 mg	TID	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 12
LEVOFLOXACIN	0.3 g	BID	Y-M: 20[redacted] / 12	Y-M: 20[redacted] / 14
ACETYLCYSTEINE	0.2 g	TID	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 31
AMINOPHYLLINE;CHLORPHENAMINE;METHOXYPHENAMINE;NOSCAPINE	2 OTHER: PILL	TID	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 31
BROMHEXINE	16 mg	TID	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 31
LEVOFLOXACIN	0.5 g	QD	Y-M: 20[redacted] / 25	Y-M: 20[redacted] / 31
AMINOPHYLLINE	0.25 g	QD	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 3
LEVOFLOXACIN	0.3 g	QD	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 3
SODIUM CHLORIDE	250 mL	QD	Y-M: 20[redacted] / 3	Y-M: 20[redacted] / 3
AMBROXOL	60 mg	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 5
CEFOTAXIME;SULBACTAM	3 g	OTHER: Q8H	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 14
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 14
POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC	2 mL	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 14
SODIUM CHLORIDE	10 mL	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 5
SODIUM CHLORIDE	100 mL	OTHER: Q8H	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 14
SODIUM CHLORIDE	100 mL	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 5
TUBERCULIN	50 IU	QD	Y-M: 20[redacted] / 5	Y-M: 20[redacted] / 5
AMOXICILLIN;SULBACTAM	6 g	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 37
CEFEPIME	2 g	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 37
DEXAMETHASONE	10 mg	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 37

Event #1: 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	[redacted]20[redacted] / 43
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	61
Duration of AE	19 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	CREATINE PHOSPHATE KINASE 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	[redacted]20[redacted] / 43
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	61
Duration of AE	19 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 - Creatine Phosphokinase (CPK) Elevation

Event Description	CREATINE KINASE ISOENZYME 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	[redacted]20[redacted] / 43
Age at AE Onset	4[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	65 (3 DAYS AFTER LAST TREATMENT)
Duration of AE	23 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 of Interest - Serious Infections

Event Description	PULMONARY INFECTION
Preferred term	肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	4[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY -3): NPTST161-COVID-19 STATUS DETERMINATION: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	63 (1 DAY AFTER LAST TREATMENT)
Duration of AE	7 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 #5: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections

Event Description	PULMONARY INFECTION
Preferred term	肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 63 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 5): Albumin: 33.83 [40 - 55] G/L; Hemoglobin: 115 [120 - 160] G/L; Platelets: 359 [100 - 300] 10^9/L; [redacted]20[redacted] (RX DAY 6): Occult Blood: + [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 12): Hemoglobin: 112 [120 - 160] G/L; Platelets: 400 [100 - 300] 10^9/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	CONSIDER RELATED TO THE STUDY OF DRUGS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は中国の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，投与57日後＊　及び投与63日後＊　に肺感染症の事象を発現した。関連する病歴は，潰瘍性大腸炎，気管支炎，肺気腫，現喫煙者（1 日 1 箱を 30 年間）及び非飲酒者であった。

Event 4 及び 5 の臨床経過：

投与57日後＊　，被験者は肺感染症を発現した。投与63日後＊　，肺感染症は消失した。投与63日後＊，被験者は肺感染症を発現した。

投与57日後＊　　，被験者は胸部 CT スキャン検査を行い，両肺に新たなびまん性すりガラス様陰影が認められた。COVID-19 ウイルス検査（鼻咽頭）が行われ，結果は陰性であった。被験者には経口の抗炎症薬が投与された。

投与65日後＊　　，被験者は息切れ及び胸痛があり，呼吸及び動作の症状がより顕著になり，入院した。COVID-19 ウイルス検査が再度行われたが，陰性であった。結核菌検査であるツベルクリン反応検査（PPD）の結果も陰性であった。抗炎症治療後，症状は改善し，投与75日後＊に被験者は退院した。

本事象により治験薬の投与は完全に中止された。

投与された薬剤は，モキシフロキサシン，オセルタミビルリン酸塩，アセチルシステイン，ブロムヘキシン塩酸塩，レボフロキサシン，アモキシシリンナトリウム・スルバクタムナトリウム合剤，デキサメタゾンリン酸エステルナトリウム，セフェピム塩酸塩水和物，セフォタキシムナトリウム・スルバクタム合剤，レボフロキサシン塩酸塩及びメトキシフェナミン化合物であった。

The patient's past medications include:

SOLU MEDROL for ULCERATIVE COLITIS ([redacted])

THALIDOMIDE for ULCERATIVE COLITIS ([redacted])

MEDROL for ULCERATIVE COLITIS ([redacted])

MESALAZINE ENEMAS for ULCERATIVE COLITIS ([redacted])

DEXAMETHASONE SODIUM PHOSPHATE for ULCERATIVE COLITIS ([redacted])

ETIASA for ULCERATIVE COLITIS ([redacted])

MESALAZINE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Lung infection (10061229) (Pneumonia (10035664)) [v.23.0] [10061229]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Lung infection (10061229) (Pneumonia (10035664)) [v.23.0] [10061229]

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 PULMONARY INFECTION

- Investigator: Considered related to the study drugs

- AbbVie: Risk factors include pre-existing bronchitis, emphysema and on-going tobacco smoking (1 PPD for 30 years).

Event of PULMONARY INFECTION

- Investigator: Not applicable.

- AbbVie: Risk factors include pre-existing bronchitis, emphysema and on-going tobacco smoking (1 PPD for 30 years).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 33.83 G/L (normal 40.00 to 55.00)

[redacted] **20[redacted] CHEST CT SCAN:** Abnormal - new diffuse ground-glass opacity in both lungs

[redacted] **20[redacted] CHEST CT SCAN:** Bilateral lungs scattered in ground glass like shadow; the overall change was little compared with before, considering the possibility of partial ventilation insufficiency or chronic inflammation. The area of the posterior segment of the upper lobe tip of the left lung and the anterior inner base segment of the lower lobe of the left lung was wider than before, except for the possibility of tuberculosis reburning, most of which were similar to before.

[redacted] **20[redacted] CHEST CT SCAN:** Calcified granulomas- absent, Pleural scarring- absent, Pleural thickening- absent, Signs of active TB- no, finding indicative of previous TB infection- yes. Inflammation of the middle lobe of the right lung with partial atelectasis is more advanced than before.

[redacted] **20[redacted] CHEST X-RAY:** Pulmonary infection.

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

[redacted] **20[redacted] COVID-19 VIRUS TEST:** nasopharyngeal swab - negative

[redacted] **20[redacted] COVID-19 VIRUS TEST:** nasopharyngeal swab - negative

[redacted] **20[redacted] COVID-19 VIRUS TEST:** nasopharyngeal swab - negative

[redacted] **20[redacted] COVID-19 VIRUS TEST:** nasopharyngeal swab: Negative

[redacted] **20[redacted] HEMOGLOBIN:** 115.00 G/L (normal 120 to 160)

[redacted] **20[redacted] HEMOGLOBIN:** 112.0 G/L (normal 120 to 160)

[redacted] **20[redacted] OCCULT BLOOD:** Positive

[redacted] **20[redacted] PLATELET COUNT:** 359.0 X10**9/L (normal 100 to 300)

[redacted] **20[redacted] PLATELET COUNT:** 400 X10**9/L (normal 100 to 300)

[redacted] **20[redacted] PPD:** Negative

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Blood creatinine phosphokinase 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
肛門膿瘍	X			X
ヘモグロビン減少				X
腸閉塞		X		
リンパ球数減少				X
リンパ球百分率減少				X

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

Medical History	Onset Year
ANAL FISTULA	20[redacted]
ANEMIA	20[redacted]
CHRONIC SUPERFICIAL - EROSIVE GASTRITIS	20[redacted]
DUODENAL BULB ULCER	20[redacted]
GASTROINTESTINAL DYSFUNCTION	20[redacted]
HEMORRHOIDS	20[redacted]
LEFT SIDED UC	20[redacted]
LIPOMA	20[redacted]
REFLUX ESOPHAGITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: LIPOMA RESECTION	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 54	54
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted] / 1	[redacted] / 198	198

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	QID	Y-M: [redacted]
MESALAZINE	1 g	QD	Y-M: [redacted]
MESALAZINE	1 g	TID	Y-M: [redacted]
ASCORBIC ACID	0.1 g	BID	Y-M: [redacted] / -121
IRON	0.1 g	QD	Y-M: [redacted] / -13
MOSAPRIDE	5 mg	BID	Y-M: [redacted] / -14
REBAMIPIDE	100 mg	TID	Y-M: [redacted] / -14

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
MESALAZINE	1 g	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 216
ASCORBIC ACID	0.1 g	BID	Y-M: 20[redacted] / -121	Y-M: 20[redacted] / 200
IRON	0.1 g	QD	Y-M: 20[redacted] / -13	Y-M: 20[redacted] / 200
MOSAPRIDE	5 mg	BID	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 11
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] / -14	Y-M: 20[redacted] / 3
CLOSTRIDIUM BUTYRICUM	20 mg	TID	Y-M: 20[redacted] / 48	ONGOING
CETIRIZINE	10 mg	OTHER: QN	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 96
TRIAMCINOLONE	RIGHT AMOUNT DAUB OTHER: UNKONWN	OTHER: RIGHT AMOUNT DAUB	Y-M: 20[redacted] / 94	Y-M: 20[redacted] / 112
TRETINOIN	RIGHT AMOUNT DAUB OTHER: UNKNOWN	OTHER: IRREGULAR MEDICATION	Y-M: 20[redacted] / 112	ONGOING
ASCORBIC ACID	10 mL	QD	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 182
CEFUROXIME	1.5 g	BID	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 182
SODIUM CHLORIDE	100 mL	BID	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 182
SODIUM CHLORIDE	250 mL	QD	Y-M: 20[redacted] / 182	Y-M: 20[redacted] / 182
CEFACLOR	0.25 g	TID	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 189
FURAZOLIDONE;INDOMETACIN	1# OTHER: COMPOUND PREPARATIONS	OTHER: QN	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 189
CAMPHOR;MENTHOL;PETROLATUM;PINUS PINASTER;SALICYLIC ACID	A MODERATE AMOUNT OF OUTER COATING OTHER: AN UNKNOWN	OTHER: A MODERATE AMOUNT OF OUTER COATING	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 189
PHELLODENDRON CHINENSE	UES AS NEEDED OTHER: UNKONWM	QD	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 193
CEFACLOR	0.375 g	BID	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 198
DEXTROMETHORPHAN	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 196	Y-M: 20[redacted] / 199
SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 198	Y-M: 20[redacted] / 199
ALBUMIN HUMAN	UNKNOWN OTHER: UNKNOWN	OTHER: UNKNOWN	Y-M: 20[redacted] / 202	Y-M: 20[redacted] / 232
METRONIDAZOLE	0.5 g	BID	Y-M: 20[redacted] / 207	Y-M: 20[redacted] / 216
SANGUISORBA OFFICINALIS	0.3 g	TID	Y-M: 20[redacted] / 207	Y-M: 20[redacted] / 213
DIOSMIN	0.45 g	BID	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 210
TRIMEBUTINE	0.1 g	TID	Y-M: 20[redacted] / 208	Y-M: 20[redacted] / 210

INFLIXIMAB	400 mg	OTHER: ONCE	Y-M: 20[redacted] / 216	Y-M: 20[redacted] / 216
METRONIDAZOLE	0.5 g	QD	Y-M: 20[redacted] / 217	ONGOING

Event #1: Event of Interest - Lymphopenia

Event Description	THE PERCENTAGE OF LYMPHOCYTES DECREASED
Preferred term	リンパ球百分率減少
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	256 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	242 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 - Lymphopenia

Event Description	LYMPHOCYTE COUNT DECREASED
Preferred term	リンパ球数減少
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 82
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	256 (4 DAYS AFTER LAST TREATMENT)
Duration of AE	175 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: AE Leading to Discontinuation of Study Drug

Event Description	INTESTINAL OBSTRUCTION
Preferred term	腸閉塞
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 252
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	254 (2 DAYS AFTER LAST TREATMENT)
Duration of AE	3 DAYS
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

Event #4: Serious Adverse Event, Event of Interest - Serious Infections

Event Description	CRISSUM ABSCESS(AROUND THE ANUS)
Preferred term	肛門膿瘍
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 256 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 202): Albumin: 33.9 [40 - 55] G/L; Hemoglobin: 105 [130 - 175] G/L; Leukocytes: 8.14 [3.5 - 9.5] 10^9/L; Lymphocytes: 0.3 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 4.1 [20 - 50] %; NPTST205-ERYTHROCYTE SEDIMENTATION RATE: 111 [NOT REPORTED - NOT REPORTED] mm/h; Neutrophils: 6.6 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 81 [40 - 75] %; [redacted]20[redacted] (RX DAY 208): Hemoglobin: 97 [130 - 175] G/L; Leukocytes: 3.13 [3.5 - 9.5] 10^9/L; Lymphocytes: 0.3 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 10.2 [20 - 50] %; [redacted]20[redacted] (RX DAY 212): Albumin: 24.5 [40 - 55] G/L; Hemoglobin: 86 [130 - 175] G/L; Lymphocytes: 0.4 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 10 [20 - 50] %; NPTST015-ALBUMIN PERCENTAGE: 43.9 [55.8 - 66.1] %; NPTST064-BEFORE THE ALBUMIN: 0.08 [0.2 - 0.43] G/L; NPTST205-ERYTHROCYTE SEDIMENTATION RATE: 87 [NOT REPORTED - NOT REPORTED] mm/h; NPTST512-TOTAL PROTEIN: 49.3 [65 - 85] G/L; [redacted]20[redacted] (RX DAY 216): Albumin: 28 [40 - 55] G/L; Hemoglobin: 83 [130 - 175] G/L; Leukocytes: 6.5 [3.5 - 9.5] 10^9/L; Lymphocytes: 0.5 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 7.2 [20 - 50] %; NPTST015-ALBUMIN PERCENTAGE: 49.7 [55.8 - 66.1] %; NPTST064-BEFORE THE ALBUMIN: 0.12 [0.2 - 0.43] G/L; NPTST205-ERYTHROCYTE SEDIMENTATION RATE: 41 [NOT REPORTED - NOT REPORTED] mm/h; NPTST512-TOTAL PROTEIN: 52.1 [65 - 85] G/L; Neutrophils: 4.92 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 75.6 [40 - 75] %

Microbiology

[redacted]20[redacted] (RX DAY 204): BLOOD NPTST460-SALMONELLA.SHIGELLA: NEGATIVE

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	IT IS ASSOCIATED WITH UC DISEASE ACTIVITY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #5: Event of Interest - Lymphopenia

Event Description	LYMPHOCYTE COUNT DECREASED
Preferred term	リンパ球数減少
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 256 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]

Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
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 - Lymphopenia

Event Description	THE PERCENTAGE OF LYMPHOCYTES DECREASED
Preferred term	リンパ球百分率減少
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 256 (4 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
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 - Anemia

Event Description	HEMOGLOBIN IS REDUCED
Preferred term	ヘモグロビン減少
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 262 (10 DAYS AFTER LAST TREATMENT)
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は中国の 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，膿瘍（肛門周辺）の事象を発現した。関連する病歴は，潰瘍性大腸炎，痔瘻，慢性の表在性びらん性胃炎，十二指腸球部の潰瘍，逆流性食道炎，胃腸障害，貧血，非喫煙者及び非飲酒者であった。

Event 4 の臨床経過：

投与256日後＊，被験者は膿瘍（肛門周辺）を発現した。

投与256日後＊　，被験者は痛みを伴う肛門周囲膿瘍のために入院した。投与258日後＊　，被験者は無痛の結腸内視鏡検査を受け，炎症性腸疾患が確認された。病理報告によると，被験者には活動性の潰瘍，内因性の腺の減少，潜在性のねじれ及び潜在性の炎症を伴う直腸粘膜の重

度の炎症が認められた。被験者は対処療法を連続して受けた。

投与262日後＊，外来及び救急科で診察したところ，被験者は肛門周囲の腫脹，痛み及び化膿性分泌物を認めた。診察の結果，痔瘻が考えられたため，被験者は肛門科に移った。投与263日後＊，超音波検査により肛門周囲の瘻孔が確認された。同日に，被験者は複雑化した痔瘻の切開排膿（痔瘻結紮療法），直腸ポリープ切除，肥大肛門乳頭切除及び外痔核切除を受けた。

投与265日後＊　，病理検査報告では，痔瘻の管壁，肛門乳頭，肛門直腸ポリープの皮膚組織，炎症細胞の角質への浸潤，骨粗鬆症の間質性浮腫，血管拡張及びうっ血，出血，扁平上皮過形成の一部，肛門乳頭の肥大，多数の急性又は慢性炎症細胞の浸潤を認める痔瘻の管壁，肉芽組織の過形成，並びにリンパ組織の限局的な領域が示された。手術はスムーズに進み，肛門周囲膿瘍は改善した。その後被験者は消化器内科に移った。投与271日後＊，被験者は退院した。
入院中に合併症は発生しなかった。

投与された薬剤は，メトロニダゾール，diosmin，phellodendron chinense，セファクロル，dragon ball ointment 及び indolomethacin・furazolidone 坐剤であった。

The patient's past medications include:

MESALAZINE ENTERIC COATED TABLETS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

MOSAPRIDE CITRATE TABLETS for MERGER DISEASE: CHRONIC GASTRITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

REBAMIPIDE for CHRONIC GASTRITIS ([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: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of CRISSUM ABSCESS (AROUND THE ANUS)

- Investigator: The patient was hospitalized with perianal abscess and had no other cause.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST CT:** Increased texture in both lungs

[redacted] **20[redacted] CONTRAST-ENHANCED CT EXAMINATION OF SMALL INTESTINES:** Thickening and enhancement of the rectum, colon, and intestinal wall were associated with inflammatory bowel disease. Small intestinal wall was slightly thickened and inflammation was possible in the 6 groups

[redacted] **20[redacted] CULTURE:** Negative for Salmonella and Shigella

[redacted] **20[redacted] ENDOSCOPY:** Inflammatory bowl disease

[redacted] **20[redacted] MRI ANUS:** Changes after complex anal fistula operation

[redacted] **20[redacted] PERINAL COLOR ULTRASOUND:** Anal fistula

[redacted] **20[redacted] PLAIN FILEM OF ABDOMEN IN RIGHT AND SUPINE POSITION:** No obvious abnormality was observed

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
好中球減少症				X
皮膚裂傷	X			

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

Medical History	Onset Year
CMV POSITIVE	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 114	58
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 369	369

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
METHYLPREDNISOLONE	20 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	20 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	32 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	20 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	300.000 mg	0.2 .6WEEK	Y-M: 20[redacted]
MESALAZINE	1 g	TID	Y-M: 20[redacted]
VEDOLIZUMAB	300.000 mg	FOLLOW PRO TOCOL	Y-M: 20[redacted]
MESALAZINE	1 g	QID	Y-M: 20[redacted]
THALIDOMIDE	50 mg	QD	Y-M: 20[redacted]
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted] / -362
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -148
MESALAZINE	1 g	QID	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] / -148	ONGOING
POTASSIUM	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51
TETANUS VACCINE	1 OTHER: SHOT	OTHER: ONCE	Y-M: 20[redacted] / 51	Y-M: 20[redacted] / 51

Event #1: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 87
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	122
Duration of AE	36 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 141
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	174
Duration of AE	34 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

Event Description	LACERATION OF SCALP (TRAUMA)
Preferred term	皮膚裂傷
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 165
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 51): Bilirubin: 24.5 [3.4 - 20.5] UMOL/L; Calcium: 2.23 [2 - 2.6] MMOL/L; Creatine Kinase: 235 [24 - 195] U/L; Creatinine: 95 [41 - 111] UMOL/L; Erythrocytes: 4.51 [4.3 - 5.8] 10^12/L; Glucose: 5.66 [3.9 - 6.1] MMOL/L; Hemoglobin: 143 [130 - 175] G/L; Leukocytes: 4.5 [3.5 - 9.5] 10^9/L; NPTST181-D - DIMER: 3480.0 [0 - 500] 099,UG/L; NPTST408-PLASMA LACTIC ACID: 3.3 [1 - 2.5] MMOL/L; NPTST424-PROTHROMBIN TIME: 11.3 [10 - 14] SEC; Platelets: 230 [125 - 350] 10^9/L; Potassium: 3.29 [3.5 - 5.3] MMOL/L

Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	189
Duration of AE	25 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	WHEN RIDING AN ELECTRIC CAR, THE FRONT CAR STOPS AND OPENS THE DOOR.BLOCKED BY A CAR DOOR, CAUSING THE CAR TO ROLL OVER AND LACERATE ITS HEAD
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #4: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 174
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	198
Duration of AE	25 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 #5: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 253
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	314
Duration of AE	62 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 #6: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 314
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	371
Duration of AE	58 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は中国の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，頭皮裂傷（外傷）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 3 の臨床経過：

投与165日後＊　　，被験者は頭皮裂傷（外傷）を発現した。投与189日後＊　　，頭皮裂傷（外傷）は消失した。

投与165日後＊　　，被験者は電気自動車に乗っていて事故に遭った。被験者は救急車で病院に到着し，活動性・滲出性の頭皮裂傷（右頭頂部からわずかに側頭部にかかる 3 cm の裂傷），頭痛，右顔面皮膚の挫傷，左肘の圧痛（明らかな変形はなし）を呈していた。検体検査，画像診断及び診察を行った。頭皮裂傷のデブリードマン及び縫合が行われた。水分補給による体系的な治療が行われた。痛みは改善し，明らかな出血はなくなった。同日に被験者は退院した。

投与された薬剤は，tetanus vaccine であった。

The patient's past medications include:

METHYLPREDNISOLONE for ULCERATIVE COLITIS ([redacted])

SOLU MEDROL for ULCERATIVE COLITIS ([redacted])

SULFASALAZINE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

HYDROCORTISONE SODIUM SUCCINATE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

THALIDOMIDE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Scalp laceration (10066049) (Skin laceration (10058818)) [v.24.0] [10066049]

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 LACERATION OF SCALP (TRAUMA)

- Investigator: When riding an electric car, the front car stops and opens the door. Blocked by a car door, causing the car to roll over and lacerate its head.

- AbbVie: Event is more likely related to a motor vehicle accident.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** on admission: 143/93 mmHg

[redacted] **20[redacted] BLOOD PRESSURE:** on discharge: 133/83 mmHg

[redacted] **20[redacted] BODY TEMPERATURE:** on admission: 37.5 degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** on discharge:: 37.2 degrees C

[redacted] **20[redacted] CREATINE KINASE:** 235 U/L

[redacted] **20[redacted] CRP:** <1 MG/L

[redacted] **20[redacted] CT HEAD:** bilateral frontotemporal subdural effusion

[redacted] **20[redacted] CT HEAD:** SLIGHT SUBDURAL EFFUSION IN BILATERAL FRONTOTEMPORAL AREA

[redacted] **20[redacted] D DIMER:** 3480.0 G/L

[redacted] **20[redacted] HEMOGLOBIN:** 143 G/L

[redacted] **20[redacted] LACTIC ACID:** 3.3 MMOL/L

[redacted] **20[redacted] OXYGEN SATURATION:** on admission: 98%

[redacted] **20[redacted] OXYGEN SATURATION:** on discharge: 99%

[redacted] **20[redacted] PLATELET COUNT:** 230 X10**9/L

[redacted] **20[redacted] POTASSIUM:** 3.29 L

[redacted] **20[redacted] PULSE RATE:** on admission: 84 bpm

[redacted] **20[redacted] PULSE RATE:** on discharge:: 80 bpm

[redacted] **20[redacted] RBC:** 4.51 X10**9/L

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

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

[redacted] **20[redacted] WBC:** 4.5 X10**9/L (normal 3.5 to 9.5)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
白内障	X			
肝損傷				**X**

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

Medical History	Onset Year
BRONCHITIS	20[redacted]
COMPLETE RIGHT BUNDLE BRANCH BLOCK	20[redacted]
HEMATURESIS	20[redacted]
LEFT SIDED UC	20[redacted]
PROTEINURIA	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 370	370

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACONITUM KUSNEZOFFII;HERBAL NOS	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AUCKLANDIA COSTUS;COPTIS SPP.;CORYDALIS YANHUSUO;PRUNUS MUME;ZINGIBER OFFICINALE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
DEXAMETHASONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
LEVOGLUTAMIDE	NOT REPORTED	OTHER: UK	Y-M: 20[redacted]
PLANT ALKALOIDS AND OTHER NATURAL PRODUCTS	0.600 g	TID	Y-M: 20[redacted]
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	0.500 g	TID	Y-M: 20[redacted]
MESALAZINE	0.5 g	TID	Y-M: 20[redacted]
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	0.500 g	TID	Y-M: 20[redacted] / -262
MESALAZINE	1 g	TID	Y-M: 20[redacted] / -262
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	0.500 g	TID	Y-M: 20[redacted] / -206
HYDROCORTISONE	60 mL	BID	Y-M: 20[redacted] / -206
MESALAZINE	1 g	TID	Y-M: 20[redacted] / -206
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	0.500 g	TID	Y-M: 20[redacted] / -218
MESALAZINE	1 g	TID	Y-M: 20[redacted] / -218
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / -218
TEPRENONE	50.000 mg	TID	Y-M: 20[redacted] / -218
MESALAZINE	1 g	TID	Y-M: 20[redacted] / -150
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -108
PREDNISONE	12.5 mg	QD	Y-M: 20[redacted] / -2
CAMELLIA SINENSIS	6 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
ACONITUM KUSNEZOFFII;HERBAL NOS	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]	Not reported
AUCKLANDIA COSTUS;COPTIS SPP.;CORYDALIS YANHUSUO;PRUNUS MUME;ZINGIBER OFFICINALE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]	Not reported
DEXAMETHASONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]	Not reported
LEVOGLUTAMIDE	NOT REPORTED	OTHER: UK	Y-M: 20[redacted]	Not reported
PLANT ALKALOIDS AND OTHER NATURAL PRODUCTS	0.600 g	TID	Y-M: 20[redacted]	Not reported
MESALAZINE	1 g	TID	Y-M: 20[redacted] / -206	Not reported
BACILLUS SUBTILIS;ENTEROCOCCUS FAECIUM	0.500 g	TID	Y-M: 20[redacted] / -218	Not reported
MESALAZINE	1 g	TID	Y-M: 20[redacted] / -218	Not reported
MESALAZINE	1000 mg	TID	Y-M: 20[redacted] / -108	Y-M: 20[redacted] / 266
LEVOFLOXACIN	1 mL	QID	Y-M: 20[redacted] / 117	Y-M: 20[redacted] / 118
TROPICAMIDE	1 mL	BID	Y-M: 20[redacted] / 118	Y-M: 20[redacted] / 122
DEXAMETHASONE;TOBRAMYCIN	1 OTHER: APPROPRIATE AMOUNT	TID	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 122
DEXAMETHASONE;TOBRAMYCIN	1 mL	QID	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 122
MESALAZINE	1 g	QD	Y-M: 20[redacted] / 253	Y-M: 20[redacted] / 297
MESALAZINE	1 g	BID	Y-M: 20[redacted] / 267	ONGOING
MESALAZINE	1 g	QD	Y-M: 20[redacted] / 310	ONGOING
GLYCYRRHIZIC ACID	150 mg	TID	Y-M: 20[redacted] / 320	Y-M: 20[redacted] / 329
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	137.15 g	QD	Y-M: 20[redacted] / 371	Y-M: 20[redacted] / 371

CAMELLIA SINENSIS	6 g	QD	Y: 19[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	CATARACT
Preferred term	白内障
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 164
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 117): Basophils: 0.03 [0 - 0.06] 10^9/L; Basophils/Leukocytes: 0.5 [0 - 1] %; Eosinophils: 0.13 [0.02 - 0.52] 10^9/L; Eosinophils/Leukocytes: 2.3 [0.4 - 8] %; Erythrocytes: 4.51 [4.3 - 5.8] 10^12/L; Glucose: 5.18 [3.89 - 6.11] MMOL/L; Hematocrit: 0.434 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 142 [130 - 175] G/L; Leukocytes: 5.46 [3.5 - 9.5] 10^9/L; Lymphocytes: 1.7 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 31.2 [20 - 50] %; Monocytes: 0.43 [0.1 - 0.6] 10^9/L; Monocytes/Leukocytes: 7.9 [3 - 10] %; NPTST020-ALY#: 0.0 [0 - 0.2] 10^9/L; NPTST331-MCH: 31.4 [27 - 34] PG; NPTST332-MCHC: 327 [326 - 354] G/L; NPTST334-MCV: 96.1 [82 - 100] FL; NPTST352-MPV: 8.2 [6.5 - 12] FL; NPTST397-PCT: 0.167 [0.108 - 0.282] %; NPTST398-PDW: 15.8 [9 - 17] %; NPTST441-RDW-CV: 11 [11 - 16] %; NPTST442-RDW-SD: 40.4 [35 - 56] FL; Neutrophils: 3.17 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 58.1 [40 - 75] %; Platelets: 202 [100 - 300] 10^9/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	176
Duration of AE	13 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	AGE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Event of Interest - Hepatic Disorder

Event Description	HEPATIC INJURY
Preferred term	肝損傷
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 367
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	428 (1 DAY AFTER LAST TREATMENT)
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

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は中国の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，白内障の事象を発現した。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164日後＊　，被験者は白内障を発現した。投与176日後＊　，白内障は消失した。

投与の約2ヵ月後＊，被験者は白内障（非重篤）を発現し，眼科の受診を勧められた。

投与174日後＊　，被験者は入院した。血糖値測定，血液のルーチン検査，12 誘導心電図及び眼の超音波検査（A・B モード）を行った。投与175日後＊ ，左眼の白内障に対する超音波水晶体乳化吸引術及び眼内レンズの埋め込みを局所麻酔下で行った。投与176日後＊　，右眼

の白内障に対する超音波水晶体乳化吸引術及び眼内レンズの埋め込みを局所麻酔下で行った。術後は抗炎症治療及び抗感染症治療を行った。これらの手術は，本治験の同意説明文書へ署名する前には予定されていなかった。投与177日後＊，被験者は退院した。

投与された薬剤は，レボフロキサシン塩酸塩，トブラマイシン・デキサメタゾン合剤，チモロールマレイン酸塩及び recombinant bovine basic fibroblast growth factor であった。

The patient's past medications include:

COMPOUND GLUTAMINE ENTERSOLUBLE for ULCERATIVE COLITIS ([redacted])

LIVE C-BACILLUS SUBTILIS AND EF for ULCERATIVE COLITIS ([redacted])

LIVE C-BACILLUS SUBTILIS AND EF E-COATED CAPSULES for ULCERATIVE COLITIS ([redacted])

TEPRENONE for ULCERATIVE COLITIS ([redacted])

HYDROCORTISONE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Cataract (10007739) (Cataract (10007739)) [v.24.0] [10007739]

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 CATARACT

- Investigator: age

- AbbVie: Risk factor includes advanced age. The prevalence of cataract increases with advancing age. Global prevalence of cataracts in adults over age 50 was estimated to be 47.8 percent.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] COVID-19 TEST:** Tested negative for COVID-19

[redacted] **20[redacted] ECG:** 1. Sinus rhythm (NCS), 2. Extreme right axis deviation, 3. Complete right bundle branch block, CS, associated with the history of complete right bundle branch block, 4. High right ventricular voltage (NCS)

[redacted] **20[redacted] EYE EXAMINATION:** Examination of binocular external eye and anterior segment showed no abnormality. The pupil of the right eye is round and the pupil of the left eye is oval left eye pupil2.5 x 3.5mm, there is a reflection of light. The lens cortex of both eyes is yellowish and cloudy, more severe in the left eye. There was mild liquefaction of the vitreous in both eyes, and clear optic disc edges could be seen in the fundus of both eyes. C/D＜0.3, age-related degeneration of the posterior polar retina is present, the vascular distribution was generally normal, with pigmentation in macular area and absence of fovea reflection. The macular area of the right eye can be seen with yellowish-white punctures oozing out, intraocular pressure tod 14.5mmhg, tos12.3mmhg

[redacted] **20[redacted] GLUCOSE:** 5.18 MMOL/L (normal 3.89 to 6.11)

[redacted] **20[redacted] HEMOGLOBIN:** 142 G/L (normal 130 to 175)

[redacted] **20[redacted] HEPATITIS B TEST:** Unown

[redacted] **20[redacted] HEPATITIS C TEST:** Unknown

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

[redacted] **20[redacted] OPHTHALMIC AB ULTRASOUND EXAMINATION:** None

[redacted] **20[redacted] PDW:** 15.8 No units (normal 9 to 17)

[redacted] **20[redacted] PLATELET COUNT:** 202 X10**9/L (normal 100 to 300)

[redacted] **20[redacted] SYPHILIS TEST:** Unknown

Unknown date URINE TEST: Weak positive occult blood (NCS)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.46 X10**9/L (normal 3.5 to 9.5)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Liver Injury: Asymptomatic. History of use of herbal supplements or teas.

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
好中球数減少				X
クリプトコッカス性肺炎	X	X		X

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

Medical History	Onset Year
BROKEN LEFT THUMB AND INDEX FINGER	19[redacted]
COUGH	19[redacted]
LEFT SIDED UC	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: THE LEFT THUMB AND INDEX FINGER SUTURE SURJUERY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 263	263

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	TID	Y-M: 20[redacted] / -270
BIFIDOBACTERIUM BIFIDUM;LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS CASEI;LACTOBACILLUS SALIVARIUS;STREPTOCOCCUS LACTIS	500.000 mg	TID	Y-M: 20[redacted] / -108
LEVOGLUTAMIDE	3.000 OTHER: TABLET	TID	Y-M: 20[redacted] / -108
PREDNISONE	30 mg	TID	Y-M: 20[redacted] / -118
LEUCOGEN	20 mg	TID	Y-M: 20[redacted] / -38
MESALAZINE	0.5 g	TID	Y-M: 20[redacted] / -41

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
LEUCOGEN	20 mg	TID	Y-M: 20[redacted] / -38	Y-M: 20[redacted] / 86
MESALAZINE	0.5 g	TID	Y-M: 20[redacted] / -41	Y-M: 20[redacted] / 273
LEUCOGEN	20 mg	TID	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 247
AMBROXOL	30 mg	TID	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 259
BORNEOL;CANARIUM ALBUM;CICADA SLOUGH;GLYCYRRHIZA SPP.;IRIS DOMESTICA;MENTHA CANADENSIS;PLATYCODON GRANDIFLORUS;PRUNUS MUME	0.4 g	TID	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 259
EPHEDRINE;GUAIFENESIN;PHOLCODINE	10 mL	QD	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 259
KETOTIFEN	1.38 mg	QD	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 273
LEVOFLOXACIN	0.4 g	QD	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 259
MONTELUKAST	10 mg	QD	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 273
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	10 mL	TID	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 259
AMBROXOL	10 mL	TID	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 273
BUDESONIDE;FORMOTEROL	160/4.5 ug	BID	Y-M: 20[redacted] / 264	Y-M: 20[redacted] / 273
ACETYLCYSTEINE	3 mL	BID	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 276
IOVERSOL	100 mL	QD	Y-M: 20[redacted] / 275	Y-M: 20[redacted] / 275
SODIUM CHLORIDE	250 mL	QD	Y-M: 20[redacted] / 275	Y-M: 20[redacted] / 275
ASCORBIC ACID	2 g	QD	Y-M: 20[redacted] / 276	Y-M: 20[redacted] / 276
CALCIUM CHLORIDE;DEXTRAN;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	250 mL	QD	Y-M: 20[redacted] / 276	Y-M: 20[redacted] / 276
CEFUROXIME	1.5 g	QD	Y-M: 20[redacted] / 276	Y-M: 20[redacted] / 276
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 276	Y-M: 20[redacted] / 276

POTASSIUM	10 mL	QD	Y-M: 20[redacted] / 276	Y-M: 20[redacted] / 276
PYRIDOXINE	200 mg	QD	Y-M: 20[redacted] / 276	Y-M: 20[redacted] / 276
SODIUM CHLORIDE	100 mL	QD	Y-M: 20[redacted] / 276	Y-M: 20[redacted] / 276
TRANEXAMIC ACID	2 g	QD	Y-M: 20[redacted] / 276	Y-M: 20[redacted] / 276
AMINOPHYLLINE	0.25 g	BID	Y-M: 20[redacted] / 277	Y-M: 20[redacted] / 285
CEFUROXIME	1.5 g	BID	Y-M: 20[redacted] / 277	Y-M: 20[redacted] / 277
CEFUROXIME	1.5 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 277	Y-M: 20[redacted] / 279
TERBUTALINE	5 mg	TID	Y-M: 20[redacted] / 277	Y-M: 20[redacted] / 285
TRAMADOL	0.1 g	OTHER: EVERY EIGHT HOURS	Y-M: 20[redacted] / 277	Y-M: 20[redacted] / 281
ENOXAPARIN	0.4 mL	QD	Y-M: 20[redacted] / 278	Y-M: 20[redacted] / 285
CEFUROXIME	1.5 g	QD	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 279
AMMONIA;BENZOIC ACID;CAMPHOR;GLYCEROL;GLYCYRRHIZA SPP.;GUAIFENESIN;ILLICIUM VERUM;PAPAVER SOMNIFERUM	10 mL	TID	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 290
PARACETAMOL;TRAMADOL	37.5 mg	OTHER: EVERY 6 HOURS	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 285
PARACETAMOL;TRAMADOL	37.5 mg	TID	Y-M: 20[redacted] / 282	Y-M: 20[redacted] / 289
MESALAZINE	0.5 g	TID	Y-M: 20[redacted] / 287	ONGOING
AMBROXOL	30 mg	TID	Y-M: 20[redacted] / 292	Y-M: 20[redacted] / 298
AMBROXOL	10 mL	TID	Y-M: 20[redacted] / 299	Y-M: 20[redacted] / 309
GLYCYRRHIZIC ACID	150 mg	TID	Y-M: 20[redacted] / 311	ONGOING
LEUCOGEN	20 mg	TID	Y-M: 20[redacted] / 311	ONGOING
FLUCONAZOLE	0.4 g	QD	Y-M: 20[redacted] / 364	ONGOING
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	137.15 g	QD	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 367
PROPOFOL	1 OTHER: RIGHT AMOUNT	QD	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 367

Event #1: Event of Interest - Neutropenia

Event Description	NEUTROPHIL COUNT DECREASED
Preferred term	好中球数減少
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 88
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	141
Duration of AE	54 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, AE Leading to Discontinuation of Study Drug, Event of Interest-Serious Infections, Event of Interest-Opportunistic Infection excluding Tuberculosis and Herpes Zoster

Event Description	PULMONARY CRYPTOCOCCUS NEOFORMANS INFECTION
Preferred term	クリプトコッカス性肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 313
Age at AE Onset	5[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 316): NPTST500-THE CAPSULAR ANTIGEN OF CRYPTOC: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 359): NPTST037-ANTIGEN TITER DETECTION OF CRYP: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST500-THE CAPSULAR ANTIGEN OF CRYPTOC: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology	
NOT REPORTED	
AE Stopped Initial 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]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は中国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺クリプトコッカス・ネオフォルマンス感染の事象を発現した。関連する病歴は，咳嗽，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313日後＊，被験者は肺クリプトコッカス・ネオフォルマンス感染を発現した。

本事象発現前の投与から約6ヵ月後＊，被験者は喘息（非重篤）と診断され，投与から約9ヵ月後＊に慢性気管支炎（非重篤）と診断された。

投与313日後＊　，被験者は，30 年間の病歴として報告された反復する咳嗽及び痰が 1 ヵ月前から悪化したため，病院を受診した。入院時の診断は，咳喘息，慢性気管支炎の急性発症，性状不明の両肺多発小結節及び高脂血症（非重篤）であった。同日，CT スキャン検査が行われて両側多発小結節が認められ，被験者は治療を受けた。投与316日後＊　，被験者は入院した。入院後，被験者は気道過敏性を抑えるための去痰薬による治療，抗ロイコトリエン治療を受け，気管支拡張が実施された。危険因子は職業性曝露であった。近医は小結節を取り除くための胸部手術を勧めた。投与319日後＊　，被験者は退院した。投与330日後＊　，被験者は手術のために再入院した。投与333日後＊　，被験者は胸腔鏡下切除術を受け，本手術では右肺上葉の肺尖区の部分切除，胸膜癒着焼灼術，肺の修復及び閉鎖式胸腔ドレナージが行われた。投与373日後＊，病理再報告では，クリプトコッカス・ネオフォルマンスでよくみられる真菌胞子が示された。

治験薬の投与は，肺クリプトコッカス・ネオフォルマンス感染のため完全に中止され，投与456日後＊，被験者は同意撤回し，治験を中止した。

投与された薬剤は，アセチルシステイン，terbutaline sulphate，アミノフィリン，トラマドール塩酸塩，エノキサパリンナトリウム，compound glycyrrhiza，モンテルカストナトリウム，レボフロキサシン塩酸塩，ケトチフェンフマル酸塩，モンテルカストナトリウム，compound pholcodine，アンブロキソール塩酸塩，gan ju bing mei，アンブロキソール塩酸塩，zhike pingchuan tangjiang，

ブデソニド，formoterol，フルコナゾール，paracetamol・トラマドール塩酸塩，vitamin B6 及びセフロキシムナトリウムであった。

The patient's past medications include:

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

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

COMPOUND GLUTAMINE ENTERSOLUBLE CAPSULES for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LIVE COMBINED BIFIDOBACTERIUM LACTOBACILLUS AND ENTEROCOCCUS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pulmonary cryptococcosis (10037371) (Pneumonia cryptococcal (10067565)) [v.24.0] [10037371]

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 PULMONARY CRYPTOCOCCUS NEOFORMANS INFECTION

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ACID FAST STAINING:** Negative

[redacted] 20[redacted] **ANTIGEN TITER DETECTION OF CRYPTOCOCCUS:** Negative

[redacted] 20[redacted] **BLOOD PRESSURE:** 144/88 mmHg

[redacted] 20[redacted] **CAPSULAR ANTIGEN OF CRYPTOCOCCUS NEOFORMANS/GERTH:** Negative

[redacted] 20[redacted] **CAPSULAR ANTIGEN OF CRYPTOCOCCUS NEOFORMANS/GERTH:** Negative

[redacted] 20[redacted] **CHEST CT SCAN:** Diagnostic comments: Spertering chronic inflammation in both lungs (PI considers as CS, which is associated with asthma). Low density lesions in the left lobe of liver and right kidney (PI considers as NCS). Old fractures of left clavicle; bilateral fractures of multiple calcaneal ribs with callus growth (PI considers as NCS). No obvious thickening of the bilateral pleura, no enlarged lymph nodes were observed in the bilateral hilum and mediastinum.

[redacted] 20[redacted] **CHEST CT SCAN:** 1. New solid enchantment was added to the posterior segment of the right upper lobe, the border was rough, the diameter was about 0.9cm, and the inflammatory nodule? except for the placeholder? It is recommended to combine related examinations and follow up closely(PI considers as CS, which is related to pulmonary nodules). 2. There are multiple solid small nodules scattered in both lungs. What is the nature? follow up is recommended. 3. Both lungs are scattered in the same chronic disease as before. (PI considers 2 and 3 as CS, which is related to asthma) 4. Scan and change the old fractures of the left clavicle and multiple ribs on both sides. 5. Multiple cystic low-density shadows in the liver. Considering the possibility of cyst formation, it is recommended to combine with related examinations. The right kidney low density lesion is the same as before, it is recommended to combine related examinations (PI considers 4 and 5 as NCS)

[redacted] 20[redacted] **CHEST CT SCAN:** Chest enhanced ct reexamination, compared with the previous film (20[redacted].[redacted].[redacted]), showed: A nodular shadow of increased density was observed in the posterior segment of the right upper lobe, with a length of about 1.4cm, rough boundary, and inhomogeneous enhancement on enhanced scan: inflammatory nodules no exceptions to placeholders more than before, it is recommended to review after treatment. Double lung scattered in a number of solid small nodules shadow, nature roughly the same as before, follow-up is recommended. Scattering chronic lesions in both lungs are the same as before. Chest enhanced CT reexamination: No obvious abnormalities were observed in the heart and large vessels: no mass and enlarged lymph nodes were observed in the mediastinum. Old fractures of left clavicle and bilateral multiple calcaneal ribs were the same as before. Abdominal enhanced CT showed: Multiple small round unenhanced low-density shadows were scattered in the liver, with clear boundaries. The larger ones were located in the iv segment of the liver, with a long diameter of about 1.1cm: small hepatic cysts were considered. Abdominal enhanced CT showed: Several round low-density shadows without enhancement were observed in the parenchyma of both kidneys, with clear boundaries. The larger one was located in the right kidney, with a length of about 2.9cm: several cysts in both kidneys. No obvious abnormalities were observed in gallbladder, pancreas, spleen, bladder and prostate. No definite enlarged lymph nodes observed in retroperitoneal and pelvic cavity: no effusion observed in abdominal and pelvic cavity.

[redacted] 20[redacted] **CHEST CT SCAN:** Conclusion: Postoperative changes of the upper lobe of the right lung, no definite abnormal density shadow was observed in the operative area, please follow up. Chronic inflammation is scattered in both lungs, and bilateral pleura thickens and adhesions. Small nodules scattered in both lungs, multi-system inflammatory nodules, or other? Please follow up. Bilateral partial ribs may be old fractures.

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

[redacted] 20[redacted] **COLOR ULTRASOUND ABDOMINAL FULL SET:** Liver: normal shape and size, smooth liver capsule, even parenchyma echo, no obvious mass occupying. the hepatic vein ran naturally and the portal vein was not dilated. CDFI: No abnormal blood flow signal was observed in liver parenchyma. Gallbladder: Normal in shape and size, smooth in wall and clear in contour, no abnormal echo observed in bladder, and no expansion of intrahepatic and extrahepatic bile ducts. The pancreas was regular shape, normal size, clear outline, even echo of pancreatic parenchyma, no dilation of the main pancreatic duct. Spleen: normal shape and size, clear outline, splenic portal incise visible, parenchymal echo uniform, no splenic vein dilation observed. Kidney: Both kidneys had clear outline, normal shape and size, even parenchyma echo, clear boundary between skin and medulla, no separation of collection system was observed anechoic mass size of about 3.0 2.7cm was observed in the right kidney, clear boundary, regular, good internal permeability sound, no obvious mass occupying the left kidney. CDFI: no abnormal blood flow signal in and around the anechoic kidney. Ureter: Bilateral ureteral dilation is not present. Bladder: Filling difference 8. Prostate: Normal shape and size, clear contour, smooth capsule, even parenchyma echo, no abnormal echo observed in the anterior gland. CDFI: no abdormal blood flow signal was found in the anterior gland, suggestions: right renal cysts (PI thinks its NCS).

[redacted] 20[redacted] **COLOR ULTRASOUND SHALLOW SURFACE BLOCK:** Superficial mass: no abnormally enlarged lymph nodes observed in bilateral neck and bilateral supraclavicular fossa. CDFI: no abnormal blood flow signal was observed

[redacted] 20[redacted] **COVID TEST:** Nasopharyngeal swab-Negative

[redacted] 20[redacted] **CT CHEST PLAIN SCAN:** Chest CT reexamination showed that compared to previous film (20[redacted]) the following findings were found: The postoperative changes of the right chest: Volume reduction of the right upper lobe of the lung, irregular mass shadow of the right upper lobe and hilar region, dense strip shadow inside, shadow of a drainage tube in the right thoracic cavity and gas accumulation in the right chest wall. Double lung scattered in a number of solid small nodules shadow with the previous, nature follow up is recommended. (PI considered as CS, which is related to asthma). Diffuse patchy shadows in both lungs, thickened interlobular septa in the lower lobe of the right lung, double pneumonia lesions are considered, and interstitial changes in the lower lobe of the right lung are recommended for reexamination (PI considered as CS, which is related to right pulmonary nodules resection). No definite abnormalities were found in the heart and large vessels; no mass or enlarged lymph node was observed in the mediastinum. Old fractures of left clavicle and bilateral multiple calcaneal ribs were the same as before. (PI considers and NCS). No effusion in bilateral pleural cavity. Small hepatic cyst and right renal cyst were scanned as before (PI consider as NCS).

[redacted] 20[redacted] **CT CHEST PLAIN SCAN:** Chestal CT reexamination, compared with the previous film (20[redacted]) showed the following: Post operative changes of the right chest: volume of the right upper lobe was reduced, irregular mass shadow of the right upper lobe and hilar region was similar to that before, dense stripe shadow was observed inside, and gas accumulation in the right chest wall was less than that before. Double lung scattered in a number of solid small nodules shadow with the previous, nature, follow up is recommended. (PI considered as CS, which is related to asthma). Blurred patches in both lungs increased, some lesions were absorbed, and the thickening of interlobular septa in the lower lobe of the right lung was significantly less than before. Considering the double pneumonia lesions, it is recommended to reexamine. (PI consider as CS, which is related to right pulmonary nodules resection). No definite abnormalities were found in the heart and large vessels; no mass or enlarged lymph node was observed in the mediastinum. Old fractures of left clavicle and bilateral multiple calcaneal ribs were the same as before. (PI consider as NCS).

A small amount of effusion in the right pleural cavity. (PI consider as CS, which is related to right pulmonary nodules resection). Scanning and small hepatic cyst were the same as before. (PI consider as NCS).

[redacted] 20[redacted] **HEAD CT SCAN:** There was no obvious abnormal density shadow in the intracranial, no obvious dilation, compression or displacement in the ventricle, cistern and sulcus. The midline structure is centered. Focal depression of the left zygomatic arch. Locally, the bone is slightly thicker. Conclusion: No obvious intracranial abnormalities were observed. Old injury of the left zygomatic arch or others? Please combine with clinical. Right upper frontal sinus cyst.

[redacted] 20[redacted] **MR PLAIN SCANNING OF THE BRAIN:** Diagnostic comments: Abnormal white matter signal, Fazekas level 1 (PI consider as NCS) 2. right maxillary inflammation was detected by scanning (PI consider as NCS)

[redacted] 20[redacted] **MYCOBACTERIUM TUBERCULOSIS COMPLEX GROUP NUCLEIC ACID TEST:** Negative

[redacted] 20[redacted] **PATHOLOGICAL DIAGNOSIS REPORT:** Pathological diagnosis:chronic granulomatous inflammation in the upper lobe of the right lung,accompanied by fibrous hyperplasia,and acid-fast staining was needed to exclude tuberculosis. Specimen name:group 2, group 4, group 7, group 10;clinical diagnosis:type i membrane occupying;as seen by the naked eye,there was 1 lymph node in the"second group",the maximum diameter was 0.5cm,and all lymph nodes were sent."group 4 lymph node"1 lymph node,maximum diameter 0.8cm,all sent;"group 7 lymph nodes"included 2 lymph nodes with maximum diameter of 1cm-2.5cm,all of which were sent."group 10 lymph node"1 lymph node,maximum diameter 0.5cm,all sent.;pathological diagnosis: "second,fourth,seventh,tenth group lymph nodes"chronic inflammation,accompanied by charcoal deposition. Gross eye observation: "group 12 lymph node" gray-brown irregular tissue, 0.5cm×0.3cm×0.1cm, all sent. Pathological diagnosis: "group 12 lymph nodes" was carbon deposition of fibrous connective tissue Gray-white gray-brown tissue, 1cm×1cm×0.3cm, medium quality, selected pathological diagnosis: "right upper lobe" giant cell granulomatous inflammation, fibrosis.tuberculosis cannot be ruled out, and further acid-fast staining and tuberculosis dna testing are required. Rereport: Acid fast staining results: negative

[redacted] 20[redacted] **PATHOLOGICAL REPORT:** Lesion site: upper lobe of right lung Specimen type: excised Pathological diagnosis: chronic inflammation with granuloma formation, histochemical staining and immunohistochemical detection are recommended for further analysis. Histochemical staining: the pathogen was silver hexaamine (+), I-As (+), mucilage carb (+), acid fast (+), Immunohistochemistry showed CD68(PGM-1) (+) and ALK-1 (-) in tissue cells.Theere 2 IgG4 positive cells /HPF. Pathological diagnosis: Chronic inflammation with non caseous granuloma formation, fungal spores can be found, prone to cyptococcus neoforans.

[redacted] 20[redacted] **PULMONARY FUNCTION REPORT:** V75, V50, BR slightly decreased, V25, MMEF moderate decreased, VE> 10L. Bronchodilation test was positive (FEV1 increased but 15.98%R with an absolute increase of 460mL) (30 Min after inhalation of 400ug salbutamol). Patient with mild airflow limitation in the air duct, moderate airflow limitation in the small airways, and slide decrease in ventilation reserve function. Hyperventilation and impaired lung function. (PI thinks it's CS, which is associated with asthma).

[redacted] 20[redacted] **PULMONARY FUNCTION REPORT:** MMEF, MVV, and BR were slightly decreased, and V25 was moderately decreased. Patient had mild limitation of small airway flow, mild decrease of ventilation

reserve function and mild impairment of lung function. (PI considers as CS, which is related to asthma)

ChangeHistory

On [redacted] 20[redacted], received updates to suspect drug information.

On [redacted] 20[redacted], received updates to patient demographics, treatment drug information, laboratory/diagnostic procedures and narrative description.

On [redacted] 20[redacted], received updates to reporter alternative etiology, company alternative etiology, concomitant drug information, past drug information, laboratory/diagnostic procedures and narrative description.

On [redacted] 20[redacted], received updates to treatment drug information, laboratory/diagnostic procedures and narrative description.

On [redacted] 20[redacted], received updates to event information, reporter opinion of causality, company opinion of causality, reporter alternative etiology, company alternative etiology, concomitant drug information, treatment drug information and narrative description.

On [redacted] 20[redacted], received updates to laboratory/diagnostic procedures and narrative description.

On [redacted] 20[redacted], received updates to event information, reporter opinion of causality, reporter alternative etiology, concomitant drug information, treatment drug information, laboratory/diagnostic procedures and narrative description. The event of "RIGHT PULMONARY NODULE (FUNGAL INFECTION)" was amended to "RIGHT PULMONARY NODULES (CRYPTOCOCCUS NEOFORMANS INFECTION)".

On [redacted] 20[redacted], received updates to event information, reporter alternative etiology, past drug information, laboratory/diagnostic procedures, narrative description and medical history. The event of "RIGHT PULMONARY NODULES (CRYPTOCOCCUS NEOFORMANS INFECTION)" was amended to "PULMONARY CRYPTOCOCCUS NEOFORMANS INFECTION". The event of "RIGHT PULMONARY NODULES (CRYPTOCOCCUS NEOFORMANS INFECTION)" was amended to "RIGHT PULMONARY NODULES".

On [redacted] 20[redacted], received updates to patient demographics, medical history, event information, reporter opinion of causality, company opinion of causality, reporter alternative etiology, company alternative etiology, concomitant drug information, treatment drug information, laboratory/diagnostic procedures and narrative description. The event of "RIGHT PULMONARY NODULES" was removed.

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
クリプトコッカス性肺炎	X	X		X

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

Medical History	Onset Year
ALANINE AMINOTRANSFERASE INCREASED	20[redacted]
CHOLESTEROL REDUCTION	20[redacted]
HEPATITIS B CORE ANTIBODY POSITIVE	20[redacted]
HYPERURICEMIA	20[redacted]
LEFT SIDED UC	20[redacted]
MILD THALASSEMIA	20[redacted]
NEUTROPHIL COUNT INCREASED	20[redacted]
PERIPHERAL WHITE BLOOD CELL INCREASED	20[redacted]
TACHYCARDIA SINUS	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[redacted] / 1	[redacted] / 56	56
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	[redacted] / 57	[redacted] / 112	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted] / 1	[redacted] / 161	161

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1 g	TID	Y-M: [redacted]
LEVOGLUTAMIDE	2.000 OTHER: S	TID	Y-M: [redacted] / -342
ALPHA-AMYLASE SWINE PANCREAS;CELLULASE;LIPASE;PROTEASE NOS	1.000 OTHER: S	TID	Y-M: [redacted] / -196
ANTIDIARRHEAL MICROORGANISMS	2.000 g	TID	Y-M: [redacted] / -196
SULFASALAZINE	0.5 g	OTHER: QN	Y-M: [redacted] / -176
MESALAZINE	1 g	TID	Y-M: [redacted] / -112
MESALAZINE	1.2 g	TID	Y-M: [redacted] / -58

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	
MESALAZINE	1.2 g	TID	Y-M: 20[redacted] / -58	ONGOING
CALCIUM SULFATE;DRYOPTERIS CRASSIRHIZOMA;EPHEDRA SPP.;FORSYTHIA SUSPENSA;GLYCYRRHIZA GLABRA;HOUTTUYNIA CORDATA;ISATIS TINCTORIA;LONICERA JAPONICA;MENTHOL;POGOSTE MON CABLIN;PRUNUS SPP.;RHEUM SPP.;RHOD	6 g	TID	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 156
ERYTHROMYCIN	0.25 g	TID	Y-M: 20[redacted] / 156	Y-M: 20[redacted] / 157
AMBROXOL	30 mg	BID	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 182
MOXIFLOXACIN	250 mL	QD	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 170
SODIUM CHLORIDE	100 mL	BID	Y-M: 20[redacted] / 161	Y-M: 20[redacted] / 182
FLUCONAZOLE;SODIUM CHLORIDE	300 mL	QD	Y-M: 20[redacted] / 166	Y-M: 20[redacted] / 166
FLUCONAZOLE;SODIUM CHLORIDE	200 mL	QD	Y-M: 20[redacted] / 167	Y-M: 20[redacted] / 181
LIDOCAINE	1 mg	QD	Y-M: 20[redacted] / 169	Y-M: 20[redacted] / 169
SOLUTIONS AFFECTING THE ELECTROLYTE BALANCE	500 mL	QD	Y-M: 20[redacted] / 173	Y-M: 20[redacted] / 173
POTASSIUM	20 mL	QD	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 174
NIFEDIPINE	30 mg	QD	Y-M: 20[redacted] / 176	Y-M: 20[redacted] / 182
FLUCONAZOLE	400 mg	QD	Y-M: 20[redacted] / 182	ONGOING
FLUCYTOSINE	1.5 g	QID	Y-M: 20[redacted] / 182	ONGOING
AGRIMONIA PILOSA;FORSYTHIA SUSPENSA;GLYCYRRHIZA SPP.;INDIGO;PAEONIA X SUFFRUTICOSA	1.35 g	TID	Y-M: 20[redacted] / 203	ONGOING
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	137.15 g	QD	Y-M: 20[redacted] / 246	Y-M: 20[redacted] / 246

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest-Serious Infections, Event of Interest-Opportunistic Infection excluding Tuberculosis and Herpes Zoster

Event Description	CRYPTOCOCCAL PNEUMONIA
Preferred term	クリプトコッカス性肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 267
Age at AE Onset	6[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 158): Basophils: 0.05 [0 - 0.1] 10^9/L; Basophils/Leukocytes: 0.4 [0 - 1] %; Eosinophils: 0.12 [0.02 - 0.5] 10^9/L; Eosinophils/Leukocytes: 1.1 [0.5 - 5] %; Erythrocytes: 4.59 [4.3 - 5.7] 10^12/L; Hematocrit: 0.313 [0.39 - 0.49] FRACTION OF 1; Hemoglobin: 101 [120 - 160] G/L; Leukocytes: 11.09 [4 - 10] 10^9/L; Lymphocytes: 1.19 [0.8 - 4] 10^9/L; Lymphocytes/Leukocytes: 10.7 [20 - 40] %; Monocytes: 0.7 [0 - 0.84] 10^9/L; Monocytes/Leukocytes: 6.3 [3 - 8] %; NPTST050-AVERAGE CORPUSCULAR HEMOGLOBIN: 22 [27 - 34] PG; NPTST147-COEFFICIENT OF VARIATION OF RED: 16.6 [0 - 15] UNIT NOT REPORTED; NPTST259-H-CRP: 19.57 [0.5 - 10] MG/L; NPTST338-MEAN CORPUSCULAR HEMOGLOBIN CON: 323 [320 - 380] G/L; NPTST340-MEAN CORPUSCULAR VOLUME: 68.2 [79 - 101] FL; NPTST342-MEAN PLATELET VOLUME: 10.5 [7.1 - 13.1] FL; NPTST378-P-LCC: 77 [30 - 90] UNIT NOT REPORTED; NPTST379-P-LCR: 34.1 [9 - 50] %; NPTST397-PCT: 0.236 [0.108 - 0.282] %; NPTST409-PLATELET DISTRIBUTION WIDTH: 15.9 [8 - 19.8] UNIT NOT REPORTED; NPTST488-STANDARD DEVIATION OF RED BLOOD: 40.5 [35 - 56] UNIT NOT REPORTED; Neutrophils: 9.03 [2.3 - 7.7] 10^9/L; Neutrophils/Leukocytes: 81.5 [50 - 70] %; Platelets: 225 [100 - 450] 10^9/L; [redacted]20[redacted] (RX DAY 162): Alanine Aminotransferase: 22 [NOT REPORTED - 50] IU/L; Albumin: 43.6 [40 - 55] G/L; Alkaline Phosphatase: 49 [51 - 160] U/L; Aspartate Aminotransferase: 22 [NOT REPORTED - 40] IU/L; Basophils: 0.04 [0 - 0.06] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 1] %; Bilirubin: NEGATIVE [3 - 19] umol/L; Calcium: 2.28 [2.11 - 2.52] MMOL/L; Chloride: 103.7 [99 - 110] MMOL/L; Cholesterol: 3.79 [2.8 - 5.7] MMOL/L; Creatine Kinase: 237 [19 - 226] U/L; Creatinine: 88 [68 - 108] UMOL/L; Eosinophils: 0.11 [0.02 - 0.52] 10^9/L; Eosinophils/Leukocytes: 0.9 [0.4 - 8] %; Erythrocytes: NIL [NOT REPORTED - NOT REPORTED] /HPF; Erythrocytes: 4.56 [4.3 - 5.8] 10^12/L; Glucose: 6.24 [3.9 - 5.9] MMOL/L; Glucose: NEGATIVE [4.6 - 6.4] mmol/L; HDL Cholesterol: 1.23 [0.9 - NOT REPORTED] mmol/L; Hematocrit: 0.32 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 98 [130 - 175] G/L; Ketones: NEGATIVE [NOT REPORTED - NOT REPORTED] mmol/L; LDL Cholesterol: 2.19 [NOT REPORTED - 4] mmol/L; Leukocytes: NIL [0 - 1] /HPF; Leukocytes: 11.76 [3.5 - 9.5] 10^9/L; Leukocytes: 0.001 [0 - 0.011] 10^9/L; Lymphocytes: 1.01 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 8.6 [20 - 50] %; Monocytes: 0.66 [0.1 - 0.6] 10^9/L; Monocytes/Leukocytes: 5.6 [3 - 10] %; NPTST006-A/G: 1.48 [1.2 - 2.4] RATIO; NPTST012-AFP: 1.40 [NOT REPORTED - 7] ng/mL; NPTST013-AG: 18.7 [12 - 20] MMOL/L; NPTST033-ANTI-HCV: 0.039 [0 - 0.9] UNIT NOT REPORTED; NPTST042-APTT: 29.6 [24.8 - 33.8] SEC; NPTST043-APTT RATIO: 1.07 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST044-ASPERGILLUS GALACTOMANNAN: 0.05 [NOT REPORTED - 0.5] UNIT NOT REPORTED; NPTST047-AST/ALT: 1.00 [NOT REPORTED - NOT REPORTED] RATIO; NPTST049-ATIII: 88.3 [75 - 125] %; NPTST052-BACT: 0 [NOT REPORTED - 230] /uL; NPTST072-BLA%: / [NOT REPORTED - 0] %; NPTST073-BLD: NEGATIVE [NOT REPORTED - NOT REPORTED] cells/uL; NPTST094-CA-125: 6.64 [NOT REPORTED - 24] U/mL; NPTST095-CA15-3: 13.20 [NOT REPORTED - 24] U/mL; NPTST096-CA19-9: 3.33 [NOT REPORTED - 30] U/mL; NPTST097-CA72-4: ?1.50 [NOT REPORTED - 6.5] U/mL; NPTST105-CAST: 0 [0 - 2] /UL; NPTST106-CD3: 48.40 [66.9 - 83.1] %; NPTST107-CD3 COUNT: 475 [941 - 2226] CELLS/UL; NPTST108-CD4: 33.90 [33.19 - 47.85] %; NPTST109-CD4 COUNT: 333 [471 - 1220] CELLS/UL; NPTST110-CD4/CD8: 2.95 [0.97 - 2.31] UNIT NOT REPORTED; NPTST111-CD8: 11.5 [20.4 - 34.7] %; NPTST112-CD8 COUNT: 113 [303 - 1003] CELLS/UL; NPTST113-CEA: 1.50 [NOT REPORTED - 5] ng/mL; NPTST143-CO2: 22.6 [18 - 28] MMOL/L; NPTST149-COLOR AND DESCRIPTION: YELLOW , SOFT FECES [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST150-COLOR AND TURBIDITY: YELLOW;CLEAR [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST152-COMBINED DETECTION OF HIV ANTIG: 0.204 [0 - 1] UNIT NOT REPORTED; NPTST153-COMMON EPITHELIAL CELL: A LITTLE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST154-CONDUCTIVI: 7 [19.8 - 42.5] UNIT NOT REPORTED; NPTST165-CRP: 19.40 [NOT REPORTED - 5] mg/L; NPTST174-CYFRA21-1: 1.75 [NOT REPORTED - 3] ng/mL; NPTST175-CYS-C: 0.97 [0.51 - 1.09] MG/L; NPTST182-D-DIMER: 1.42 [NOT REPORTED - 0.55] UNIT NOT REPORTED; NPTST185-DFIB: 5.99 [NOT REPORTED - NOT REPORTED] g/L; NPTST186-DIRECT BILIRUBIN: 8.9 [NOT REPORTED - 8.8] umol/L; NPTST195-EC-1: 1 [0 - 6] /UL; NPTST196-EGFR: 79.06 [56 - 122] ML/MIN/1.73M2; NPTST207-ESR: 54.0 [NOT REPORTED - 43] mm/h; NPTST212-FAT DROPLET: NIL [NOT REPORTED - NOT REPORTED] /HPF; NPTST214-FDP: 2.8 [NOT REPORTED - 5] mg/L; NPTST229-FIB: 3.57 [2 - 4] G/L; NPTST237-FUNGAL 1, 3-B-D GLUCAN: ?37.00 [0 - 95] pg/mL; NPTST247-GGT: 16 [NOT REPORTED - 60] IU/L; NPTST250-GLB: 29.5 [20 - 40] G/L; NPTST257-GRANULAR CASTS: NIL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST261-HBDH: 138 [72 - 182] IU/L; NPTST274-HEPATITIS B CORE ANTIBODY SEMI-: 0.008 [1 - NOT REPORTED] UNIT NOT REPORTED; NPTST275-HEPATITIS B E ANTIBODY SEMI-QUA: 0.602 [1 - NOT

REPORTED] UNIT NOT REPORTED; NPTST276-HEPATITIS B SURFACE ANTIBODY QU: 8.360 [0 - 10] IU/L; NPTST277-HEPATITIS B SURFACE ANTIGEN SEM: 0.338 [0 - 0.9] UNIT NOT REPORTED; NPTST294-IBIL: 18.4 [NOT REPORTED - 20] umol/L; NPTST295-IL-6: 17.70 [0 - 7] PG/ML; NPTST307-INR: 1.10 [0.88 - 1.15] SEC; NPTST317-LDH: 186 [120 - 250] IU/L; NPTST321-LEU: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST326-LIKE YEAST: NIL [NOT REPORTED - NOT REPORTED] /HPF; NPTST331-MCH: 21.5 [27 - 34] PG; NPTST332-MCHC: 302 [316 - 354] G/L; NPTST334-MCV: 71.1 [82 - 100] FL; NPTST343-METARUBRICYTE: 0 [NOT REPORTED - 1] UNIT NOT REPORTED; NPTST344-MG: 0.95 [0.75 - 1.02] MMOL/L; NPTST364-NON-HDL-C: 2.56 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST366-NSE: 9.54 [NOT REPORTED - 20.4] ng/mL; NPTST371-OB(IMMUNIZATION): NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST388-PATHOLOGICAL CAST: 0 [NOT REPORTED - NOT REPORTED] /uL; NPTST397-PCT: ?0.02 [NOT REPORTED - 0.046] ng/mL; NPTST400-PHAGOCYTE: NIL [NOT REPORTED - NOT REPORTED] /HPF; NPTST412-PO4: 0.99 [0.85 - 1.51] MMOL/L; NPTST415-PRO: NEGATIVE [NOT REPORTED - NOT REPORTED] cells/uL; NPTST428-PT: 11.8 [9.6 - 12.8] SEC; NPTST433-PUS CELLS: NONE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST433-PUS CELLS: NIL [NOT REPORTED - NOT REPORTED] /HPF; NPTST436-RBC-1: 0 [0 - 3] UNIT NOT REPORTED; NPTST437-RBC-2: 1 [0 - 11] /UL; NPTST441-RDW-CV: 18.3 [11.5 - 14.5] %; NPTST442-RDW-SD: 44.3 [37 - 54] FL; NPTST470-SEMI-QUANTIFICATION OF HEPATITI: 0.143 [0 - 1] UNIT NOT REPORTED; NPTST472-SG: 1.010 [1.003 - 1.03] UNIT NOT REPORTED; NPTST476-SMALL ROUND EPITHELIAL CELL: NIL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST489-STARCH GRANULE: NIL [NOT REPORTED - NOT REPORTED] /HPF; NPTST499-TBA: 3.3 [NOT REPORTED - 15] umol/L; NPTST509-TOTAL BILIRUBIN: 27.3 [5 - 28] UMOL/L; NPTST515-TP: 73.1 [65 - 85] G/L; NPTST520-TREPONEMA PALLIDUM ANTIBODY: 0.104 [0 - 1] UNIT NOT REPORTED; NPTST526-TT: 16.5 [14 - 22] SEC; NPTST527-TT RATIO: 1.01 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST532-UREA: 4.4 [3.6 - 9.5] MMOL/L; NPTST545-VISCOSE RAYON: NIL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST548-WBC-1: 0 [0 - 5] UNIT NOT REPORTED; Neutrophils: 9.95 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 84.6 [40 - 75] %; Nitrite: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Platelets: 208 [100 - 300] 10^9/L; Potassium: 4.26 [3.5 - 5.3] MMOL/L; Sodium: 140.7 [137 - 147] MMOL/L; Triglycerides: 1.21 [0.29 - 1.83] MMOL/L; Urate: 430 [240 - 490] UMOL/L; Urobilinogen: NEGATIVE [NOT REPORTED - NOT REPORTED] umol/L; pH: 5.50 [4.6 - 8] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 163): NPTST168-CRYPTOCOCCUS NEOFORMANS/CRYPTOC: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST362-NEOCOCCUS/CRYPTOCOCCUS GERTH AN: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 169): Chloride: 124 [120 - 130] MMOL/L; Erythrocytes: 0 [3.8 - 5.8] 10^12/L; Glucose: 4.21 [2.5 - 4.4] MMOL/L; NPTST148-COLOR: COLORLESS [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST168-CRYPTOCOCCUS NEOFORMANS/CRYPTOC: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST363-NM-TP: 0.24 [0.15 - 0.45] G/L; NPTST368-NUCLEATED CELLS: 1 [0 - 10] 10^6/L; NPTST433-PUS CELLS: NIL [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST519-TRANSPARENCY: TRANSPARENT [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 170): Alanine Aminotransferase: 28 [NOT REPORTED - 50] IU/L; Alanine Aminotransferase: 26 [NOT REPORTED - 50] IU/L; Albumin: 43 [40 - 55] G/L; Alkaline Phosphatase: 53 [51 - 160] U/L; Aspartate Aminotransferase: 25 [NOT REPORTED - 40] IU/L; Basophils: 0.03 [0 - 0.06] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 1] %; Bilirubin: 24.7 [5 - 28] UMOL/L; Calcium: 2.16 [2.11 - 2.52] MMOL/L; Cholesterol: 3.23 [2.8 - 5.7] MMOL/L; Creatine Kinase: 139 [19 - 226] U/L; Eosinophils: 0.15 [0.02 - 0.52] 10^9/L; Eosinophils/Leukocytes: 1.6 [0.4 - 8] %; Erythrocytes: 4.55 [4.3 - 5.8] 10^12/L; Glucose: 4.96 [3.9 - 5.9] MMOL/L; HDL Cholesterol: 0.84 [0.9 - NOT REPORTED] mmol/L; Hematocrit: 0.33 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 98 [130 - 175] G/L; LDL Cholesterol: 1.73 [NOT REPORTED - 4] mmol/L; Leukocytes: 9.48 [3.5 - 9.5] 10^9/L; Lymphocytes: 1.26 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 13.3 [20 - 50] %; Monocytes: 0.83 [0.1 - 0.6] 10^9/L; Monocytes/Leukocytes: 8.8 [3 - 10] %; NPTST006-A/G: 1.44 [1.2 - 2.4] RATIO; NPTST013-AG: 20.2 [12 - 20] MMOL/L; NPTST047-AST/ALT: 0.96 [NOT REPORTED - NOT REPORTED] RATIO; NPTST072-BLA%: / [NOT REPORTED - 0] %; NPTST121-CL: 102.9 [99 - 110] MMOL/L; NPTST163-CREA: 85 [68 - 108] UMOL/L; NPTST165-CRP: 9.08 [NOT REPORTED - 5] mg/L; NPTST175-CYS-C: 0.93 [0.51 - 1.09] MG/L; NPTST183-DBIL: 7.6 [NOT REPORTED - 8.8] umol/L; NPTST196-EGFR: 82.45 [56 - 122] ML/MIN/1.73M2; NPTST204-EPO: 130.00 [3.7 - 29.5] MIU/ML; NPTST207-ESR: 46.0 [NOT

REPORTED - 43] mm/h; NPTST228-FERRITIN: 151.00 [24 - 336] NG/ML; NPTST247-GGT: 16 [NOT REPORTED - 60] IU/L; NPTST250-GLB: 29.8 [20 - 40] G/L; NPTST261-HBDH: 173 [72 - 182] IU/L; NPTST294-IBIL: 17.1 [NOT REPORTED - 20] umol/L; NPTST317-LDH: 227 [120 - 250] IU/L; NPTST331-MCH: 21.5 [27 - 34] PG; NPTST332-MCHC: 302 [316 - 354] G/L; NPTST334-MCV: 71.4 [82 - 100] FL; NPTST343-METARUBRICYTE: 0 [NOT REPORTED - 1] /100 CELLS; NPTST344-MG: 0.92 [0.75 - 1.02] MMOL/L; NPTST364-NON-HDL-C: 2.39 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST412-PO4: 0.85 [0.85 - 1.51] MMOL/L; NPTST441-RDW-CV: 19.5 [11.5 - 14.5] %; NPTST442-RDW-SD: 47.4 [37 - 54] FL; NPTST490-STFR: 3.53 [0.76 - 1.76] MG/L; NPTST499-TBA: 4.3 [NOT REPORTED - 15] umol/L; NPTST515-TP: 72.8 [65 - 85] G/L; NPTST521-TRF: 2.49 [2.5 - 4.3] G/L; NPTST532-UREA: 3.1 [3.6 - 9.5] MMOL/L; Neutrophils: 7.2 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 76 [40 - 75] %; Potassium: 3.54 [3.5 - 5.3] MMOL/L; Sodium: 142.5 [137 - 147] MMOL/L; Triglycerides: 1.7 [0.29 - 1.83] MMOL/L; Urate: 342 [240 - 490] UMOL/L; [redacted]20[redacted] (RX DAY 174): Albumin: 41.2 [40 - 55] G/L; Alkaline Phosphatase: 51 [51 - 160] U/L; Aspartate Aminotransferase: 23 [NOT REPORTED - 40] IU/L; Basophils: 0.03 [0 - 0.06] 10^9/L; Basophils/Leukocytes: 0.4 [0 - 1] %; Bilirubin: 25 [5 - 28] UMOL/L; Calcium: 2.19 [2.11 - 2.52] MMOL/L; Chloride: 102.1 [99 - 110] MMOL/L; Creatine Kinase: 94 [19 - 226] U/L; Creatinine: 84 [68 - 108] UMOL/L; Eosinophils: 0.16 [0.02 - 0.52] 10^9/L; Eosinophils/Leukocytes: 2.1 [0.4 - 8] %; Erythrocytes: 4.61 [4.3 - 5.8] 10^12/L; Glucose: 5.3 [3.9 - 5.9] MMOL/L; HDL Cholesterol: 0.83 [0.9 - NOT REPORTED] mmol/L; Hemoglobin: 100 [130 - 175] G/L; LDL Cholesterol: 1.81 [NOT REPORTED - 4] mmol/L; Leukocytes: 7.71 [3.5 - 9.5] 10^9/L; Lymphocytes: 1.56 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 20.2 [20 - 50] %; Monocytes: 0.72 [0.1 - 0.6] 10^9/L; Monocytes/Leukocytes: 9.4 [3 - 10] %; NPTST006-A/G: 1.34 [1.2 - 2.4] UNIT NOT REPORTED; NPTST013-AG: 18.9 [12 - 20] MMOL/L; NPTST047-AST/ALT: 0.82 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST072-BLA%: / [NOT REPORTED - 0] %; NPTST143-CO2: 23.1 [18 - 28] MMOL/L; NPTST165-CRP: 5.57 [NOT REPORTED - 5] mg/L; NPTST175-CYS-C: 1.00 [0.51 - 1.09] MG/L; NPTST183-DBIL: 8.3 [NOT REPORTED - NOT REPORTED] umol/L; NPTST196-EGFR: 83.64 [56 - 122] ML/MIN/1.73M2; NPTST207-ESR: 37.0 [NOT REPORTED - 43] mm/h; NPTST247-GGT: 18 [NOT REPORTED - 60] IU/L; NPTST250-GLB: 30.8 [20 - 40] G/L; NPTST261-HBDH: 160 [72 - 182] IU/L; NPTST294-IBIL: 16.7 [NOT REPORTED - 20] umol/L; NPTST295-IL-6: 2.47 [0 - 7] PG/ML; NPTST317-LDH: 204 [120 - 250] IU/L; NPTST331-MCH: 21.7 [27 - 34] PG; NPTST332-MCHC: 305 [316 - 354] G/L; NPTST334-MCV: 71.1 [82 - 100] FL; NPTST343-METARUBRICYTE: 0 [NOT REPORTED - 1] /100 CELLS; NPTST344-MG: 0.92 [0.75 - 1.02] MMOL/L; NPTST364-NON-HDL-C: 2.52 [NOT REPORTED - NOT REPORTED] mmol/L; NPTST397-PCT: ?0.02 [NOT REPORTED - 0.046] ng/mL; NPTST412-PO4: 1.11 [0.85 - 1.51] MMOL/L; NPTST441-RDW-CV: 19.7 [11.5 - 14.5] %; NPTST442-RDW-SD: 47.3 [37 - 54] FL; NPTST499-TBA: 13.5 [NOT REPORTED - 15] umol/L; NPTST515-TP: 72.0 [65 - 85] G/L; NPTST532-UREA: 2.9 [3.6 - 9.5] MMOL/L; Neutrophils: 5.24 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 67.9 [40 - 75] %; Platelets: 132 [100 - 300] 10^9/L; Potassium: 3.12 [3.5 - 5.3] MMOL/L; Sodium: 141 [137 - 147] MMOL/L; Triglycerides: 1.86 [0.29 - 1.83] MMOL/L; Urate: 344 [240 - 490] UMOL/L; [redacted]20[redacted] (RX DAY 179): Basophils: 0.04 [0 - 0.06] 10^9/L; Basophils/Leukocytes: 0.5 [0 - 1] %; Eosinophils: 0.3 [0.02 - 0.52] 10^9/L; Eosinophils/Leukocytes: 3.8 [0.4 - 8] %; Erythrocytes: 4.84 [4.3 - 5.8] 10^12/L; Hematocrit: 0.35 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 106 [130 - 175] G/L; Leukocytes: 7.77 [3.5 - 9.5] 10^9/L; Lymphocytes: 1.72 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 22.1 [20 - 50] %; Monocytes: 0.7 [0.1 - 0.6] 10^9/L; Monocytes/Leukocytes: 9 [3 - 10] %; NPTST072-BLA%: / [NOT REPORTED - 0] %; NPTST165-CRP: 2.93 [NOT REPORTED - 5] mg/L; NPTST168-CRYPTOCOCCUS NEOFORMANS/CRYPTOC: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST207-ESR: 36.0 [NOT REPORTED - 43] mm/h; NPTST331-MCH: 21.9 [27 - 34] PG; NPTST332-MCHC: 307 [316 - 354] G/L; NPTST334-MCV: 71.3 [82 - 100] FL; NPTST343-METARUBRICYTE: 1 [NOT REPORTED - 1] UNIT NOT REPORTED; NPTST441-RDW-CV: 19.9 [11.5 - 14.5] %; NPTST442-RDW-SD: 47.8 [37 - 54] FL; Neutrophils: 5.02 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 64.6 [40 - 75] %; Platelets: 153 [100 - 300] 10^9/L; [redacted]20[redacted] (RX DAY 181): NPTST167-CRYPTOCOCCUS ANTIGEN TITER TEST: 1:5 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 191): Alanine Aminotransferase: 24 [NOT REPORTED - 50] IU/L; Albumin: 50.4 [40 - 55] G/L; Alkaline Phosphatase: 56 [51 - 160] U/L; Aspartate Aminotransferase: 26 [NOT REPORTED - 40] IU/L; Basophils: 0.02 [0 - 0.06] 10^9/L; Basophils/Leukocytes: 0.2 [0 - 1] %; Creatinine: 97 [68 - 108] UMOL/L; Eosinophils: 0.23 [0.02 - 0.52] 10^9/L; Eosinophils/Leukocytes: 2.7 [3 - 10] %; Erythrocytes: 5.47 [4.3 - 5.8] 10^12/L; Hematocrit: 0.38 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 118 [130 - 175] G/L; Leukocytes: 8.55 [3.5 - 9.5] 10^9/L; Lymphocytes: 2.07 [1.1 - 3.2] 10^9/L; Lymphocytes/Leukocytes: 24.2 [20 - 50] %; Monocytes: 0.45 [0.1 - 0.6]

10^9/L; NPTST005-A/A: 1.08 [NOT REPORTED - NOT REPORTED] RATIO; NPTST006-A/G: 1.50 [1.2 - 2.4] RATIO; NPTST072-BLA%: / [NOT REPORTED - NOT REPORTED] %; NPTST116-CHE: 7824 [4900 - 11900] IU/L; NPTST175-CYS-C: 1.09 [0.51 - 1.09] MG/L; NPTST183-DBIL: 6.9 [NOT REPORTED - 8.8] umol/L; NPTST196-EGFR: 70.28 [56 - 122] 099,ML/MIN/1.73M3; NPTST247-GGT: 22 [NOT REPORTED - 60] IU/L; NPTST250-GLB: 33.5 [20 - 40] G/L; NPTST294-IBIL: 17.8 [NOT REPORTED - 20] umol/L; NPTST332-MCHC: 311 [316 - 354] G/L; NPTST334-MCV: 69.3 [82 - 100] FL; NPTST441-RDW-CV: 18.7 [11.5 - 14.5] %; NPTST442-RDW-SD: 46.2 [37 - 54] FL; NPTST499-TBA: 1.8 [NOT REPORTED - 10] umol/L; NPTST515-TP: 83.9 [65 - 85] G/L; NPTST532-UREA: 4.5 [3.6 - 9.5] MMOL/L; Neutrophils: 5.78 [1.8 - 6.3] 10^9/L; Neutrophils/Leukocytes: 67.6 [40 - 75] %; Neutrophils/Leukocytes: 5.3 [3 - 10] %; Platelets: 134 [100 - 300] 10^9/L; Urate: 545 [240 - 490] UMOL/L; [redacted]20[redacted] (RX DAY 202): Alanine Aminotransferase: 28 [NOT REPORTED - 50] IU/L; Albumin: 48.5 [40 - 55] G/L; Alkaline Phosphatase: 51 [51 - 160] U/L; Aspartate Aminotransferase: 28 [NOT REPORTED - 40] IU/L; Bilirubin: 23.2 [5 - 28] UMOL/L; Creatinine: 86 [68 - 108] UMOL/L; Glucose: 5.32 [3.9 - 5.9] MMOL/L; Hematocrit: 0.36 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 113 [130 - 175] G/L; NPTST006-A/G: 1.44 [1.2 - 2.4] RATIO; NPTST047-AST/ALT: 1.00 [NOT REPORTED - NOT REPORTED] RATIO; NPTST175-CYS-C: 0.98 [0.51 - 1.09] MG/L; NPTST250-GLB: 33.7 [20 - 40] G/L; NPTST447-RET: 0.1536 [0.024 - 0.084] 10^12/L; NPTST515-TP: 82.2 [65 - 85] G/L; NPTST532-UREA: 6.2 [3.6 - 9.5] MMOL/L; Platelets: 83 [100 - 300] 10^9/L; Urate: 476 [240 - 490] UMOL/L; [redacted]20[redacted] (RX DAY 209): Hematocrit: 0.38 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 119 [130 - 175] G/L; Leukocytes: 10.53 [3.5 - 9.5] 10^9/L; NPTST372-OCCULT BLOOD: WEAKLY POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; Neutrophils: 7.02 [1.8 - 6.3] 10^9/L; Platelets: 99 [100 - 300] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 162): SPUTUM NPTST007-ACID FAST STAINING OF SMEAR: NEGATIVE-NO ACID-FAST BACILLI WERE FOUND; SPUTUM NPTST238-FUNGAL CULTURE: POSITIVE-A LITTLE CANDIDA GLABRATA; SPUTUM NPTST256-GRAM-STAINED SMEAR: NEGATIVE-NO FUNGUS DETECTED. MIXED FLORA OF UPPER RESPIRATORY TRACT, SQUAMOUS EPITHELIAL CELLS>25/LP WHITE BLOOD CELLS<10/LP NON-DEEP SPUTUM EXPECTORATION.; SPUTUM NPTST480-SPUTUM AND PHARYNGEAL BACTERIA: NEGATIVE-NORMAL MIXED FLORA GROWTH, HAEMOPHILUS IS NOT ISOLATED; [redacted]20[redacted] (RX DAY 169): CEREBROSPINAL FLUID NPTST008-ACID-RESISTANT STAIN OF SMEAR: NEGATIVE-NO ACID-FAST BACILLI WERE FOUND; CEREBROSPINAL FLUID NPTST115-CEREBROSPINAL FLUID BACTERIAL C: NEGATIVE-NO BACTERIAL GROWTH; CEREBROSPINAL FLUID NPTST256-GRAM-STAINED SMEAR: NEGATIVE-NO FUNGI, NO BACTERIA; CEREBROSPINAL FLUID NPTST479-SMEAR INK STAINING: NEGATIVE-NO CRYPTOCOCCUS WAS FOUND

AE Stopped Initial 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]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は中国の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，クリプトコッカス性肺炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，軽度のサラセミア，末梢の白血球増加，非喫煙者及び非飲酒者であった。

Event 1 の臨床経過：

投与267日後＊，被験者はクリプトコッカス性肺炎を発現した。

投与270日後＊　，被験者は風邪をひいた。投与273日後＊ ，被験者はクリプトコッカス性肺炎，右肺の複数の層状陰影，潰瘍性大腸炎，グレード 2 の高血圧の中等度のリスク及び軽度のサラセミアの初期診断があり入院した。被験者は感染症に対してモキシフロキサシン，去痰剤としてムコソルバンを投与された。関連する検査結果を合わせると，右肺のクリプトコッカス性肺炎の診断が考えられ，フルコナゾールが開始された。入院中，被験者の血圧が上昇した（最大で 166/92 mmHg）。高血圧と考えられ，baxinton による治療が開始された。被験者の咳嗽及び痰は改善し，その結果，モキシフロキサシンの投与は中止された。投与294日後＊　，被験者は退院した。退院後，被験者は 4 ヵ月にわたって抗クリプトコッカス療法を受けた。4 ヵ月の治療後，被験者に明らかな咳嗽及び痰の症状は認められなかった。被検者の状態は安定しており，呼吸器治療は継続された。

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，ムコソルバン，フルコナゾール，モキシフロキサシン塩酸塩・塩化ナトリウム合剤，アンブロキソール塩酸塩，フルシトシン，lian hua qing wen ke li（漢方薬），エリスロマイシンエチルコハク酸エステル及びフルコナゾール・塩化ナトリウム合剤であった。

The patient's past medications include:

COMPOUND GLUTAMINE ENTERSOLUBLE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COMPOUND DIGESTIVE ENZYME for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LIVE COMBINED BIFIDOBACTERIUM AND LACTOBACILLUS for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

Causality for UPADACITINIB (Blinded)

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1) Pneumonia cryptococcal (10067565) (Pneumonia cryptococcal (10067565)) [v.24.0] [10067565]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)----------

Event of CRYPTOCOCCAL PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] A-THALASSEMIA (CLINICAL) (A-TH):** 1. THE PATIENT'S A-THALASSEMIA GENOTYPE IS -A3.7/ AA, AND HE IS A CARRIER OF THE A-THALASSEMIA DELETION GENE. THE CLINICAL MANIFESTATIONS ARE MILD ANEMIA OR NO SYMPTOMS 2. HOWEVER, THE POSSIBILITY OF OTHER RARE MUTATIONS CANNOT BE RULED OUT

[redacted] **20[redacted] ACID FAST STAINING OF SMSPUTUM):** NO ACID-FAST BACILLI WERE FOUND

[redacted] **20[redacted] ACID-RESISTANT STAIN OF SMEAR (CEREBOSPINAL FLUID):** NO ACID-FAST BACILLI WERE FOUND

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 22 IU/L (normal <50)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 49 IU/L (normal 51 to 160)

[redacted] **20[redacted] ANTI-HCV:** 0.039 COI (normal 0 to 0.9)

[redacted] **20[redacted] ASPARTATE AMINO TRANSFERASE:** 22 IU/L (normal <40)

[redacted] **20[redacted] ASPERGILLUS GALACTOMANNAN:** 0.05 GMI (normal <0.5)

[redacted] **20[redacted] B-THALASSEMIA (CLINICAL) (B-TH):** 1.CARRIERS OF THE B-THALASSEMIA MUTANT GENE 2. THE POSSIBILITY THAT THIS SUBJECT HAS OTHER RARE HBB GENE MUTATIONS IS NOT EXCLUDED

[redacted] **20[redacted] BLOOD PRESSURE:** 157/85 mmHg

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

[redacted] **20[redacted] CD3:** 48.40 % (normal 66.9 to 83.1)

[redacted] **20[redacted] CD3 COUNT:** 475 CELL/UL (normal 941 to 2226)

[redacted] **20[redacted] CD4:** 33.90 % (normal 33.19 to 47.85)

[redacted] **20[redacted] CD4 COUNT:** 333 CELL/UL (normal 471 to 1220)

[redacted] **20[redacted] CD8:** 11.5 % (normal 20.4 to 34.7)

[redacted] **20[redacted] CD8 COUNT:**113 CELL/UL (normal 303 to 1003)

[redacted] **20[redacted] CHEST CT:** Flat sweep results show: 1. The lower right lung leaf multiple nodules, clumps density increase shadow and flaky grinding glass shadow, the largest is located in the lower right lung leaf base section, size of about 39mm X 29mm X 40mm, edge blur, grinding glass shadow, part of which see bronchial signs, small air bubbles: consider infectious lesions may be, excluding special types of infection may be combined with clinical laboratory examination. 2. Double lung dispersion. Increased shadow in speckled density. 3. Aortic hardening.

[redacted] **20[redacted] CHEST CT SCAN:** IMAGING FINDINGS:THE CHEST WAS SYMMETRICAL.THERE WERE SCATTERED NODULES,PATCHY CONSOLIDATION SHADOWS AND A FEW SMALL PATCHY GROUND GLASS SHADOWS IN THE LOWER LOBE OF THE RIGHT LUNG.THE AIR BRONCHIAL SIGN WAS SEEN INSIDE,THE LARGER ONE WAS ABOUT 3.0×2.8CM, AND THE ADJACENT PLEURA WAS SLIGHTLY THICKENED.THE VEINS OF BOTH LUNGS WERE NORMAL,AND NO STENOSIS,OCCLUSION OR ENLARGEMNT OF TRACHEA,LOBES AND SEGMENTAL BRONCHUS WERE OBSERVED.NO HILAR OR MEDIASTINAL LYMPH NODE ENLARGEMENT WAS OBSERVED. IMAGING FINDINGS:NO ENLARGEMENT OF THE HEART,CALCIFICATION OF THE AORTIC WALL AND LEFT CORONARY WALL,NO EFFUSION IN THE PERICARDIUM, AND NO EFFUSION IN BILATERAL PLEURAL CAVITY.

[redacted] **20[redacted] CHEST CT SCAN:** IMAGING FINDINGS:THE CHEST WAS SYMMETRICAL.THERE WERE SCATTERED NODULES,PATCHY CONSOLIDATION SHADOWS AND A FEW SMALL PATCHY GROUND GLASS SHADOWS IN THE LOWER LOBE OF THE RIGHT LUNG.THE AIR BRONCHIAL SIGN WAS SEEN INSIDE,THE LARGER ONE WAS ABOUT 3.0×2.8CM,AND THE ADJACENT PLEURA WAS SLIGHTLY THICKENED.THE VEINS OF BOTH LUNGS WERE NORMAL,AND NO STENOSIS,OCCLUSION OR ENLARGEMENT OF TRACHEA,LOBES AND SEGMENTAL BRONCHUS WERE OBSERVED.NO HILAR OR MEDIASTINAL LYMPH NODE

ENLARGEMENT WAS OBSERVED.

[redacted] 20[redacted] **CHEST CT SCAN:** Image findings: Chest symmetry, nodules, patch consolidation shadows and a few patch ground glass shadows in the lower lobe of the right lung, air bronhial sign, accompanied by a few cable shadow. The veins of both lungs were normal, no stenosis, occlusion or enlargement of trachea, lobe, and segmental bronchi were observed, and no enlargement of hilar and mediastinal lymph nodes were observed. There was no enlargement of the heart, calcification of the aortic wall and the left coronary wall, and no pericardium effusion. No effusion in both pleural cavities. Conclusion: 1. The infection of the lower lobe of the right lung. Compared with the old CT film of 20[redacted]-[redacted]-[redacted], the lesions were obviously absorbed and reduced. 2. Calcification of the aortic wall and left coronary artery wall.

[redacted] 20[redacted] **CHEST CT SCAN:** Image findings: symmetrical thorax, scattered nodules, patchy consolidation shadows and a few patch ground glass shadows in the lower lobe of the right lung, with blurred edges, air bronchial signs, accompanied by a few strip shadows. There is calcification in the basal segment of the right lower lobe. The veins of both lungs were normal, no stenosis, occlusion or enlargement of trachea. lobe, and segmental bronchi were observed, and no enlargement oh hilar and mediastinal lymph nodes were observed. There was no enlargement of the heart, calcification of the aortic wall and the left coronary wall, and no pericardium effusion. No effusion in both pleural cavities. The cortical morphology of the fourth rib of the left anterior rib is irregular.

[redacted] 20[redacted] **CHEST CT SCAN:** Imaging findings: the thorax was symmetrical and bilateral lung field transmittance was normal. In the lower lobe of the right lung, there were a few small nodules connected by strip shadow and patchy consolidation shadows, with blurred edges and air brochial signs in the consolidation area. A small solid nodule about 0.4cm in diameter was observed in the posterior segment of the upper lobe apex of the lung. There is calcification in the basal segment of the right lower lobe. The veins of the two lungs were normal, and no stenosis, occlusion or enlargement of trachea, lobe or segmental bronchus was observed. Hilar and mediastinal lymh nodes were not swollen. There was no enlargement of the heart, little calcification of the aortic wall, no effusion in the pericardium, and no effusion in the bilateral pleural cavity Conclusions: The infection foci in the lower lobe of the right lung was partially absorbed and reduced compared with the old CT film of 202-7-1. 2. There were solid small nodules in the posterior segment of the upper lobe apex of the left lung and multiple inflammatory nodules. No significant changes were observed compared with the previous one, 3. Calcification foci in the basal segment of the right lower lobe. 4. A little calcification of the aortic wall.

[redacted] 20[redacted] **COMBINED DETECTION OF HIV ANTIGEN AND ANTIBODY:** 0.204 COI (normal 0 to 1)

[redacted] 20[redacted] **COVID-19 VIRUS TEST:** Nasopharyngeal swab - Negative

[redacted] 20[redacted] **CREATINE KINASE:** 237 IU/L (normal 19 to 226)

[redacted] 20[redacted] **CREATININE:** 88 umol/L (normal 68 to 108)

[redacted] 20[redacted] **CRP:** 19.40 MG/L (normal <5.0)

[redacted] 20[redacted] **CRYPTOCOCCUS NEOFORMANS/CRYPTOCOCCUS GUTTATA CAPSULAR ANTIGEN:** Positive

[redacted] 20[redacted] **CRYPTOCOCCUS NEOFORMANS/CRYPTOCOCCUS GUTTATA CAPSULAR ANTIGEN:** Negative

[redacted] 20[redacted] **CRYPTOCOCCUS NEOFORMANS/CRYPTOCOCCUS GUTTATA CAPSULAR ANTIGEN:** Positive

[redacted] 20[redacted] **D-DIMER:** 1.42 MG/1 FEU (normal <0.55)

[redacted] 20[redacted] **DIRECT BILIRUBIN:** 8.9 umol/L (normal <8.8)

[redacted] 20[redacted] **ECG:** 1. SINUS RHYTHM 2. NORMAL ECG

[redacted] 20[redacted] **ECG:** 1. SINUS RHYTHM 2. NORMAL ECG

[redacted] 20[redacted] **EGFR:** 79.06 ML/MIN/1.73M^2 (normal 56 to 122)

[redacted] 20[redacted] **ESR:** 54.0 MM/HR (normal <43)

[redacted] 20[redacted] **FUNGAL 1, 3-B-D GLUCAN:** <37.00 pg/ml (0-95)

[redacted] 20[redacted] **GGT:** 16 IU/L (normal <60)

[redacted] 20[redacted] **GLUCOSE:** 6.24 MMOL/L (normal 3.90 to 5.90)

[redacted] 20[redacted] **GRAM-STAINED SMEAR (CEREBROSPINAL FLUID):** NO FUNGI, NO BACTERIA

[redacted] 20[redacted] **GRAM-STAINED SMEAR (SPUTUM):** NO FUNGUS DETECTED. MIXED FLORA OF UPPER RESPIRATORY TRACT, SQUAMOUS EPITHELIAL CELLS>25/LP WHITE BLOOD CELLS<10/LP NON-DEEP SPUTUM EXPECTORATION.

[redacted] 20[redacted] **H-CRP:** 19.57 MG/L (normal 0.5 to 10)

[redacted] 20[redacted] **HEMATOCRIT:** 31.3 % (normal 39 to 49)

[redacted] 20[redacted] **HEMATOCRIT:** 0.32 L/L (normal 0.40 to 0.50)

[redacted] 20[redacted] **HEMOGLOBIN:** 101 G/L (normal 120 to 160)

[redacted] 20[redacted] **HEMOGLOBIN:** 98 G/L (normal 130 to 175)

[redacted] 20[redacted] **HEMOGLOBIN:** 100 G/L (normal 130 to 175)

[redacted] 20[redacted] **HEMOGLOBIN:** 118 G/L (normal 130 to 175)

[redacted] 20[redacted] **IL-6:** 17.70 PG/ML (normal 0.0 to 7.0)

[redacted] 20[redacted] **LDH:** 186 IU/L (normal 120 to 250)

[redacted] 20[redacted] **LUMBAR PUNCTURE:** INITIAL PRESSURE: 190CMH20, FINAL PRESSURE: 125CMH20, CEREBROSPINAL FLUID EXAMINATION SHOWED NO OBVIOUS ABNORMITY.

[redacted] 20[redacted] **LYMPHOCYTES %:** 10.7 % (normal 20 to 40)

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 1.01 X10**9/L (normal 1.1 to 3.2)

[redacted] 20[redacted] **MONOCYTES %:** 6.3 % (normal 3 to 8)

[redacted] 20[redacted] **MONOCYTES ABS:** 0.70 X10**9/L (normal 0 to 0.84)

[redacted] 20[redacted] **MRI HEAD AXIAL CORONAL SAGITTAL GENERAL SCAN:** IMAGING FINDINGS: NO ABNORMAL SIGNAL SHADOW WAS OBSERVED IN THE BRAIN PARENCHYMA, AND NO OBVIOUS ABNORMAL ENHANCEMENT WAS OBSERVED AFTER ENHANCEMENT.NO WIDENING OF SULCUS AND CISTERN, NO EXPANSION OF EACH VENTRICLE SYSTEM, NO DEVIATION OF MIDLINE STRUCTURE, NO ABNORMALITY OF BONE SIGNAL IN SKULL.THE MUCOSA OF THE RIGHT MAXILLARY SINUS AND ETHMOID SINUS WAS SLIGHTLY THICKENED. SUMMARY COMMENTS: 1. NO INTRACRANIAL ABNORMALITIES WERE OBSERVED.2. PARASINUSITIS.PI CONSIDER THIS IS NCS.

[redacted] 20[redacted] **NEOCOCCUS/CRYPTOCOCCUS GERTH ANTIGEN:** NEGATIVE

[redacted] 20[redacted] **NEUTROPHILS %:** 81.5 % (normal 50 to 70)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 9.03 X10**9/L (normal 2.3 to 7.7)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 9.95 X10**9/L (normal 1.8 to 6.3)

[redacted] 20[redacted] **PATHOLOGICAL DIAGNOSIS REPORT:** The naked eye can see: "right lower lung": 1 gray cord tissue, 1.5cm in length, 0.1cm in diameter. Lesion site: right lower lung; sample type: puncture; pathological diagnosis: chronic granulomatous inflammation, need to be diagnosed by special staining and otherassistance.

[redacted] 20[redacted] **PATHOLOGICAL DIAGNOSIS REPORT:** No positive mycobacterium was detected in the acid-fast staining of the right lower lung, while positive spherical fungus and mucocarasin (-) were detected in both hexamine silver staining and PAS staining. Combined with morphology, fungal infection, propensity for fungal infection, propensity for histoplasmosis, please consider in combination with other clinical laboratory tests.

[redacted] 20[redacted] **PLATELET COUNT:** 225 X10**9/L (normal 100 to 450)

[redacted] 20[redacted] **PLATELET COUNT:** 208 X10**9/L (normal 100 to 300)

[redacted] 20[redacted] **PULSE:** 100 BPM

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.59 X10**12/L (normal 4.30 to 5.70)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.56 X10**12/L (normal 4.30 to 5.8)

[redacted] **20[redacted] SMEAR INK STAINING (CEREBROSPINAL FLUID):** NO CRYPTOCOCCUS WAS FOUND

[redacted] **20[redacted] SPUTUM AND PHARYNGEAL BACTERIA CULTURE:** NORMAL MIXED FLORA GROWTH, HAEMOPHILUS IS NOT ISOLATED

[redacted] **20[redacted] SPUTUM FUNGAL CULTURE:** Positive- A little candida glabrata

[redacted] **20[redacted] TOTAL BILIRUBIN:** 27.3 umol/L (normal 5.0 to 28.0)

[redacted] **20[redacted] TREPONEMA PALLIDUM ANTIBODY:** 0.104 COI (normal 0 to 1)

[redacted] **20[redacted] ULTRASOUND: LYMPH NODES:** NO ABNORMALLY LARGE LYMPH NODES OBSERVED IN BILATERAL NECK

[redacted] **20[redacted] UREA:** 4.4 MMOL/L (normal 3.6 to 9.5)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.09 X10**9/L (normal 4 to 10)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.76 X10**9/L (normal 3.5 to 9.5)

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	3[redacted]	MALE	WHITE

Medical History	Onset Year
ANXIETY DISORDERS	20[redacted]
HYPOCHROMIC ANEMIA	20[redacted]
HYPOVITAMINOSIS VITAMIN D3	20[redacted]
LEFT SIDED UC	20[redacted]
SWELLING OF THE WRIST	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	0.7 PACK	16	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 66	66
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	[redacted] / 69	[redacted] / 112	44
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted] / 1	[redacted] / 99	99

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]
PREDNISONE	30 mg	BID	Y-M: 20[redacted]
ANTIBIOTICS	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CORTICOSTEROIDS	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
CALCIUM CARBONATE	600 mg	QD	Y-M: 20[redacted]
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	7.500 mg/kg	0-2-6 WEEK	Y-M: 20[redacted]
ADALIMUMAB	160.000 mg	EVERY 14 DAYS	Y-M: 20[redacted]
VEDOLIZUMAB	300.000 mg	0-2-6 WEEK	Y-M: 20[redacted]
CIPROFLOXACIN	200 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]
TOFACITINIB	10.000 mg	NOT REPORTED	Y-M: 20[redacted]
CIPROFLOXACIN	200 mg	BID	Y-M: 20[redacted] / -292
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / -292
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -292
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / -296
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -296
METHYLPREDNISOLONE	16 mg	BID	Y-M: 20[redacted] / -196
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / -198
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / -198
CIPROFLOXACIN	200 mg	BID	Y-M: 20[redacted] / -204
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / -204
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -204
CIPROFLOXACIN	200 mg	BID	Y-M: 20[redacted] / -148
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -148
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -148
AZATHIOPRINE	50 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
SERTRALINE	50 mg	QD	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 80
ALANINE;ARGININE;ASPARTIC ACID;GLUCOSE;GLUTAMIC ACID;GLYCINE;GLYCINE MAX;HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE;METHIONINE;OLEA EUROPAEA;PHENYLALANINE;PROLINE;SERINE;THREONINE;TRYPTOPHAN, L-;TYROSINE;VA	900 mL	OTHER: CONTINUOSLY 18 HOURS	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 51
ASCORBIC ACID;IRON	320/60 mg	BID	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 80
CALCIUM CARBONATE	600 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 80
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
ENTEROCOCCUS FAECALIS;ESCHERICHIA COLI;LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS HELVETICUS	2 mL	TID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 102
ERDOSTEINE	300 mg	BID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
GLUCONATE SODIUM;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	100 ML/HOUR mL	OTHER: CONTINUOSLY 6AM-10PM	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
IRON	100 mg	BID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 91
IRON	62.5 mg	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
METRONIDAZOLE	500 mg	BID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 102
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
MIRTAZAPINE	15 mg	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
NADROPARIN	0.4 mL	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
NUTRIENTS NOS	200 mL	BID	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
PREDNISONE	20 mg	QD	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92
SERTRALINE	100 mg	QD	Y-M: 20[redacted] / 81	ONGOING
TRAZODONE	75 mg	QD	Y-M: 20[redacted] / 81	ONGOING
ZOLPIDEM	10 mg	PRN	Y-M: 20[redacted] / 81	Y-M: 20[redacted] / 92

COLECALCIFEROL	20 gtt	OTHER: WEEKLY	Y-M: 20[redacted] / 92	ONGOING
IRON	100 mg	QD	Y-M: 20[redacted] / 92	ONGOING
METHYLPREDNISOLONE	16 mg	QD	Y-M: 20[redacted] / 93	ONGOING

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

Event Description	RELAPS OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 193
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 81): Albumin: 44 [35 - 55] G/L; Bilirubin: 2 [0 - 0] UNIT NOT REPORTED; Erythrocytes: 4.55 [4 - 5.8] 10^12/L; Glucose: 8.32 [3.9 - 5.6] MMOL/L; Hematocrit: 0.362 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 120 [135 - 175] G/L; Ketones: 2 [0 - 0] UNIT NOT REPORTED; Leukocytes: 5.4 [4 - 10] 10^9/L; NPTST165-CRP: 34.9 [0 - 10] MG/L; Platelets: 396 [150 - 400] 10^9/L; Potassium: 4.56 [3.8 - 5.2] MMOL/L; Protein: 69.3 [64 - 80] G/L; pH: 6.0 [6 - 7] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 81): STOOL NPTST125-CLOSTRIDIUM DIFFICILE: NEGATIVE; OTHER NOSE NPTST393-PCR COVID-19 VIRAL TEST: NEGATIVE; [redacted]20[redacted] (RX DAY 84): OTHER BIOPSY NPTST139-CMV INFECTION: NEGATIVE; [redacted]20[redacted] (RX DAY 86): OTHER NOSE NPTST393-PCR COVID-19 VIRAL TEST: POSITIVE-CORONAVIRUS

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RELAPS OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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）の治験で盲検化された治験薬が投与され，潰瘍性大腸炎の再燃の事象を発現した。関

連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 0.7 箱を 16 年間）及び元飲酒者（1 日 2–4 杯）であった。

Event 1 の臨床経過：

投与193日後＊　　，被験者は潰瘍性大腸炎の再燃を発現した。投与304日後＊，潰瘍性大腸炎の再燃は消失した。

入院前の 投与192日後＊　　，被験者は摂氏 38.4°C，夜間には摂氏 38.8°C の発熱があった。被験者の消化器内科医は被験者へ病院に行くように勧めた。

投与193日後＊　，被験者は入院した。被験者は 1 日 10 回の排便及び直腸出血があり，食事ができず，飲み物しか摂取できない状態であった。被験者は摂氏 38.4°C の発熱もあった。検体検査及び診断検査が行われた。入院中，被験者はプロテイン飲料，スープ又はピューレを摂取し，排便回数は 1 日 6–10 回であった。投与198日後＊　　，被験者は COVID-19 の検査に陽性（非重篤）であった。被験者は COVID-19 の症状はなかった。投与198日後＊　，COVID-19 への感染のため，治験薬の投与は中断された。投与204日後＊，被験者は安定した状態で退院し，投与210日後＊まで隔離された。

投与された薬剤は，メドロール，entizol，hylac forte，prednisone，シプロフロキサシン，efloran，erdomed，ferrlecit，plasmalyte solution 及びソル・メドロールであった。

The patient's past medications include:

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

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

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

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

NOLPAZA for PROPHYLAXIS OF HYPERSECRETION OF HYDROCHLORIC ACID ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

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

SOLUMEDROL 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])

CIPROFLOXACIN 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])

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

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Ulcerative colitis relapse (10082448) (Colitis ulcerative (10009900)) [v.24.0] [10082448]

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 RELAPSE OF ULCERATIVE COLITIS

- Investigator: Relapse of ulcerative colitis

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 44.0 G/L (normal 35 to 55)

[redacted] **20[redacted] BODY TEMPERATURE:** 38.4 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 38.8 Degrees C

[redacted] 20[redacted] **BODY WEIGHT:** 6[redacted] KG

[redacted] 20[redacted] **CLOSTRIDIUM DIFFICILE TEST:Stool:** Negative

[redacted] 20[redacted] **CMV:** Negative

[redacted] 20[redacted] **CRP:** 34.9 MG/L (normal >0)

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

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

[redacted] 20[redacted] **GLUCOSE:** 8.32 MMOL/L (normal 3.9 to 5.6)

[redacted] 20[redacted] **HEMATOCRIT:** 36.2 % (normal 40.0 to 50.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 120 G/L (normal 135 to 175)

[redacted] 20[redacted] **COVID-19 NASOPHARYNGEAL SWAB:** Positive

[redacted] 20[redacted] **PCR COVID-19 VIRAL TEST:** Negative

[redacted] 20[redacted] **PCR COVID-19 VIRAL TEST:** Positive for Coronavirus

[redacted] 20[redacted] **PLATELET COUNT:** 396 X10**9/L (normal 150 to 400)

[redacted] 20[redacted] **POTASSIUM:** 4.56 MMOL/L (normal 3.8 to 5.2)

[redacted] 20[redacted] **PROTEIN:** 69.3 G/L (normal 64 to 80)

[redacted] 20[redacted] **RED BLOOD CELLS:** 4.55 X10**12/L (normal 4 to 5.8)

[redacted] 20[redacted] **SIGMOIDOSCOPY:** Relapse of Ulcerative Colitis, Mayo 3

[redacted] 20[redacted] **ULTRASOUND OF ABDOMEN:** Border-width of sigmoideum and descendent

[redacted] 20[redacted] **WBC:** 5.4 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			

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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 33	33

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	32 mg	TID	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	9 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	75 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	75 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	TID	Y-M: 20[redacted]
IRON	500.000 mg	NOT REPORTED	Y-M: 20[redacted]
RED BLOOD CELLS	900.000 mL	NOT REPORTED	Y-M: 20[redacted]
IRON	500.000 mg	NOT REPORTED	Y-M: 20[redacted]
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / -253
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -253
AZATHIOPRINE	150 mg	OTHER: 1 TABL X 3 TIMES PER DAY	Y-M: 20[redacted] / -266
INTRAUTERINE CONTRACEPTIVE DEVICE	N/A OTHER: NON APLICABLE	OTHER: N/A	Y-M: 20[redacted] / -219
IRON	500.000 mg	NOT REPORTED	Y-M: 20[redacted] / -71
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / -35

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
INTRAUTERINE CONTRACEPTIVE DEVICE	N/A OTHER: NON APLICABLE	OTHER: N/A	Y-M: 20[redacted] / -219	ONGOING
BUDESONIDE	9 mg	TID	Y-M: 20[redacted] / 1	ONGOING
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 22
CIPROFLOXACIN	400 mg	BID	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 31
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 23	Y-M: 20[redacted] / 31

Event #1: Serious Adverse Event

Event Description	ULCERATIVE COLITIS WORSENING
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 78
Age at AE Onset	2[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 23): Erythrocytes: 4 [3.8 - 5.5] 10^12/L; Hemoglobin: 111 [110 - 150] G/L; Leukocytes: 8.1 [3.8 - 10] 10^9/L; NPTST099-CALPROTECTINE: > 3000 [49 - 49] MG/KG; NPTST165-CRP: 83.4 [NOT REPORTED - 5] mg/L; NPTST215-FE: 2.0 [9 - 30] UMOL/L; Platelets: 827 [150 - 400] 10^9/L

Microbiology

[redacted]20[redacted] (RX DAY 23): STOOL NPTST100-CAMPYLOBACTER: NEGATIVE; STOOL NPTST124-CLOSTRIDIUM DEFICILE: NEGATIVE; STOOL NPTST458-SALMONELLA: NEGATIVE; STOOL NPTST475-SHIGELLA: NEGATIVE; STOOL NPTST554-YERSINIA: NEGATIVE

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	WORSENING OF ULCERATIVE COLITIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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）の治験で盲検化された治験薬が投与され，潰瘍性大腸炎の悪化を発現した。関連する病歴は，潰瘍性大腸炎（全大腸炎型），貧血，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78日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与257日後＊　，潰瘍性大腸炎の悪化は消失した。

本事象の発現前，投与70日後＊　　に被験者は潰瘍性大腸炎の悪化（非重篤）を発現し始めた。

投与78日後＊　　，被験者は 1 日 10 回以上の排便や血便があり入院した。被験者の状態は入院中に改善したが，寛解には至らなかった。投与86日後＊，被験者は退院した。

投与された薬剤は，メトロニダゾール，シプロフロキサシン，メチルプレドニゾロン及びプレドニゾロンであった。

The patient's past medications include:

MESALAMINE for ULCERATIVE COLITIS ([redacted])

METHYLPREDNISOLONE for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

ERYTHROCYTE MASS for ANEMIA ([redacted])

MONOFER for ANEMIA ([redacted])

CIPROFLOXACINE for ULCERATIVE COLITIS ([redacted])

METRONIDAZOLE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　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: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of ULCERATIVE COLITIS WORSENING

- Investigator: Worsening of ulcerative colitis.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CALPROTECTINE:** >3000 (<49-49)

[redacted] **20[redacted] CAMPYLOBACTER:** Negative

[redacted] **20[redacted] CLOSTRIDIUM DEFICILE:** Negative

[redacted] **20[redacted] CRP:** 83.4 mg/L (normal <5.0)

[redacted] **20[redacted] FE:** 2.0 umol/L (normal 9.0 to 30.0)

[redacted] **20[redacted] HEMOGLOBIN:** 111 G/L (normal 110 to 150)

[redacted] **20[redacted] PLATELET COUNT:** 827 X10**9/L (normal 150 to 400)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.00 X10**12/L (normal 3.8 to 5.50)

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

[redacted] **20[redacted] SHIGELLA:** Negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.1 X10**9/L (normal 3.8 to 10.0)

[redacted] **20[redacted] YERSINIA:** 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
肝障害	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 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
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

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

M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1 [redacted]20[redacted] / 319	319

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	5.000 mg/kg	EVERY 8 WEEKS	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted] / -216
AZATHIOPRINE	250 mg	QD	Y-M: 20[redacted] / -160
TACROLIMUS	5 mg	BID	Y-M: 20[redacted] / -102
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -103
PANTOPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -110
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / -110
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -97
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -71
MIDAZOLAM	3 mg	OTHER: ONCE	Y-M: 20[redacted] / -77
PROPOFOL	130 mg	OTHER: ONCE	Y-M: 20[redacted] / -77
MESALAZINE	NOT REPORTED	OTHER: UNK	Y: 20[redacted]
DOMPERIDONE	10 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
LECITHIN	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 187	Y-M: 20[redacted] / 199
SPIRULINA SPP.	1 OTHER: CAPSULE	QD	Y-M: 20[redacted] / 187	Y-M: 20[redacted] / 199
CALCIUM CARBONATE;COLECALCIFEROL	500 mg	QD	Y-M: 20[redacted] / 207	Y-M: 20[redacted] / 232
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / 207	Y-M: 20[redacted] / 220

Event #1: Serious Adverse Event, Event of Interest - Hepatic Disorder

Event Description	HEPATOPATHY
Preferred term	肝障害
AE Onset Date / Initial Rx Day	[redacted] / 254
Age at AE Onset	[redacted]

Laboratory Testing

[redacted] (RX DAY -90): Alanine Aminotransferase: 126 [6 - 43] U/L; NPTST247-GGT: 85 [10 - 61] U/L; NPTST273-HEPATITIS B AND <C: NEGATIVE [NOT REPORTED - 0] UNIT NOT REPORTED; [redacted] (RX DAY -83): Alanine Aminotransferase: 77 [6 - 43] U/L; NPTST247-GGT: 71 [10 - 61] U/L; [redacted] (RX DAY -77): Alanine Aminotransferase: 44 [6 - 43] U/L; [redacted] (RX DAY 201): NPTST035-ANTI-MITOCHONDRIALE AK-SCREEN: NEG [0 - 0] UNIT NOT REPORTED; NPTST036-ANTI-NEUTRO.-CYTOPL. AK: NEG [0 - NOT REPORTED] UNIT NOT REPORTED; NPTST040-ANTINUKLEARE-AK: NEG [0 - NOT REPORTED] UNIT NOT REPORTED; NPTST137-CMV IGG: NEG [0 - 0] IU/mL; NPTST138-CMV IGM: NEG [0 - 0] UNIT NOT REPORTED; NPTST189-EBV IGG: POS [0 - 0] UNIT NOT REPORTED; NPTST190-EBV IGM: GRENZW. [0 - 0] UNIT NOT REPORTED; NPTST269-HEP A: NEG [0 - 0] UNIT NOT REPORTED; NPTST271-HEP B: NEG [0 - 0] UNIT NOT REPORTED; NPTST272-HEP C: NEG [0 - 0] UNIT NOT REPORTED; NPTST288-HSV IGG: POS [0 - 0] UNIT NOT REPORTED; NPTST289-HSV IGM: NEG [0 - 0] UNIT NOT REPORTED; [redacted] (RX DAY 208): Alanine Aminotransferase: 1626 [0 - 50] U/L; Alkaline Phosphatase: 191 [40 - 130] U/L; Aspartate Aminotransferase: 900 [0 - 50] U/L; Bilirubin: 32.155313 [3.420778 - 17.10389] UMOL/L; NPTST240-G-GLUTAMYLTRANSFERRIN: 439 [0 - 60] U/L; [redacted] (RX DAY 209): Alanine Aminotransferase: 1870 [0 - 50] U/L; Alkaline Phosphatase: 199 [40 - 130] U/L; Aspartate Aminotransferase: 956 [0 - 50] U/L; Bilirubin: 37.28648 [3.420778 - 17.10389] UMOL/L; NPTST240-G-GLUTAMYLTRANSFERRIN: 464 [0 - 60] U/L; [redacted] (RX DAY 211): Alanine Aminotransferase: 1455 [0 - 50] U/L; Alkaline Phosphatase: 204 [40 - 130] U/L; Aspartate Aminotransferase: 488 [0 - 50] U/L; Bilirubin: 20.18259 [3.420778 - 17.10389] UMOL/L; NPTST239-G-GLUTAMYLTRANSFERRI: 449 [0 - 50] U/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	268
Duration of AE	15 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	ALCOHOL, CONMEDS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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）の治験で盲検化された治験薬が投与され，肝障害の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），脂肪肝，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254日後＊，被験者は肝障害を発現した。投与268日後＊，肝障害は消失した。

投与263日後＊　，被験者は肝酵素の検査値が高かったため入院した。被験者に他の症状はなかった。投与268日後＊　，被験者は退院した。因果関係が疑われた薬を再開したところ，再開後も被験者の肝酵素値は正常のままであった。ALT はまだわずかに高値であったが，改善していた。

本事象に関連する危険因子は，3 日連続の極端なアルコール摂取並びにレシチン及びスピルリナを含む栄養補助食品の摂取であった。被験者は国外への旅行歴はなく，刺鍼法の経験もなく，タトゥーも入れていなかった。

投与された薬剤は，prednisolon であった。

The patient's past medications include:

PREDNISOLON for ULCERATIVE COLITIS and ULCERATIVE COLITIS ([redacted])

Causality for ABT-494 (Blinded)

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1)　Hepatopathy (10059616)　(Liver disorder (10024670))　[v.21.1]　[10059616]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for ABT-494 (Blinded)

Event of HEPATOPATHY

- Investigator: Alcohol, concomitant medications.

- AbbVie: Event is more likely related to pre-existing hepatic steatosis. Pre-existing ulcerative colitis is an additional risk factor.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 126 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 77 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE**: 44 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 44 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 370 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 510 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 839 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 1626 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 1870 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 1455 U/L (normal <50)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 166 U/L (normal <50)

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 73 U/L

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 35 U/L

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 81 U/L

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 191 U/L

[redacted] **20[redacted] ALKALINE PHOSPHATASE:** 199 U/L

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 204 U/L

[redacted] 20[redacted] **ANTI-MITOCHONDRIALE AK-SCREEN:** Negative

[redacted] 20[redacted] **ANTI-NEUTRO.-CYTOPL.AK:** Negative

[redacted] 20[redacted] **ANTINUKLEÄRE-AK:** Negative

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

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 34 U/L (normal <50)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 241 U/L (normal <50)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 288 U/L (normal <50)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 402 U/L (normal <50)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 900 U/L (normal <50)

[redacted] 20[redacted] **ASPATATE AMINO TRANSFERASE:** 488 U/L (normal <50)

[redacted] 20[redacted] **BILIRUBIN:** 0.6 mg/dL (normal 0.2 to 1.0)

[redacted] 20[redacted] **BILIRUBIN:** 1.2 mg/dL (normal 0.2 to 1.0)

[redacted] 20[redacted] **BILIRUBIN:** 1.1 mg/dL (normal 0.2 to 1.0)

[redacted] 20[redacted] **BILIRUBIN:** 2.4 mg/dL (normal 0.2 to 1.0)

[redacted] 20[redacted] **BILIRUBIN:** 2.33 mg/dL (normal 0.2 to 1.0)

[redacted] 20[redacted] **BILIRUBIN:** 1.88 mg/dL (normal 0.2 to 1.0)

[redacted] 20[redacted] **BILIRUBIN:** 2.18 mg/dL (normal 0.2 to 1.0)

[redacted] 20[redacted] **BILIRUBIN:** 1.18 mg/dL (normal 0.2 to 1.0)

[redacted] 20[redacted] **CMV IGG:** Negative

[redacted] 20[redacted] **CMV IGM:** Negative

[redacted] 20[redacted] **CREATININE:** 1.28 mg/dL

[redacted] 20[redacted] **EBV IGG:** Positive

[redacted] 20[redacted] **EBV IGM:** Borderline

[redacted] **20[redacted] GGT:** 85 U/L (normal 0 to 60)

[redacted] **20[redacted] GGT:** 71 U/L (normal 0 to 60)

[redacted] **20[redacted] GGT:** 439 U/L (normal 0 to 60)

[redacted] **20[redacted] GGT:** 464 U/L (normal 0 to 60)

[redacted] **20[redacted] GGT:** 449 U/L (normal 0 to 60)

[redacted] **20[redacted] HEP A:** Negative

[redacted] **20[redacted] HEP B:** Negative

[redacted] **20[redacted] HEP C:** negative

[redacted] **20[redacted] HEPATITIS B SCREEN:** Negative

[redacted] **20[redacted] HEPATITIS C SCREEN:** Negative

[redacted] **20[redacted] HSV IGG:** Positive

[redacted] **20[redacted] HSV IGM:** Negative

[redacted] **20[redacted] LIVER PUNCTURE:** VITAL LIVER PARENCHYMA WITH LITTLE INTERFACE INFLAMMATION

[redacted] **20[redacted] ULTRASOUND:** 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
軟骨軟化症	X			

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

Medical History	Onset Year
ERYTHEMA MIGRANS	20[redacted]
HYPERTENSIS	19[redacted]
LEFT SIDED UC	20[redacted]
NEPHROLITHIASIS	20[redacted]
PENICILLIN ALLERGY	19[redacted]
PNEUMONIA	19[redacted]
RHEMATISM	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted] / 1	[redacted] / 308	308

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: [redacted]
USTEKINUMAB	390.000 mg	NOT REPORTED	Y-M: [redacted] / -211
CORTISONE	80 mg	QD	Y-M: [redacted] / -136
DOXYCYCLINE	500 mg	BID	Y-M: [redacted] / -70
AMLODIPINE;VALSARTAN	12,5 mg	QD	Y: [redacted]
METHOTREXATE	NOT REPORTED	1 time per week	Y: [redacted]
ADALIMUMAB	160.000 mg	EOW	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
DOXYCYCLINE	500 mg	BID	Y-M: [redacted] / -70	Y-M: [redacted] / 306
DEQUALINIUM;POLIDOCANOL;SULFANILAMIDE;TALC;ZINC	80 mg	BID	Y-M: [redacted] / 72	ONGOING
METAMIZOLE	30 gtt	PRN	Y-M: [redacted] / 72	ONGOING
AMLODIPINE;VALSARTAN	12,5 mg	QD	Y: [redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	CHONDROMALACIA LEFT KNEE
Preferred term	軟骨軟化症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 216
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	216
Duration of AE	1 DAY
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	AGE RETATED WEARING
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はドイツの 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，左膝の軟骨軟化症の事象を発現した。

Event 1 の臨床経過：

投与216日後＊　，被験者は左膝の軟骨軟化症を発現した。投与216日後＊　，左膝の軟骨軟化症は消失した。

投与216日後＊　　，被験者は運動時の膝の痛みのため入院した。被験者は関節鏡検査，徒手リンパドレナージ及び理学療法を受けた。投与217日後＊，被験者は退院した。

The patient's past medications include:

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

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

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

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

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

PENICILLIN for UNKNOWN INDICATION

Causality for UPADACITINIB (Blinded)

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1) Chondromalacia (10008729) (Chondromalacia (10008729)) [v.23.1] [10008729]

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 CHONDROMALACIA LEFT KNEE

- Investigator: Age related wearing.

- AbbVie: Chondromalacia of the knee is usually the result of repetitive trauma due to squatting/kneeling and other activities, thus, it is inconsistent with mechanism of action of the study drug. Additional risk factor is being overweight.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 26.9 kg/m2

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
基底細胞癌	X			X
脳血管発作	X			X
帯状疱疹				X
脂漏性角化症	X			

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	7[redacted]	MALE	WHITE

Medical History	Onset Year
ASTHMA	19[redacted]
BIPEDAL PITTING OEDEMA	20[redacted]
CATARACTS	NOT REPORTED
CHRONIC COUGH	20[redacted]
DECREASED EJECTION FRACTION	20[redacted]
DECREASED ENERGY LEVELS (COLITIS SYMPTOM)	20[redacted]
FRACTURED CLAVICLE	19[redacted]
INCREASED BOWEL MOTIONS	20[redacted]
INTERMITTENT CHEST PAIN	20[redacted]
IRON DEFICIENCY ANAEMIA	20[redacted]
LEFT SIDED UC	20[redacted]
MACULAR EYE DEGENERATION	20[redacted]
MITRIAL REGURURATION	NOT REPORTED
PERMANENT ATRIAL FIBRILATION	20[redacted]
PURE HYPERCHOLESTERAEMIA	20[redacted]
RESTLESS LEG SYNDROME	20[redacted]
RIGHT FOOT DROP	20[redacted]
SINUSITUS	20[redacted]
VARICOSE VEINS	19[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): FLEXIBLE SIGMOIDOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: ANGIOGRAM	20[redacted]
PRIOR PROCEDURES: BRONCOSCOPY	20[redacted]
PRIOR PROCEDURES: BRONSCHOSCOPY	20[redacted]
PRIOR PROCEDURES: CARDIOVERSION	20[redacted]
PRIOR PROCEDURES: COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: LIGATION OF VARICOSE VEINS	19[redacted]
PRIOR PROCEDURES: NASAL ENDOSCOPY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS2 ABT-494 (OL)	45 mg	ORAL	QD	[redacted]20[redacted] / 57	[redacted]20[redacted] / 113	57
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 364	364

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
WARFARIN	7-8 mg	OTHER: ALTERNATE DAYS	Y-M: 20[redacted]
MESALAZINE	4.8 g	QID	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	700.000 mg	6 WEEKS	Y-M: 20[redacted]
IRON	100 mg/kg	PRN	Y-M: 20[redacted]
FUROSEMIDE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300.000 mg	2 WEEKS	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -361
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -148
AFLIBERCEPT	0.05 OTHER: MG/ML	OTHER: ONCE EVERY 6 MONTHS	Y-M: 20[redacted] / -113
FENTANYL	50 OTHER: MCG	OTHER: ONCE DURING ENDOSCOPY	Y-M: 20[redacted] / -119
MIDAZOLAM	4 mg	OTHER: ONCE-DURING SCOPE	Y-M: 20[redacted] / -119
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 OTHER: SACHETS	OTHER: ONCE PRIOR TO ENDOSCOPY	Y-M: 20[redacted] / -120
DIFLUCORTOLONE;ISOCONAZOLE	TOPICAL APPICATION TO AFFECTED AREA OTHER: TOPICAL APPLICATION TO AFFECTED AREA	BID	Y-M: 20[redacted] / -43
BUDESONIDE	6 mg	QD	Y-M: 20[redacted] / -1
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / -1
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / -10
AFLIBERCEPT	0.05 mg	OTHER: EVERY 6 MONTHS	Y-M: 20[redacted] / -3
MIDAZOLAM	4 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / -7
BISOPROLOL	10 mg	QD	Y: 20[redacted]
ESOMEPRAZOLE	20 mg	QD	Y: 20[redacted]

ATORVASTATIN	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	
MESALAZINE	1 g	NOT REPORTED	Not reported	Not reported
WARFARIN	7-8 mg	OTHER: ALTERNATE DAYS	Y-M: 20[redacted]	Y-M: 20[redacted] / 56
IRON	100 mg/kg	PRN	Y-M: 20[redacted]	ONGOING
FUROSEMIDE	40 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 186
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -148	Y-M: 20[redacted] / -2
DIFLUCORTOLONE;ISOCONAZOLE	TOPICAL APPICATION TO AFFECTED AREA OTHER: TOPICAL APPLICATION TO AFFECTED AREA	BID	Y-M: 20[redacted] / -43	ONGOING
BUDESONIDE	6 mg	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 28
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 5
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / -10	Y-M: 20[redacted] / -3
AFLIBERCEPT	0.05 mg	OTHER: EVERY 6 MONTHS	Y-M: 20[redacted] / -3	Y-M: 20[redacted] / -3
MIDAZOLAM	4 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -7
BUDESONIDE	3 mg	QD	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 56
FENTANYL	50 OTHER: MCG	OTHER: ONCE ONLY	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 50
MIDAZOLAM	4 mg	OTHER: ONCE ONLY	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 50
OXYGEN	3 L	PRN	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 56
PARACETAMOL	1 g	QID	Y-M: 20[redacted] / 55	ONGOING
ACETYLSALICYLIC ACID	300 mg	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 61
ATORVASTATIN	40 mg	QD	Y-M: 20[redacted] / 56	ONGOING
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 186
BISOPROLOL	5 mg	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 173
CYCLIZINE	50 mg	TID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
METOCLOPRAMIDE	10 mg	TID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 57
PROCHLORPERAZINE	10 mg	TID	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 59
SODIUM CHLORIDE	1000 mL	OTHER: OVER 12 HOURS	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 56
QUININE	300 mg	QD	Y-M: 20[redacted] / 57	Y-M: 20[redacted] / 59

CYCLIZINE	50 mg	PRN	Y-M: 20[redacted] / 58	Y-M: 20[redacted] / 66
PROCHLORPERAZINE	5 mg	QD	Y-M: 20[redacted] / 59	ONGOING
LACTULOSE	15 mL	TID	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 67
SENNA ALEXANDRINA	2 OTHER: PILLS	QD	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 64
APIXABAN	2.5 mg	BID	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 64
APIXABAN	5 mg	BID	Y-M: 20[redacted] / 64	ONGOING
IRON	1 g	OTHER: STAT DOSE	Y-M: 20[redacted] / 67	Y-M: 20[redacted] / 67
ALUMINIUM HYDROXIDE;MAGNESIUM CARBONATE	10-15 mL	PRN	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 72
BISOPROLOL	2.5 mg	QD	Y-M: 20[redacted] / 173	Y-M: 20[redacted] / 183
LIDOCAINE	2 %	PRN	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 183
BUMETANIDE	1 mg	QD	Y-M: 20[redacted] / 186	ONGOING
AFLIBERCEPT	0.05 mg	OTHER: 6 MONTHLY	Y-M: 20[redacted] / 305	Y-M: 20[redacted] / 305
BISOPROLOL	10 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 56
ESOMEPRAZOLE	20 mg	QD	Y: 20[redacted]	ONGOING
ATORVASTATIN	10 mg	QD	Y: 20[redacted]	Y-M: 20[redacted] / 56

Event #1: Event of Interest - Herpes Zoster

Event Description	SHINGLES
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 90
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	120
Duration of AE	31 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 - Adjudicated MACE *

Event Description	POSTERIOR CIRCULATION STROKE
Preferred term	脳血管発作
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 168
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 55): Alanine Aminotransferase: 28 [0 - 41] U/L; Albumin: 45 [35 - 52] G/L; Alkaline Phosphatase: 70 [40 - 130] U/L; Aspartate Aminotransferase: 28 [0 - 40] U/L; Bilirubin: 11 [0 - 24] UMOL/L; Calcium: 2.29 [2.2 - 2.55] MMOL/L; Cholesterol: 3.6 [0 - 5.2] MMOL/L; Creatinine: 81 [59 - 104] UMOL/L; Eosinophils: 0 [0.02 - 0.5] 10^9/L; Erythrocytes: 3.61 [4.5 - 6.5] 10^12/L; HDL Cholesterol: 1.07 [0 - 1.45] MMOL/L; Hematocrit: 0.36 [0.4 - 0.54] FRACTION OF 1; Hemoglobin: 123 [130 - 180] G/L; LDL Cholesterol: 2.5 [0 - 2.59] MMOL/L; Leukocytes: 15.06 [4 - 11] 10^9/L; Monocytes: 1.4 [0.2 - 1] 10^9/L; NPTST014-ALBUMIN ADJUSTED CALCIUM: 2.19 [2.2 - 2.55] MMOL/L; NPTST087-C-REACTIVE PROTEIN: 3 [0 - 5] MG/L; NPTST117-CHLORIDE: 102 [98 - 107] MMOL/L; NPTST251-GLOBULIN: 27 [20 - 35] G/L; NPTST307-INR: 1.4 [NOT REPORTED - NOT REPORTED] RATIO; NPTST330-MAGNESIUM: 0.86 [0.66 - 0.99] MMOL/L; NPTST331-MCH: 34.1 [27.5 - 31.5] PG; NPTST332-MCHC: 34.6 [30 - 35] G/DL; NPTST334-MCV: 98.3 [78 - 98] FL; NPTST421-PROTHROBIN TIME: 13.7 [9.9 - 12] SEC; NPTST524-TROPONINS T-HS: 16 [0 - 14] NG/ML; NPTST532-UREA: 5.8 [2.8 - 8.1] MMOL/L; Neutrophils: 12.24 [2 - 7.5] 10^9/L; Platelets: 229 [140 - 450] 10^9/L; Potassium: 3.8 [3.5 - 5.1] MMOL/L; Protein: 72 [66 - 87] G/L; Sodium: 142 [136 - 145] MMOL/L; Triglycerides: 0.97 [0 - 2.26] MMOL/L; [redacted]20[redacted] (RX DAY 59): Albumin: 38 [39 - 51] G/L; Bilirubin: 23 [1 - 21] UMOL/L; Creatinine: 58 [64 - 104] UMOL/L; NPTST086-C- REATIVE PROTEIN: 35.4 [0 - 5] MG/L; NPTST227-FERRITAN: 1926.7 [20 - 270] NG/ML; NPTST308-IRON: 5 [12 - 31] UMOL/L; NPTST516-TRANSFERRIN: 1.6 [2 - 3.6] G/L; NPTST517-TRANSFERRIN SAT.: 12 [21 - 45] %; Potassium: 3.6 [3.7 - 5.4] MMOL/L; [redacted]20[redacted] (RX DAY 62): Erythrocytes: 4.39 [4.5 - 5.5] 10^12/L; Leukocytes: 7.6 [4 - 10] 10^9/L; Lymphocytes: 2.2 [1 - 3] 10^9/L; Monocytes: 0.9 [0.2 - 1] 10^9/L; NPTST312-LACTATE: 3.8 [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST331-MCH: 29.8 [27 - 32] PG; Neutrophils: 3.7 [2 - 7] 10^9/L; [redacted]20[redacted] (RX DAY 69): Albumin: 37 [39 - 51] G/L; Basophils: 0.14 [0 - 0.1] 10^9/L; Eosinophils: 0.28 [0 - 0.5] 10^9/L; Erythrocytes: 4.12 [4.5 - 5.5] 10^12/L; Leukocytes: 6.2 [4 - 10] 10^9/L; NPTST086-C- REATIVE PROTEIN: 6.6 [0 - 5] MG/L; NPTST165-CRP: 6.6 [0 - 5] MG/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	191
Duration of AE	24 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HISTORY OF ATRIAL FIBRILATION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, LIFE THREATENING

Event #3: Serious Adverse Event, Event of Interest - Possible Malignancies, Event of Interest - Malignancy, Event of Interest - Non-melanoma Skin Cancer (NMSC)

Event Description	SKIN BASAL CELL CARINOMA OF RIGHT TEMPLE
Preferred term	基底細胞癌
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 219
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 182): NPTST389-PATHOLOGY: NODULAR BCC [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	296
Duration of AE	78 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	? SUN EXPOSURE- FARMER
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #4: Serious Adverse Event

Event Description	SEBORRHEIC KERATOSIS- LEFT SIDE OF NECK
Preferred term	脂漏性角化症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 295
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 182): NPTST390-PATHOLOGY OF BIOPSY: SEBORRHEIC KERATOSIS [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	295
Duration of AE	1 DAY
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	OCCUPATION- SKIN EXPOSURE - FARMING BACKGROUND
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Event #5: 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 WITH SUPERFICIAL AND NODULAR GROWING PATTERN - RIGHT TEMPLE- SKIN
Preferred term	基底細胞癌
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 447
Age at AE Onset	7[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 334): NPTST280-HISTOLOGY: BASAL CELL CARCINOMA [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	447
Duration of AE	1 DAY
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	OCCUPATION- SUN EXPOSURE- FARMING BACKGROUND
Discontinued Study Drug Due to the Event	NO
SAE Criteria	IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はアイルランドの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，後方循環脳卒中の事象を発現した。関連する病歴は，静脈瘤，永続性の心房細動，純型高コレステロール血症，潰瘍性大腸炎，鉄欠乏性貧血，歩行時の圧痕浮腫，駆出率の低下，エネルギーレベルの低下（大腸炎の症状），断続的な胸痛，非喫煙者，禁酒及び僧帽弁逆流であった。

Event 2 の臨床経過：

投与から約3ヵ月後＊，被験者は髄膜脳症の病変を伴う帯状疱疹を発現し，投与から約4ヵ月後＊に消失した。

投与168日後＊，被験者は後方循環脳卒中を発現した。

投与168日後＊　，被験者は虚血性脳卒中で救急治療室を受診し，そのまま入院した。被験者は左腕，左脚及び右脚の運動や感覚の喪失を経験した。被験者はまた，失語症，嚥下障害，構語障害，浮動性めまい，急性回転性めまい，軽度の past-pointing，半盲，眼振，急性錯乱及び意識低下の症状及び徴候があった。

退院時の要約：被験者は発症の 1 週間前に結腸内視鏡検査を受け，数日間ワルファリンを中止していた。被験者は治療レベルの通常用量のワルファリンを再開していなかった。被験者は入院 4 日前から食事量が減り，よく眠れなくなっていた。投与168日後＊　，被験者は頭痛及び浮動性めまいを訴え，椅子の上で倒れた。6 人がかりで被験者を起こした。被験者はまた，嘔吐，腹痛，回転性めまい，右側の顔面下垂及び視力障害があった。発熱，胸痛及び息切れはなかった。腹部は柔らかく，膨満感はなく，マーフィー徴候は陰性であった。神経学的検査では，筋力，緊張，感覚，反射及び協調は正常であった。被験者は主観的及び客観的な視力喪失があった。NIHSS（National Institutes of Health Stroke Scale）スコアは 6 であった。入院中，被験者は CT による腸間膜血管造影検査を受けたが，正常であった。被験者は不特定の静脈内輸液，プロトンポンプ阻害薬（PPI）及び鎮痛薬で治療を受けた。

被験者には症状はあるが大きな障害はなく，日常の業務や活動をすべて行うことができた。

投与190日後＊，被験者は退院した。投与191日後＊，後方循環脳卒中は消失した。

投与された薬剤は，プロクロルペラジン，アピキサバン，アスピリン，アトルバスタチン，メトクロプラミド，cyclizine，ビソプロロール，ラクツロース，キニーネ及びセンナであった。

The patient's past medications include:

ASACOLON for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

SALOFALK for ULCERATIVE COLITIS

Causality for UPADACITINIB (Blinded)

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1) Stroke (10042244) (Cerebrovascular accident (10008190)) [v.22.1] [10042244]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of POSTERIOR CIRCULATION STROKE

- Investigator: History of Atrial fibrillation.

- AbbVie: Risk factors include pre-existing atrial fibrillation, hypercholesterolemia, advanced age and recent interruption of warfarin for colonoscopy .

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL X-RAY:** Normal bowel gas pattern. No radiographic sign of obstruction or perforation.

[redacted] **20[redacted] ABSOLUTE EOSINOPHIL:** 0.00 X10**9/L (normal 0.02 to 0.5)

[redacted] **20[redacted] ABSOLUTE MONOCYTE:** 1.40 X10**9/L (normal 0.2 to 1.0)

[redacted] **20[redacted] ABSOLUTE NEUTROPHIL:** 12.24 X10**9/L (normal 2.0 to 7.5)

[redacted] **20[redacted] ALBUMIN:** 45 G/L (normal 35 to 52)

[redacted] **20[redacted] ALBUMIN:** 37 G/L (normal 39 to 51)

[redacted] **20[redacted] ALBUMIN ADJUSTED CALCIUM:** 2.19 MCMOL/L (normal 2.20 to 2.55)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 70 IU/L (normal 40 to 130)

[redacted] 20[redacted] **ALT:** 28 U/L (normal 0 to 41)

[redacted] 20[redacted] **AST:** 28 U/L (normal 0 to 40)

[redacted] 20[redacted] **BASOPHILS ABS:** 0.14 X10**9/L (normal 0 to 0.1)

[redacted] 20[redacted] **BILIRUBIN:** 11 umol/L (normal 0 to 24)

[redacted] 20[redacted] **BILIRUBIN:** 23 G/L (normal 1 to 21)

[redacted] 20[redacted] **BLOOD CULTURE:** No growth after 1 day

[redacted] 20[redacted] **BLOOD PRESSURE:** 141/65 mmHg

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

[redacted] 20[redacted] **BLOOD UREA:** 5.8 MMOL/L (normal 2.8 to 8.1)

[redacted] 20[redacted] **C- REATIVE PROTEIN:** 35.4 MG/L (normal 0 to 5)

[redacted] 20[redacted] **C- REATIVE PROTEIN:** 6.6 MG/L (normal 0 to 5)

[redacted] 20[redacted] **C-REACTIVE PROTEIN:** 3 MG/L (normal 0 to 5)

[redacted] 20[redacted] **CALCIUM:** 2.29 MMOL/L (normal 2.20 to 2.55)

[redacted] 20[redacted] **CHEST X-RAY:** AP erect projection. Cardiac and mediastinal contours are unremarkable. Hear size cannot be assessed. There is minor basal atelectasis but not consolidation or effusion is present. No subphrenic free air.

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

[redacted] 20[redacted] **CHOLESTEROL:** 3.6 MMOL/L (normal 0 to 5.2)

[redacted] 20[redacted] **CREATININE:** 81 umol/L (normal 59 to 104)

[redacted] 20[redacted] **CREATININE:** 58 umol/L (normal 64 to 104)

[redacted] 20[redacted] **CT ANGIO ARCH, CAROTIDS AND INTRACRANIAL:** THE COMMON AND INTERNAL CAROTID ARTERIES ARE PATENT BILATERALLY. NO SIGNIFICANT PROXIMALICA STENOSIS OR EVIDENCE OF DISSECTION. THE ORIGIN OF THE LEFT VERTEBRAL ARTERY IS POORLY EVALUATED DUE TO MOTION ARTEFACT. OTHERWISE THE VERTEBRAL ARTERIES ARE PATENT BILATERALLY. DOMINANTLEFT VERTEBRAL ARTERY. THE LEFT PROXIMAL PICA IS PATENT. THE BASILAR ARTERY IS PATEN. FOCAL ATTENUATION OF THE LEFT MID PCA (DISTAL AMBIENT SEGMENT APPROXIMATELY IMAGE 405) BUT NO PROXIMAL OCCLUSION. IMPRESSION: NO BASILAR ARTERY

OCCLUSION OR PROXIMAL OCCLUSION.

[redacted] 20[redacted] **CT ANGIOGRAM- MESENTERIC ARTERY:** IMAGING OBTAINED DURING PEAK ARTERIAL ENHANCEMENT. THE AORTA, COELIAC ARTERY AND SUPERIOR MESENTERIC ARTERY ENHANCE NORMALLY. NO BOWEL DILATION, PERFORATION AND FREE FLUID. IN THE LOWER CHEST , THE HEART IS ENLARGED. SMALL RIGHT EFFUSION. MINOR RIGHT BASAL INFILTRATE. IMPREESION: NO SIGNIFICANT ACUTE INTRA-ABDOMINAL PATHOLOGY.

[redacted] 20[redacted] **CT BRAIN:** LARGE LEFT PCA TERRITORY INFARCT INVOLVING THE ENTIRE LEFT OCCIPITAL LOBE. BIULATERAL CEREBELLAR HEMISPHERE INFARCTS , MORE EXTENSIVE ON THE LEFT. NO ACUTE INTRACRANIAL HEMISPHERE INFARCTS , MORE EXTENSIVE ON THE LEFT. NO ACUTE INTRACRANIAL HAEMHORRAGE OR CT EVIDENCE OF AN ANTERIOR CIRCULATION INFARCT. NO HYDROCEPHALUS AT THIS TIME HOWEVER CONSIDE SHORT INTERVAL FOLLOW UP CT BRAIN GIVEN THE RISK OF POSTERIOR FOSSA MASS EFFECT. FINDINGS DISCUSSED WITH THER REFERRING TEAM AT THE TIME OF REPORTING.

[redacted] 20[redacted] **CT BRAIN:** THERE IS A LARGE INFARCT OCCUPYING THE LEFT OCCIPITAL LOBE. THERE IS MIXED AREAS OF ATTENUATION WITHIN LIKELY REPRESENTING INFARCT MATURATION, NO DEFINITE HAEMORRHAGE VISULALISED. BILARTERAL CEREBELLAR LOBE INFARCTS, EXTENSIVE IN THE LEFT HEMISPHERE. NO MASS LIKE EFFECT DEMONSTRATED. IMPRESSION: NO EVIDENCE OF HAEMORRHAGIC TRANSFORMATION.

[redacted] 20[redacted] **ECG:** Atrial Fibrillation.

[redacted] 20[redacted] **EOSINOPHILS ABS:** 0.28 X10**9/L (normal 0 to 0.5)

[redacted] 20[redacted] **FERRITAN:** 1926.7 NG/ML (normal 20 to 270)

[redacted] 20[redacted] **GLOBULIN:** 27 G/L (normal 20 to 35)

[redacted] 20[redacted] **HB:** 12.3 G/DL (normal 13.0 to 18.0)

[redacted] 20[redacted] **HCT:** 0.36 Ratio (normal 0.40 to 0.54)

[redacted] 20[redacted] **HDL CHOLESTEROL:** 1.07 MMOL/L (normal 0 to 1.45)

[redacted] 20[redacted] **HEART RATE:** 75 MIN

[redacted] 20[redacted] **INR:** 1.4 Ratio

[redacted] 20[redacted] **IRON:** 5 umol/L (normal 12 to 31)

[redacted] 20[redacted] **LDL CHOLESTEROL:** 2.5 MMOL/L (normal 0 to 2.59)

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 2.2 X10**9/L (normal 1 to 3)

[redacted] **20[redacted] MAGNESIUM:** 0.86 MMOL/L (normal 0.66 to 0.99)

[redacted] **20[redacted] MCH:** 34.1 PG (normal 27.5 to 31.5)

[redacted] **20[redacted] MCH:** 29.8 PG (normal 27 to 32)

[redacted] **20[redacted] MCHC:** 34.6 G/DL (normal 30.0 to 35.0)

[redacted] **20[redacted] MCV:** 98.3 FL (normal 78 to 98)

[redacted] **20[redacted] MONOCYTES ABS:** 0.9 X10**9/L (normal 0.2 to 1)

[redacted] **20[redacted] NEUTROPHILS ABS:** 3.7 X10**9/L (normal 2 to 7)

[redacted] **20[redacted] PLATELET COUNT:** 229 X10**9/L (normal 140 to 450)

[redacted] **20[redacted] POTASSIUM:** 3.8 MMOL/L (normal 3.5 to 5.1)

[redacted] **20[redacted] PROTEIN:** 72 G/L (normal 66 to 87)

[redacted] **20[redacted] PT:** 13.7 MMOL/L (normal 9.9 to 12.0)

[redacted] **20[redacted] RBC:** 3.61 X10**12/L (normal 4.5 to 6.5)

[redacted] **20[redacted] RED BLOOD CELLS:** 13.3 X10**12/L (normal 11.5to 14.5)

[redacted] **20[redacted] RED BLOOD CELLS:** 4.12 X10**12/L (normal 4.5 to 5.5)

[redacted] **20[redacted] RESPIRATION:** 16 MIN

[redacted] **20[redacted] SERIAL TROPONINS:** 16 ng/L (normal <14)

[redacted] **20[redacted] SERIAL TROPONINS:** 21 ng/L (normal <14)

[redacted] **20[redacted] SERIAL TROPONINS:** 22 ng/L (normal <14)

[redacted] **20[redacted] SODIUM:** 142 MMOL/L (normal 136 to 145)

[redacted] **20[redacted] SWALLOW STUDY:** Failed

[redacted] **20[redacted] SWALLOW STUDY:** Repeat: Passed

[redacted] **20[redacted] TRANSFERRIN:** 1.6 G/L

[redacted] **20[redacted] TRANSFERRIN SAT:** 12 % (normal 21 to 45)

[redacted] **20[redacted] TRIGLYCERIDES:** 0.97 MMOL/L (normal 0 to 2.26)

[redacted] 20[redacted] **WBC:** 15.06 X10**9/L (normal 4.0 to 11.0)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 7.6 X10**9/L (normal 4 to 10)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はアイルランドの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，右側頭部の皮膚基底細胞癌の事象を発現した。関連する病歴は，喘息，永続性の心房細動，純型高コレステロール血症，潰瘍性大腸炎，歩行時の圧痕浮腫，駆出率の低下，断続的な胸痛，非喫煙者及び非飲酒者であった。

Event 3 の臨床経過：

投与から約8ヵ月後＊，被験者は右側頭部の皮膚基底細胞癌を発現した。投与296日後＊，右側頭部の皮膚基底細胞癌は消失した。

投与から約8ヵ月＊，被験者は病変群のためにかかりつけ医から紹介された。投与295日後＊，被験者は日帰り手術で右側頭部の皮膚病変の切除を受けた。同日，右側頭部の皮膚病変の病理報告で基底細胞癌が指摘された。

この被験者における追加の危険因子は，農業従事者であることであった。

投与された薬剤は，lignacaine であった。

The patient's past medications include:

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

PREDNISOLONE 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])

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

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

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

SALOFALK for ULCERATIVE COLITIS

Causality for UPADACITINIB (Blinded)

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1) Basal cell carcinoma (10004146) (Basal cell carcinoma (10004146)) [v.24.0] [10004146]

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 SKIN BASAL CELL CARCINOMA OF RIGHT TEMPLE

- Investigator: Sun Exposure-Farmer

- AbbVie: Risk factors include advanced age, Caucasian race, and occupation as a farmer.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] BODY WEIGHT: 7[redacted] KG
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はアイルランドの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，頚部左側の脂漏性角化症の事象を発現した。

Event 4 の臨床経過：

投与295日後＊ ，被験者は頚部左側の脂漏性角化症を発現した。投与295日後＊ ，頚部左側の脂漏性角化症は消失した。

被験者は病変群のためにかかりつけ医から紹介された。被験者は左頚部の皮膚病変の切除を受けた。病理学的には脂漏性角化症であり，完全に切除された。

被験者は農業従事者であるため，危険因子には日光への露出が多いことが含まれた。

The patient's past medications include:

ASACOLON for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

AZOTHIOPRINE for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

SALOFALK for ULCERATIVE COLITIS

Causality for UPADACITINIB (Blinded)

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1) Seborrheic keratosis (10039791) (Seborrhoeic keratosis (10039796)) [v.23.1] [10039791]

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 SEBORRHEIC KERATOSIS LEFT SIDE OF NECK

- Investigator: occupation- skin exposure - Farming background

- AbbVie: Seborrheic keratosis is one of the most common noncancerous skin growths in older adults. Subject's advanced age and Caucasian race are additional risk factors.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] SKIN BIOPSY:** Seborrheic keratosis
Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はアイルランドの 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，表在性及び結節性の成長パターンを伴う基底細胞癌（右側頭部）を発現した。関連する病歴は，潰瘍性大腸炎，非喫煙者及び禁酒であった。

Event 5 の臨床経過：

投与441日後＊　，被験者は表在性及び結節性の成長パターンを伴う基底細胞癌（右側頭部）を発現した。投与447日後＊　，表在性及び結節性の成長パターンを伴う基底細胞癌（右側頭部）は消失した。

投与447日後＊　，被験者は右側頭部の皮膚病変の切除生検を受けた。結果，この病変は表在性及び結節性の成長パターンを有する基底細胞癌に陽性であることが判明した。

報告された危険因子は，農業従事者であることであった。

The patient's past medications include:

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

PREDNISOLONE 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])

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

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

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

SALOFALK for ULCERATIVE COLITIS

Causality for UPADACITINIB (Blinded)

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1) Nodular basal cell carcinoma (10073093) (Basal cell carcinoma (10004146)) [v.23.1] [10073093]

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 BASAL CELL CARCINOMA WITH SUPERFICIAL AND NODULAR GROWING PATTERN - RIGHT TEMPLE SKIN

- Investigator: Occupation-sun exposure-farming background.

- AbbVie: risk factors include advanced age, caucasian race and sun exposure as reported by PI.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] HISTOLOGY LESION ON RIGHT TEMPLE:** Right temple: basal cell carcinoma with superficial and nodular growing pattern. Maximum microscopic dimension of 4.5mm; deep invasion 0.5mm to the level of interphase papillary and reticular dermis. There is no evidence of perinueral invasion.

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes Zoster: One dermatome (unknown location) involved. 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
潰瘍性大腸炎	X			

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

Medical History	Onset Year
ANEMIA: ANEMIA SECONDARY TO IBD	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
OTHER: PANCYTOPENIA DEVELOPED AS A RESULT OF USE OF HUMIRA AND IMURAN	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): FLEXIBLE SIGMOIDOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	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	11	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	CURRENT	10 SESSIONS	1	
PIPES	NEVER			

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

Study Drug Administration

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

M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 141	141

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	35.000 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40.000 mg	4 WEEKLY	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: 1 RECTAL SUPPOSITORY	PRN	Y-M: 20[redacted]
SULFASALAZINE	3 g	PRN	Y-M: 20[redacted]
AZATHIOPRINE	25 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	PRN	Y-M: 20[redacted]
SULFASALAZINE	2 g	QD	Y-M: 20[redacted]
ADALIMUMAB	40.000 mg	WEEKLY	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
VEDOLIZUMAB	300.000 mg	8 WEEKLY	Y-M: 20[redacted]
INFLIXIMAB	400.000 mg	8 WEEKLY	Y-M: 20[redacted] / -288
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -288
CALCIUM	II OTHER: CAPSULES	QD	Y-M: 20[redacted] / -79
ACICLOVIR	TOPICAL OTHER: TOPICAL	PRN	Y-M: 20[redacted] / -12
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
SULFASALAZINE	1.5 g	PRN	Y: 20[redacted]
FISH OIL	I OTHER: CAPSULE	QD	Y: 20[redacted]
HERPES ZOSTER IMMUNIZATION	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 / Stop Year-Month / RX Day	
SULFASALAZINE	2 g	QD	Y-M: 20[redacted]	ONGOING
CALCIUM	II OTHER: CAPSULES	QD	Y-M: 20[redacted] / -79	ONGOING
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 112
ENOXAPARIN	20 mg	QD	Y-M: 20[redacted] / 107	Y-M: 20[redacted] / 108
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / 113	Y-M: 20[redacted] / 119
PREDNISOLONE	25 mg	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 126
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 127	ONGOING
FISH OIL	I OTHER: CAPSULE	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	MODERATE ULCERATIVE COLITIS FLARE
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 150
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	DISEASE WORSENING. ULCERATIVE COLITIS FLARE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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，中等度の潰瘍性大腸炎の再燃の事象を発現した。関連する病歴は，元喫煙者（1 日 1 箱を 11 年間），潰瘍性大腸炎（広範囲な潰瘍性大腸炎/全大腸炎型），ヒュミラ及びイムランの使用による汎血球減少症並びに現飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与150日後＊　　，被験者は中等度の潰瘍性大腸炎の再燃の事象を発現した。投与256日後＊，中等度の潰瘍性大腸炎の再燃の事象は消失した。

投与255日後＊　　，被験者は潰瘍性大腸炎の症状悪化があり入院した。被験者は回腸瘻造設を伴う全直腸結腸切除術を受けた。投与266日後＊　　，被験者は退院した。この被験者の治験参加は完全に中止された。

投与された薬剤は，プレドニゾロン及びクレキサンであった。

The patient's past medications include:

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

COLIFOAM ENEMAS for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

VEDOLIZUMAB for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.24.0]　[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 (Blinded)

Event of MODERATE ULCERATIVE COLITIS FLARE

- Investigator: DISEASE WORSENING. ULCERATIVE COLITIS FLARE. PANPROCTOCOLECTOMY COMPLETED.

- AbbVie: EVENT MORE LIKELY RELATED TO PRE-EXISTING ULCERATIVE COLITIS.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL XRAY:** FECAL LOADING IN THE ASCENDING AND TRANSVERSE COLON WITHOUT APPRECIABLE MURAL THICKENING OR EVIDENCE OF FREE INTRAPERITONEAL GAS. NO EVIDENCE OF LARGE OR SMALL BOWEL LUMINAL DILATATION

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

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** THICKENING OF THE RECTUM AND SIGMOID COLON WITH FATTY INFILTRATION OF THE WALL INDICATING LONG-STANDING CHANGE. HOWEVER, THERE IS PROBABLE SUPERIMPOSED ACUTE SIGMOID COLITIS. NO COLLECTION.

[redacted] **20[redacted] SIGMOIDOSCOPY:** MAYO 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
帯状疱疹	X			X

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

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
OSTEOARTHRITIS	20[redacted]
OTHER: CHICKEN POX	NOT REPORTED

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SURGERY: LEFT KNEE REPLACMENT	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	40	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 48	48

M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1 [redacted]20[redacted] / 314	314

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4.8 mg	QD	Y-M: 20[redacted]
MESALAZINE	4 g	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	150.000 mg	QD	Y-M: 20[redacted]
MESALAZINE	3 g	QD	Y-M: 20[redacted]
ADALIMUMAB	180.000 mg	WEEK 0	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	380.000 mg	WEEK 0,2,6	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
GOLIMUMAB	200.000 mg	WEEK 0,2,6	Y-M: 20[redacted]
GOLIMUMAB	100.000 mg	4 WEEKLY	Y-M: 20[redacted] / -264
CALCIUM CARBONATE	2 TABS OTHER: TABLETS	QD	Y-M: 20[redacted] / -108
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -108
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -58
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -63
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -66

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / Stop Year-Month / RX Day	RX Day
CALCIUM CARBONATE	2 TABS OTHER: TABLETS	QD	Y-M: 20[redacted] / -108	ONGOING
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -108	ONGOING
BENZYLPENICILLIN	2.4 g	QID	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 168
CHLORPHENAMINE	4 g	QD	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 162
FLUCLOXACILLIN	2 g	QID	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 168
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / 162	Y-M: 20[redacted] / 182
ACICLOVIR	800 g	OTHER: 5 TIMES A DAY	Y-M: 20[redacted] / 163	Y-M: 20[redacted] / 168
ENOXAPARIN	20 mg	QD	Y-M: 20[redacted] / 163	Y-M: 20[redacted] / 167
POTASSIUM	2 OTHER: TABLES	TID	Y-M: 20[redacted] / 165	Y-M: 20[redacted] / 168
VALACICLOVIR	500 mg	TID	Y-M: 20[redacted] / 168	Y-M: 20[redacted] / 182

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

Event Description	HERPES ZOSTER 5TH CRANIAL NERVE DERMATONE
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 210
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	231
Duration of AE	22 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]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はアイルランドの 6[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，第Ｖ脳神経皮膚分節の帯状疱疹の事象を発現した。関連する病歴は，元喫煙者（1 日 0.5 箱を 40 年間），潰瘍性大腸炎（左側），現飲酒者（1 日 2 杯未満）及び水疱であった。

Event 1 の臨床経過：

投与210日後＊　，被験者は第Ｖ脳神経皮膚分節の帯状疱疹を発現した。投与231日後＊　，第Ｖ脳神経皮膚分節の帯状疱疹は消失した。

入院前の 3 日間，被験者は右目の上に痛み，腫脹及び発疹を経験した。投与210日後＊　，被験者は帯状疱疹で入院した。病変の範囲は 1 つの皮膚分節に限られていた。診断は病歴及び身体検査から行われた。投与216日後＊，被験者は退院した。

被験者は過去に帯状疱疹の病歴はなく，帯状疱疹ワクチンも接種していなかった。

投与された薬剤は，フルクロキサシリン，piriton，アシクロビル，バラシクロビル，paracetamol，ガバペンチン，クレキサン及びベンジルペニシリンであった。

The patient's past medications include:

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

GOLIMUMAB for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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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: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of HERPES ZOSTER 5TH CRANIAL NERVE DERMATONE

- Investigator: Not applicable

- AbbVie: Not applicable

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
貧血				X
血中クレアチンホスホキナーゼ増加				X
医療機器に対する不耐性	X			

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
CUTANEOUS ABSCESS	20[redacted]
CUTANEOUS FISTULA	20[redacted]
DEPRESSION	20[redacted]
EXTENSIVE UC/PANCOLITIS	19[redacted]
FIBROMIALGIA	20[redacted]
GASTRECTOMY	20[redacted]
IATROGENIC MENOPAUSE	20[redacted]
OBESITY	20[redacted]
OSTEOTOMIES	20[redacted]
RAYNAUD'S PHENOMENON	20[redacted]
RIGHT SACROILIITIS	20[redacted]
SPONDYLOARTHRITIS	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: ABDOMINAL RECONSTRUCTIVE PLASTIC SURGERY	20[redacted]
PRIOR PROCEDURES: OSTEOTOMY	20[redacted]
PRIOR PROCEDURES: SLEEVE GASTRECTOMY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 377	377

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]
MAGALDRATE	800 mg	OTHER: AS NEEDED	Y-M: 20[redacted]
INFLIXIMAB	5.000 mg/kg	AT WEEK 0, WEEK 2, WEEK 6	Y-M: 20[redacted]
MESALAZINE	1200 mg	BID	Y-M: 20[redacted]
INFLIXIMAB	5.000 mg/kg	AT WEEK 0, WEEK 2, WEEK 6	Y-M: 20[redacted]
ADALIMUMAB	160.000 mg	ONCE AT WEEK 0	Y-M: 20[redacted]
NALOXONE;OXYCODONE	10 mg	BID	Y-M: 20[redacted] / -343
BECLOMETASONE	10 mg	QD	Y-M: 20[redacted] / -278
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / -86
AMOXICILLIN;CLAVULANIC ACID	3 g	QD	Y-M: 20[redacted] / -5
MESALAZINE	1600 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	
MAGALDRATE	800 mg	OTHER: AS NEEDED	Y-M: 20[redacted]	ONGOING
MESALAZINE	1200 mg	BID	Y-M: 20[redacted]	ONGOING
NALOXONE;OXYCODONE	10 mg	BID	Y-M: 20[redacted] / -343	Y-M: 20[redacted] / 83
BECLOMETASONE	5 mg	QD	Y-M: 20[redacted] / -86	Y-M: 20[redacted] / 178
AMOXICILLIN;CLAVULANIC ACID	3 g	QD	Y-M: 20[redacted] / -5	Y-M: 20[redacted] / 2
ADEMETIONINE	400 mg	QD	Y-M: 20[redacted] / 22	Y-M: 20[redacted] / 45
FENTANYL	25 OTHER: MCG/HR	QD	Y-M: 20[redacted] / 119	ONGOING
DULOXETINE	60 mg	QD	Y-M: 20[redacted] / 294	ONGOING
ENOXAPARIN	4000 IU	QD	Y-M: 20[redacted] / 357	Y-M: 20[redacted] / 368

Event #1: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 57
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	111
Duration of AE	55 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	CK VALUE 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	[redacted]20[redacted] / 57
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	111
Duration of AE	55 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 Description	INTOLLERANCE TO PLATES
Preferred term	医療機器に対する不耐性
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 412
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	413
Duration of AE	2 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INTOLERANCE PLAQUE AND SCREWS IN OUTCOMES OF VARIZING OSTEOTOMY OF RIGHT FEMUR
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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）の治験で盲検化された治験薬が投与され，プレートに対する不耐性の事象を発現した。関連する病歴は，潰瘍性大腸炎，肥満，骨切り術，非喫煙者及び禁酒であった。

Event 3 の臨床経過：

投与412日後＊　，被験者はプレートに対する不耐性を発現した。投与413日後＊　，プレートに対する不耐性は消失した。

被験者は，投与の約6年前＊ に行った右大腿骨の骨切り術後にプレート及びスクリューに対して不耐性を示したため，投与412日後＊　に入院し，プレート及びスクリューの除去を行った。臨床経過は正常であり，投与413日後＊に被験者は良好な全身状態で退院した。

投与された薬剤は，toradol 及びクレキサンであった。

The patient's past medications include:

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

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1)　Device intolerance (10068444)　(Device intolerance (10068444))　[v.24.0]　[10068444]

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 INTOLLERANCE OF PLATES

- Investigator: INTOLERANCE PLAQUE AND SCREWS IN OUTCOMES OF VARIZING OSTEOTOMY OF RIGHT FEMUR

- AbbVie: Event more likely related to complications from plate and screws from the right femur osteotomy as noted by PI.

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
γ-グルタミルトランスフェラーゼ増加				X
膵炎	X	X		

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	3[redacted]	MALE	ASIAN

Medical History	Onset Year
CALCULUS URETERAL	20[redacted]
ECZEMA	20[redacted]
HEADACHE	20[redacted]
LEFT SIDED UC	20[redacted]
POLLINOSIS	20[redacted]
PROTEINURIA	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	1 PACK	18	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CLOSTRIDIUM BUTYRICUM	40.000 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
BUDESONIDE	2 mg	BID	Y-M: 20[redacted] / -343
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -356
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -292
LOPERAMIDE	1.000 mg	BID	Y-M: 20[redacted] / -293
PREDNISOLONE	40 mg	OTHER: ONCE	Y-M: 20[redacted] / -293
PREDNISOLONE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -241
LOPERAMIDE	1.000 mg	BID	Y-M: 20[redacted] / -141
METHYLPREDNISOLONE	500 mg	OTHER: ONCE	Y-M: 20[redacted] / -141
METHYLPREDNISOLONE	500 mg	OTHER: ONCE	Y-M: 20[redacted] / -101

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -356	Y-M: 20[redacted] / 59
PREDNISOLONE	7.5 mg	QD	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 8
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 22
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 15
ANTIBIOTICS-RESISTANT LACTIC ACID BACTERIAE	1 g	TID	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 51
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 44
CIPROFLOXACIN	200 mg	TID	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 51
LOPERAMIDE	1 mg	PRN	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 51
TIQUIZIUM	10 mg	TID	Y-M: 20[redacted] / 44	Y-M: 20[redacted] / 51
METHYLPREDNISOLONE	500 mg	OTHER: ONCE	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 54
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted] / 54	Y-M: 20[redacted] / 59
GLUCOSE;SODIUM CHLORIDE	1000 mL	OTHER: ONCE	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 59
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 60
GLUCOSE;SODIUM CHLORIDE	2000 mL	OTHER: ONCE	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
OMEPRAZOLE	20 mg	BID	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 62
PENTAZOCINE	7.5 mg	PRN	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
ULINASTATIN	50000 IU	TID	Y-M: 20[redacted] / 60	Y-M: 20[redacted] / 60
GLUCOSE;SODIUM CHLORIDE	1500 mL	QD	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 62
ULINASTATIN	50000 IU	BID	Y-M: 20[redacted] / 61	Y-M: 20[redacted] / 62
METHYLPREDNISOLONE	125 mg	BID	Y-M: 20[redacted] / 62	Y-M: 20[redacted] / 64
AMINO ACIDS NOS;ELECTROLYTES NOS;GLUCOSE;THIAMINE	1000 mL	QD	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 65
DIAZEPAM	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
DIMETICONE	10 mL	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
HYOSCINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
MAGNESIUM CITRATE	100 g	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / 63	ONGOING
METOCLOPRAMIDE	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
PETHIDINE	35 mg	OTHER: ONCE	Y-M: 20[redacted] / 63	Y-M: 20[redacted] / 63
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted] / 63	ONGOING
ALCLOMETASONE	1 g	BID	Y-M: 20[redacted] / 64	ONGOING
WHITE SOFT PARAFFIN	1 g	BID	Y-M: 20[redacted] / 64	ONGOING

CAMOSTAT	200 mg	TID	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 79

Event #1: 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	[redacted]20[redacted] / 29
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial 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, AE Leading to Discontinuation of Study Drug

Event Description	PANCREATITIS
Preferred term	膵炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 115
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 59): NPTST024-AMYLASE: 385 [43 - 116] U/L; NPTST327-LIPASE: 849 [5 - 50] U/L;
20[redacted] (RX DAY 60): NPTST024-AMYLASE: 339 [43 - 116] U/L; NPTST327-LIPASE: 622 [5 - 50] U/L;
20[redacted] (RX DAY 61): NPTST024-AMYLASE: 142 [43 - 116] U/L; NPTST327-LIPASE: 338 [5 - 50] U/L;
20[redacted] (RX DAY 62): NPTST024-AMYLASE: 92 [43 - 116] U/L; NPTST327-LIPASE: 184 [5 - 50] U/L;
20[redacted] (RX DAY 65): NPTST024-AMYLASE: 47 [43 - 116] U/L; NPTST327-LIPASE: 39 [5 - 50] U/L; [redacted]20[redacted] (RX DAY 69): NPTST024-AMYLASE: 90 [43 - 116] U/L; NPTST327-LIPASE: 163 [5 - 50] U/L; [redacted]20[redacted] (RX DAY 79): NPTST021-AMILASE: 78 [43 - 116] U/L; NPTST328-LIPAZE: 85 [5 - 50] U/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	136 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	22 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，膵炎の事象を発現した。関連する病歴は，尿管結石，潰瘍性大腸炎，現喫煙者（1 日 1 箱を 18 年間）及び現飲酒者（1 日 4 杯以上）であった。

Event 2 の臨床経過：

投与115日後＊，被験者は膵炎を発現した。投与136日後＊，膵炎は消失した。

本事象発現前の 投与101日後＊　，被験者は 2 日前から腹痛があり病院を受診し，胃腸炎（非重篤）と診断された。被験者はソルデム 3A 輸液，シプロフロキサシン，チアトン，エンテロノン及びロペミンで治療された。被験者はこの時点では入院しなかった。投与111日後＊　　，被験者は腹痛があり再度病院を受診したが，入院しなかった。腹部 CT 検査及び血液検査を受けた。潰瘍性大腸炎の悪化（非重篤）と診断され，ソル・メドロール及びラベプラゾールを投与された。投与115日後＊，被験者は 1500 mL（約 4 本）のビールを飲んだ。

投与116日後＊　　，被験者は腹痛があり入院した。上腹部の痛みがあり，アミラーゼ及びリパーゼは上昇していた。被験者は絶食し，すべての内服薬を中止した。腹部 CT 検査を受け，膵炎と診断された。投与127日後＊，症状は改善し，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。

投与された薬剤は，ミラクリッド，ソセゴン，ソル・メドロール，アセリオ及びカモスタットメシル酸塩であった。

The patient's past medications include:

MIYA BM for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

LOPEMIN for ULCERATIVE COLITIS and ACUTE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

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

PREDNISOLONE 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])

SOL-MELCORT for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　Pancreatitis (10033645)　(Pancreatitis (10033645))　[v.22.1]　[10033645]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of PANCREATITIS

- Investigator: Not applicable

- AbbVie: Risk factors include current alcohol intake of more than 4 drinks per day, current smoking of 1 pack per day for 18 years, and pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT SCAN:** There were no inflammatory findings around pancreas but suspected pancreatitis from the image of the arterial phase.

[redacted] **20[redacted] ABDOMINAL ULTRASONOGRAPHY:** Mild enlargement was detected in the pancreas body. The ultrasound did not show gallstones or duct dilation.

[redacted] **20[redacted] AMYLASE:** 385 U/L (normal 43 to 116)

[redacted] **20[redacted] AMYLASE:** 339 U/L (normal 43 to 116)

[redacted] **20[redacted] AMYLASE:** 142 U/L (normal 43 to 116)

[redacted] **20[redacted] AMYLASE:** 92 U/L (normal 43 to 116)

[redacted] **20[redacted] AMYLASE:** 47 U/L (normal 43 to 116)

[redacted] **20[redacted] AMYLASE:** 90 U/L (normal 43 to 116)

[redacted] **20[redacted] AMYLASE:** 78 U/L (normal 43 to 116)

[redacted] **20[redacted] LIPASE:** 849 U/L (normal 5 to 50)

[redacted] **20[redacted] LIPASE:** 622 U/L (normal 5 to 50)

[redacted] **20[redacted] LIPASE:** 338 U/L (normal 5 to 50)

[redacted] **20[redacted] LIPASE:** 184 U/L (normal 5 to 50)

[redacted] **20[redacted] LIPASE:** 39 U/L (normal 5 to 50)

[redacted] **20[redacted] LIPASE:** 163 U/L (normal 5 to 50)

[redacted] **20[redacted] LIPASE:** 85 U/L (normal 5 to 50)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
鉄欠乏性貧血				X
肺炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	3[redacted]	MALE	ASIAN

Medical History	Onset Year
ANAL FISTULA	20[redacted]
ATHEROMA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
INGUINAL HERNIA	19[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: OPERATION FOR ANAL FISTULA	20[redacted]
PRIOR PROCEDURES: OPERATION FOR INGUINAL HERNIA	19[redacted]
PRIOR PROCEDURES: RESECTION	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 53	53
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 1	[redacted] / 369	369

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
TACROLIMUS	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	NOT REPORTED	Y-M: 20[redacted]
PREDNISOLONE	20 mg	NOT REPORTED	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
BETAMETHASONE	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
ADALIMUMAB	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
TACROLIMUS	NOT REPORTED	NOT REPORTED	Y-M: 20[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -328
ALL OTHER NON-THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: TWICE A WEEK	Y-M: 20[redacted] / -336
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -339
PREDNISOLONE	40 mg	BID	Y-M: 20[redacted] / -340
TACROLIMUS	3 mg	BID	Y-M: 20[redacted] / -340
TACROLIMUS	1 mg	BID	Y-M: 20[redacted] / -211
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -120
DIMETICONE	100 mg	QD	Y-M: 20[redacted] / -60
FLUMAZENIL	0.5 mg	QD	Y-M: 20[redacted] / -60
FLUNITRAZEPAM	2 mg	QD	Y-M: 20[redacted] / -60
LACTULOSE	58500 mg	QD	Y-M: 20[redacted] / -60
LIDOCAINE	20 mg	QD	Y-M: 20[redacted] / -60
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	QD	Y-M: 20[redacted] / -60
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -65
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -32
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -35
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -38
SENNOSIDE A+B	24 mg	OTHER: ONCE	Y-M: 20[redacted] / -1
SODIUM PICOSULFATE	75 mg	OTHER: ONCE	Y-M: 20[redacted] / -1
PREDNISOLONE	30 mg	NOT REPORTED	Y: 20[redacted]
CORTICOSTEROIDS	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
OTHER THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: UNKNOWN	Y: 20[redacted]
CORTICOSTEROIDS	NOT REPORTED	NOT REPORTED	Y: 20[redacted]

CORTICOSTEROID NOS	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
MESALAZINE	1200 mg	TID	Y: 20[redacted]
PREDNISOLONE	15 mg	PRN	Y: 20[redacted]
TACROLIMUS	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	1200 mg	TID	Y-M: 20[redacted]	ONGOING
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -339	ONGOING
BETAMETHASONE	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 136	Y-M: 20[redacted] / 217
INFLUENZA VACCINE	0.5 mL	QD	Y-M: 20[redacted] / 204	Y-M: 20[redacted] / 204
CEFTRIAXONE	2 g	BID	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 214
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 220
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 213
IRON	40 mg	QD	Y-M: 20[redacted] / 216	Y-M: 20[redacted] / 220
HYDROCORTISONE	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 218	Y-M: 20[redacted] / 222

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 261
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	281
Duration of AE	21 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: Event of Interest - Anemia

Event Description	IRON DEFICIENCY ANEMIA
Preferred term	鉄欠乏性貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 268
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	273
Duration of AE	6 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]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺炎の事象を発現した。関連する病歴は，潰瘍性大腸炎（広範囲な潰瘍性大腸炎/全大腸炎型），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261日後＊ ，被験者は肺炎を発現した。投与281日後＊ ，肺炎は消失した。

投与261日後＊ ，被験者は発熱した。投与262日後＊ ，熱は摂氏 38.3°C まで上昇した。インフルエンザウイルス感染は陰性であった。投与264日後＊ の朝，被験者の体温は摂氏 40°C となり，他に咳嗽及び全身倦怠感の症状を訴えた。同日に被験者は入院した。CT 検査では左下

葉に硬化が認められ，肺炎と確定診断された。抗生物質が投与され，肺炎は改善した。投与275日後＊，被験者は退院した。

投与された薬剤は，カロナール，セフトリアキソンナトリウム及びレボフロキサシンであった。

The patient's past medications include:

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

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

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

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

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

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

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

PREDNISOLONE 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])

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

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] BODY TEMPERATURE:** 38.3 Degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** 40 Degrees C

[redacted] **20[redacted] CT SCAN:** A consolidation at left inferior lobe.[redacted] 20[redacted] CT SCAN: A CONSOLIDATION AT LEFT INFERIOR LOBE WAS IMPROVED BUT A RECEDING CONSOLIDATION PERSISTED.

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

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

[redacted] **20[redacted] MYCOPLASMA PNEUMONIAE ANTIGEN (QUALITATIVE):** Negative

[redacted] **20[redacted] SPUTUM EXAMINATION:** 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
貧血				X
鉄欠乏性貧血				X
ニューモシスチス・イロベチイ肺炎	X			X
静脈血栓症		X		

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	7[redacted]	FEMALE	ASIAN

Medical History	Onset Year
COLON POLYP	20[redacted]
HEADACHE	20[redacted]
HYPERLIPIDEMIA	20[redacted]
HYPERTENSION	20[redacted]
INSOMNIA	20[redacted]
LEFT SIDED UC	20[redacted]
MENOPAUSE	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: COLON POLYPECTOMY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 58	58
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 1	[redacted] / 7	7

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BETAMETHASONE	3.95 mg	QD	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
BETAMETHASONE	3.95 mg	QD	Y-M: 20[redacted]
BETAMETHASONE	3.95 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
BETAMETHASONE	3.95 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: 1-2/WEEK	Y-M: 20[redacted]
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS	1 OTHER: TABLET	TID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: 1-2/WEEK	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
TACROLIMUS	6 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5.5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5.5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]

TACROLIMUS	5 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	160.000 mg	EVERY WEEK	Y-M: 20[redacted]
ADALIMUMAB	40.000 mg	ONCE A WEEK	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
ADALIMUMAB	40.000 mg	EVERY OTHER WEEK	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: TWICE A WEEK	Y-M: 20[redacted]
AZATHIOPRINE	25 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -84
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted] / -89
PERINDOPRIL	4 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	
			RX Day	
BACILLUS MESENTERICUS;CLOSTRIDIUM BUTYRICUM;ENTEROCOCCUS FAECALIS	1 OTHER: TABLET	TID	Y-M: 20[redacted]	ONGOING
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted]	ONGOING
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]	ONGOING
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted]	ONGOING
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted]	ONGOING
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted] / -89	ONGOING
BETAMETHASONE	APPLICATION mg	PRN	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 14
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 15
BROTIZOLAM	2.5 mg	QD	Y-M: 20[redacted] / 12	ONGOING
SULFAMETHOXAZOLE;TRIMETHOPRIM	2 OTHER: TABLET	TID	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 15
AMPHOTERICIN B	1 mL	QID	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 17
MICONAZOLE	50 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 17
ATOVAQUONE	5 mL	BID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 28
DOMPERIDONE	10 mg	PRN	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 17
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 17
SODIUM CHLORIDE	20 mL	TID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 23
SULFAMETHOXAZOLE;TRIMETHOPRIM	2 OTHER: TABLET	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 16
CAFFEINE;PARACETAMOL;PROMETHAZINE;SALICYLAMIDE	1 g	TID	Y-M: 20[redacted] / 4	Y-M: 20[redacted] / 6
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 4	Y-M: 20[redacted] / 4
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted] / 4	Y-M: 20[redacted] / 22
LEVOFLOXACIN	250 mg	QD	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 7
TRANEXAMIC ACID	250 mg	TID	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 7
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 9
IRON	80 mg	QD	Y-M: 20[redacted] / 7	Y-M: 20[redacted] / 23
METHYLPREDNISOLONE	40 mg	BID	Y-M: 20[redacted] / 8	Y-M: 20[redacted] / 8
SULFAMETHOXAZOLE;TRIMETHOPRIM	3 OTHER: TABLET	TID	Y-M: 20[redacted] / 8	Y-M: 20[redacted] / 13
PREDNISOLONE	80 mg	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 10
SUVOREXANT	15 mg	QD	Y-M: 20[redacted] / 9	Y-M: 20[redacted] / 11
PERINDOPRIL	4 mg	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Serious Infections, Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zoster

Event Description	PNEUMOCYSTIS PNEUMONIA
Preferred term	ニューモシスチス・イロベチイ肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 62
Age at AE Onset	7[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 7): Eosinophils/Leukocytes: 0.2 [0.2 - 8.4] %; Leukocytes: 8.7 [3.3 - 8.6] 10^9/L; Lymphocytes/Leukocytes: 24.9 [21.2 - 51] %; Neutrophils/Leukocytes: 64.4 [38.3 - 74.7] %; [redacted]20[redacted] (RX DAY 8): NPTST051-B-D GLUCAN: 39.9 [NOT REPORTED - 20] pg/mL; NPTST310-KL-6: 541 [NOT REPORTED - 500] U/mL

Microbiology

[redacted]20[redacted] (RX DAY 7): OTHER NASAL CAVITY SWAB NPTST462-SARS-COV-2: NEGATIVE; [redacted]20[redacted] (RX DAY 8): BLOOD NPTST135-CMV ANTIGEN: NEGATIVE; OTHER NASAL CAVITY SWAB NPTST462-SARS-COV-2: NEGATIVE

AE Stopped Initial 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

Event #2: Event of Interest - Anemia

Event Description	IRON DEFICIENCY ANEMIA
Preferred term	鉄欠乏性貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 65
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial 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 #3: AE Leading to Discontinuation of Study Drug

Event Description	PHLEBOTHROMBOSIS IN HER LEFT LEG
Preferred term	静脈血栓症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 65
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial 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	YES
SAE Criteria	NONE

Event #4: Event of Interest - Anemia

Event Description	DRUG-INDUCED ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 68 (3 DAYS AFTER LAST TREATMENT)
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	90 (25 DAYS AFTER LAST TREATMENT)
Duration of AE	23 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]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 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，ニューモシスチス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），高血圧，結腸ポリープ，結腸ポリープ切除術，高脂血症，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62日後＊，被験者はニューモシスチス肺炎を発現した。

投与62日後＊　　，被験者は発熱，不快感，咳嗽，咽頭痛及び呼吸困難があり，開業医を受診した。投与64日後＊　　，被験者は発熱及び全身倦怠感があり病院を受診した。投与65日後＊，被験者は入院し，β-D-グルカン及び KL-6 が高値であることからニューモシスチスによる重症の肺炎と診断された。抗生物質の投与を開始し，ステロイドパルス療法によるソル・メド

ロールの投与とその後のプレドニンの投与に加えて，ダイフェンの投与を開始した。症状が改善したため，プレドニンの投与は徐々に中止された。ダイフェンは悪心，食欲減退及び低ナトリウム血症の副作用（非重篤）が認められたため，サムチレールに変更された。被験者の症状は改善し，投与90日後＊に退院した。

投与された薬剤は，カロナール，PL，ジスロマック，レボフロキサシン，プレドニン（プレドニゾロン），ダイフェン，トラネキサム酸，サムチレール及びフェジンであった。

The patient's past medications include:

STERONEMA for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

GCAP for ULCERATIVE COLITIS ([redacted])

PROGRAF for ULCERATIVE COLITIS ([redacted])

ADALIMUMAB for ULCERATIVE COLITIS ([redacted])

HUMIRA for ULCERATIVE COLITIS ([redacted])

IMURAN for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Pneumocystis pneumonia (10035661) (Pneumocystis jirovecii pneumonia (10073755)) [v.23.1] [10035661]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMOCYSTIS PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] B-D GLUCAN:** 39.9 PG/ML (normal 0 to 20)

[redacted] **20[redacted] CMV ANTIGEN:** Negative

[redacted] **20[redacted] CT:** Pneumonia

[redacted] **20[redacted] EOSINOPHILS:** 0.2 % (normal 0.2 to 8.4)

[redacted] **20[redacted] KL-6:** 541 U/ML (normal 0 to 500)

[redacted] **20[redacted] LYMPHOCYTES:** 24.9 % (normal 21.2 to 51)

[redacted] **20[redacted] NEUTROPHILS:** 64.4 % (normal 38.3 to 74.7)

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

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

[redacted] **20[redacted] WHITE BLOOD CELLS:** 8.7 X10**3/MCL (normal 3.3 to 8.6)

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

Reason for Narrative

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

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

Medical History	Onset Year
ASTHMA	20[redacted]
LEFT SIDED UC	20[redacted]
SACRAL PAIN	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: ABDOMINAL CT EXAMINATION	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 55	55

M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 240	240

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y-M: 19[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -221
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted] / -222
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -149
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -112
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -112
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -128
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -98
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	2 L	QD	Y-M: 20[redacted] / -64
BIFIDOBACTERIUM LACTIS	1 g	TID	Y-M: 20[redacted] / -64
DIMETICONE	5 mL	QD	Y-M: 20[redacted] / -64
FLUNITRAZEPAM	2 mg	QD	Y-M: 20[redacted] / -64
LIDOCAINE	10 mL	QD	Y-M: 20[redacted] / -64
MOSAPRIDE	10 mg	QD	Y-M: 20[redacted] / -64
PETHIDINE	1 mL	QD	Y-M: 20[redacted] / -64
SODIUM BICARBONATE	500 mL	QD	Y-M: 20[redacted] / -64
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / -65
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted] / -26
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / -27
TIPEPIDINE	20 mg	TID	Y-M: 20[redacted] / -27
PARACETAMOL	200 mg	PRN	Y-M: 20[redacted] / -41
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -41
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 L	QD	Y-M: 20[redacted] / -1
DIMETICONE	2.5 mL	QD	Y-M: 20[redacted] / -1
FAMOTIDINE	2 mL	QD	Y-M: 20[redacted] / -1
FLOMOXEF	1 g	BID	Y-M: 20[redacted] / -1
GLUCOSE	250 mL	QD	Y-M: 20[redacted] / -1
HEPARIN	5 mL	QD	Y-M: 20[redacted] / -1
MAGNESIUM CITRATE	50 g	QD	Y-M: 20[redacted] / -1
POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / -1
SODIUM BICARBONATE	500 mL	QD	Y-M: 20[redacted] / -1

SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -1
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / -2
CAFFEINE;PARACETAMOL;PROMETHAZINE;SALICYLAMIDE	1 g	TID	Y-M: 20[redacted] / -7
DEQUALINIUM	0.25 mg	PRN	Y-M: 20[redacted] / -7
MICONAZOLE	PROPER QUANTITY OTHER: N/A	TID	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
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -221	ONGOING
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted] / -26	Y-M: 20[redacted] / -17
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / -27	Y-M: 20[redacted] / -21
TIPEPIDINE	20 mg	TID	Y-M: 20[redacted] / -27	Y-M: 20[redacted] / -21
PARACETAMOL	200 mg	PRN	Y-M: 20[redacted] / -41	ONGOING
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / -41	Y-M: 20[redacted] / -27
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 L	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 1
DIMETICONE	2.5 mL	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 1
FAMOTIDINE	2 mL	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 1
FLOMOXEF	1 g	BID	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 2
GLUCOSE	250 mL	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 1
HEPARIN	5 mL	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 2
MAGNESIUM CITRATE	50 g	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 1
SODIUM BICARBONATE	500 mL	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / 1
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / -2	Y-M: 20[redacted] / -2
CAFFEINE;PARACETAMOL;PROMETHAZINE;SALICYLAMIDE	1 g	TID	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / -2
DEQUALINIUM	0.25 mg	PRN	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / 7
MICONAZOLE	PROPER QUANTITY OTHER: N/A	TID	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / 28
ACETYLCYSTEINE;ALANINE;ARGININE;ASCORBIC ACID;ASPARTIC ACID;BIOTIN;CALCIUM CHLORIDE;CYANOCOBALAMIN;FOLIC ACID;GLUCOSE;GLUTAMIC ACID;GLYCINE;HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE;MAGNESIUM SULFATE;METHI	500 mL	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 2
FLUNITRAZEPAM	2 mg	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
LIDOCAINE	10 mL	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
MOSAPRIDE	10 mg	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1

PENTAZOCINE	15 mg	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
PETHIDINE	1 mL	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 6

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

Event Description	APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 56
Age at AE Onset	2[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY -1): Leukocytes: 13.72 [3.5 - 9.7] 10^9/L; NPTST165-CRP: 0.95 [0 - 0.3] MG/DL; [redacted]20[redacted] (RX DAY 2): Leukocytes: 8.3 [3.5 - 9.7] 10^9/L; [redacted]20[redacted] (RX DAY 7): Leukocytes: 5.6 [3.5 - 9.7] 10^9/L	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	63
Duration of AE	8 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]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，虫垂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56日後＊，被験者は虫垂炎を発現した。投与63日後＊，虫垂炎は消失した。

本事象発現の 1 週間前，被験者は感冒（非重篤）を発現した。

投与55日後＊　　，被験者は発熱及び嘔吐を経験した。投与56日後＊　　，被験者は発熱及び嘔吐に加えて腹痛を訴えた。血液学的所見に基づき，血液検査及び CT スキャン検査を受けた。被験者は当初，感冒性胃腸炎と診断された。抗生物質の投与が開始され，内視鏡検査の予定が立てられた。投与56日後＊　，被験者は観察下で入院した。投与57日後＊　　，内視鏡検査で虫垂炎が確認され，抗生物質治療を継続した。被験者の症状は重くなかったため，投与58日後＊に退院した。投与63日後＊　　，経過観察が行われたところ，被験者は圧痛を訴えたが，血液検査では炎症が減少していた。

投与された薬剤は，ソリタ−T 配合顆粒 3 号，ソセゴン，パレプラス，ヘパリン Na，クラビット，ガスター，ブドウ糖及びフルマリンであった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1) Appendicitis (10003011) (Appendicitis (10003011)) [v.23.0] [10003011]

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 APPENDICITIS

- Investigator: Bacterial infectious disorders

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males and 6.7 percent in females.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT:** Appendicitis suspected, suspected gallbladder adenomyomatosis

[redacted] **20[redacted] CRP:** 0.95 mg/dL (normal 0 to 0.3)

[redacted] **20[redacted] ENDOSCOPY:** Appendicitis.

[redacted] **20[redacted] WBC:** 13.72 X10**3/MCL (normal 3.5 to 9.7)

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
貧血				X
細菌性関節炎	X	X		X
脂肪織炎	X	X		

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

Medical History	Onset Year
CATARACT	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GALL BLADDER POLYP	20[redacted]
HEPATIC CYST	20[redacted]
HYPERLIPIDEMIA	20[redacted]
HYPERTENSION	20[redacted]
HYPERURICEMIA	20[redacted]
IRRITABLE BOWEL SYNDROME	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
PRIOR PROCEDURES: CATARACT?SURGERY[LEFT EYE]	20[redacted]
PRIOR PROCEDURES: CATARACT?SURGERY[RIGHT EYE]	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	28	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 Placebo (IND)		ORAL	QD	[redacted] / 1	[redacted] / 56	56
M14-234 SS2 ABT-494 (OL)	45 mg	ORAL	QD	[redacted] / 57	[redacted] / 113	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted] / 1	[redacted] / 118	118

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4000 mg	QD	Y-M: 20[redacted]
BLINDED THERAPY	6.000 OTHER: TAB	TID	Y-M: 20[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
METRONIDAZOLE	250 mg	BID	Y-M: 20[redacted]
SULFASALAZINE	500 mg	QD	Y-M: 20[redacted]
LACTOMIN	1.5 g	BID	Y-M: 20[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	7.5 mg	QD	Y-M: 20[redacted]
ECABET	1000 mg	BID	Y-M: 20[redacted]
TRIMEBUTINE	200 mg	BID	Y-M: 20[redacted]
BENZBROMARONE	25 mg	QD	Y-M: 20[redacted]
INVESTIGATIONAL DRUG	300.000 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	7.5 mg	QD	Y-M: 20[redacted]
MESALAZINE	2400 mg	BID	Y-M: 20[redacted] / -141
FENOFIBRATE	80 mg	QD	Y-M: 20[redacted] / -155
DIMETICONE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / -127
GLUCAGON	1 mg	OTHER: ONCE	Y-M: 20[redacted] / -127
METOCLOPRAMIDE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / -127
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / -128
SODIUM PICOSULFATE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -128
CIPROFLOXACIN	100 mg	TID	Y-M: 20[redacted] / -131
CYANOCOBALAMIN	1-2 OTHER: DROP	OTHER: BID-QID	Y-M: 20[redacted] / -78
DORZOLAMIDE;TIMOLOL	1 OTHER: DROP	BID	Y-M: 20[redacted] / -78
REBAMIPIDE	100 mg	BID	Y-M: 20[redacted] / -97
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted] / -99
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted] / -57

DIMETICONE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / -57
METOCLOPRAMIDE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / -57
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / -58
SODIUM PICOSULFATE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -58
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted] / -1
DIMETICONE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / -1
GLUCAGON	1 mg	OTHER: ONCE	Y-M: 20[redacted] / -1
METOCLOPRAMIDE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / -1
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / -2
SODIUM PICOSULFATE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -2
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / -8
BCG Vaccine	NOT REPORTED	NOT REPORTED	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
LACTOMIN	1.5 g	BID	Y-M: 20[redacted]	ONGOING
TRIMEBUTINE	200 mg	BID	Y-M: 20[redacted]	ONGOING
BENZBROMARONE	25 mg	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	2400 mg	BID	Y-M: 20[redacted] / -141	ONGOING
FENOFIBRATE	80 mg	QD	Y-M: 20[redacted] / -155	ONGOING
CYANOCOBALAMIN	1-2 OTHER: DROP	OTHER: BID-QID	Y-M: 20[redacted] / -78	ONGOING
DORZOLAMIDE;TIMOLOL	1 OTHER: DROP	BID	Y-M: 20[redacted] / -78	ONGOING
REBAMIPIDE	100 mg	BID	Y-M: 20[redacted] / -97	ONGOING
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: APPLICATION	OTHER: ONCE	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
DIMETICONE	80 mg	OTHER: ONCE	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
GLUCAGON	1 mg	OTHER: ONCE	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
METOCLOPRAMIDE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / -2	Y-M: 20[redacted] / -2
SODIUM PICOSULFATE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / -2	Y-M: 20[redacted] / -2
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / -8	Y-M: 20[redacted] / 6
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 21
DIMEMORFAN	10 mg	TID	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 21
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 6
PARACETAMOL	300 mg	TID	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 18
EFINACONAZOLE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 70
LIRANAFTATE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 70
LULICONAZOLE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 70	ONGOING
TERBINAFINE	125 mg	QD	Y-M: 20[redacted] / 70	ONGOING
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 126
DIMEMORFAN	10 mg	TID	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 126
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 120

PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / 119	ONGOING
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	1000 mL	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 121
FLURBIPROFEN	40 mg	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 121
IOHEXOL	UNKNOWN mL	QD	Y-M: 20[redacted] / 120	Y-M: 20[redacted] / 120
AMIDOTRIZOIC ACID	UNKNOWN mL	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 121
AMPICILLIN;SULBACTAM	3.0 g	QID	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 129
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 121
DIMETICONE	UNKNOWN mL	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 121
LIDOCAINE	UNKNOWN mL	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 121
MIDAZOLAM	10 mg	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 121
PRONASE	20000 OTHER: UNIT	QD	Y-M: 20[redacted] / 121	Y-M: 20[redacted] / 121
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 122	Y-M: 20[redacted] / 129
CALCIUM CHLORIDE;MAGNESIUM CHLORIDE;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM CITRATE	250 mL	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	1000 mL	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
DESFLURANE	64.4 mL	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127

EPHEDRINE	5 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
FENTANYL	0.1 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
LEVOBUPIVACAINE	75 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
PHENYLEPHRINE	0.1 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
PROPOFOL	80 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
REMIFENTANIL	1.3 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
ROCURONIUM	60 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
SUGAMMADEX	200 mg	QD	Y-M: 20[redacted] / 127	Y-M: 20[redacted] / 127
AMPICILLIN;SULBACTAM	3.0 g	QD	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 130
CLINDAMYCIN	600 mg	BID	Y-M: 20[redacted] / 130	Y-M: 20[redacted] / 130
CLINDAMYCIN	600 mg	TID	Y-M: 20[redacted] / 131	Y-M: 20[redacted] / 133
AMPICILLIN	1 g	QID	Y-M: 20[redacted] / 134	Y-M: 20[redacted] / 148
AMOXICILLIN	250 mg	TID	Y-M: 20[redacted] / 149	ONGOING
CLINDAMYCIN	150 mg	TID	Y-M: 20[redacted] / 149	ONGOING

Event #1: Event of Interest - Anemia

Event Description	ANEMIA
Preferred term	貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 113
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	197
Duration of AE	85 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

Event Description	RETROPERITONEAL PANNICULITIS
Preferred term	脂肪織炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 232 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 119): NPTST416-PROCALCITONIN: 0.08 [NOT REPORTED - 0.49] ng/mL; [redacted]20[redacted] (RX DAY 120): NPTST416-PROCALCITONIN: 2.69 [NOT REPORTED - 0.49] ng/mL; [redacted]20[redacted] (RX DAY 124): NPTST432-PUROCALCITONIN: 0.43 [NOT REPORTED - 0.49] ng/mL

Microbiology

[redacted]20[redacted] (RX DAY 120): BLOOD NPTST074-BLOOD CALTURE: POSITIVE-POSITIVE FOR STREPTCOCCUS EQUISIMILIS.

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

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

Event Description	PYOGENIC ARTHRITIS OF THE KNEE
Preferred term	細菌性関節炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 233 (2 DAYS AFTER LAST TREATMENT)
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
[redacted]20[redacted] (RX DAY 121): OTHER SYNOVIAL FLUID NPTST170-CULTURE: POSITIVE-STREPTCOCCUS EQUISIMILIS; [redacted]20[redacted] (RX DAY 122): OTHER SYNOVIAL FLUID NPTST170-CULTURE: POSITIVE-STREPTCOCCUS EQUISIMILIS; [redacted]20[redacted] (RX DAY 149): OTHER SYNOVIAL FLUID NPTST170-CULTURE: NEGATIVE-NEGATIVE	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，膝の化膿性関節炎及び後腹膜の脂肪織炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 1 箱を 28 年間），過敏性腸症候群，高脂血症，高尿酸血症，高血圧及び現飲酒者（1 日 2–4 杯）であった。

Event 2 及び 3 の臨床経過：

投与232日後＊　　，被験者は後腹膜の脂肪織炎を発現した。投与233日後＊　，被験者は膝の化膿性関節炎を発現した。

投与232日後＊　，被験者は摂氏 38.7°C の発熱（非重篤）を経験した。投与233日後＊，被験者は入院し，診断検査及び治療を受けた。被験者は膝の痛みがあり，熱が摂氏 39°C に上がっていた。投与233日後＊　，プロカルシトニンの検査値が上昇し，CT 検査により後腹膜の脂肪織炎が確認された。投与237日後＊，膝の化膿性関節炎が確認された。

投与240日後＊　　，被験者は膝の化膿性関節炎の手術を受けた。投与241日後＊　，被験者は右膝の膿瘍の排膿及び摂氏 38.4°C までの発熱を経験し，さらに抗生物質療法を受けた。投与247日後＊，CT 検査により脂肪織炎の改善が確認され，熱は摂氏 37°C まで正常化した。投与253日後＊　，この被験者の治験は完全に中止された。投与262日後＊，膝の排膿は消失した。投与277日後＊，被験者は退院した。被験者は外来で膝のリハビリテーション療法を完了し，膝の状態は改善した。

投与された薬剤は，クリンダマイシンリン酸エステル，アドフィードパップ，カルボシステイン，レボフロキサシン，ダラシン，ビクシリン，アモキシシリン，アストミン，カロナール及びスルバシリンであった。

The patient's past medications include:

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

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

Causality for UPADACITINIB (Blinded)

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1)　Pyogenic arthritis (10037638)　(Arthritis bacterial (10053555))　[v.23.0]　[10037638]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2)　Panniculitis (10033675)　(Panniculitis (10033675))　[v.23.0]　[10033675]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of PYOGENIC ARTHRITIS OF THE KNEE

- Investigator: Not applicable

- AbbVie: Reported event is more likely related to concomitant retroperitoneal panniculitis. Pyogenic arthritis of the knee commonly arises from an infection that spreads from another place on the body through the blood stream to the joint.

Event of RETROPERITONEAL PANNICULITIS

- Investigator: Not applicable

- AbbVie: Risk factor includes pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD CULTURE:** POSITIVE FOR STREPTOCOCCUS EQUISIMILIS

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

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

[redacted] **20[redacted] BODY TEMPERATURE:** Up to 38.4 degrees C

[redacted] **20[redacted] BODY TEMPERATURE:** Normalized to 37 degrees C

[redacted] **20[redacted] CT:** PANICULITIS OF THE RETROPERITONEUM

[redacted] **20[redacted] CT:** Showed improvement in panniculitis and fever

[redacted] **20[redacted] PROCALCITONIN:** 0.08 NG/ML (normal <0.49)

[redacted] **20[redacted] PROCALCITONIN:** 2.69 NG/ML (normal <0.49)

[redacted] **20[redacted] PROCALCITONIN:** 0.43 NG/ML

[redacted] **20[redacted] SYNOVIAL FLUID CULTURE:** POSITIVE FOR STREPTCOCCUS EQUISIMILIS

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Anemia: 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
帯状疱疹		X		X
帯状疱疹性髄膜炎	X	X		X

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

Medical History	Onset Year
ANEMIA	NOT REPORTED
ENDOMETRIOSIS	20[redacted]
GASTRITIS	20[redacted]
HEADACHE	20[redacted]
HYPERTENSION	NOT REPORTED
LATENT TUBERCULOSIS	20[redacted]
LEFT SIDED UC	20[redacted]
LUMBER DISK HERNIATION	20[redacted]
OSTEOPOROSIS	NOT REPORTED
OVARIAN DEFICIENCY SYNDROME	20[redacted]
PERIPHERAL SENSORY NEUROPATHY	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: HYSTERECTOMY,RIGHT OVARIECTOMY	20[redacted]
PRIOR PROCEDURES: LEFT OVARIECTOMY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 169	169

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted]
ESTRADIOL	0.5 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
BETAMETHASONE	1 mg	OTHER: ONCE OR TWICE A DAY	Y-M: 20[redacted]
MESALAZINE	1200 mg	TID	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]
BETAMETHASONE	3 mg	QD	Y-M: 20[redacted]
CLOSTRIDIUM BUTYRICUM	3 OTHER: TABLETS	TID	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
PREDNISOLONE	50 mg	QD	Y-M: 20[redacted]
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: 1/30,2/1,2/4,2/6,2/8,2/13,2/15,2/18,2/20	Y-M: 20[redacted]
PREDNISOLONE	60 mg	QD	Y-M: 20[redacted]
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	75 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
LORATADINE	5 mg	QD	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -356
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -191
ISONIAZID	250 mg	QD	Y-M: 20[redacted] / -105
IRON	100 mg	QD	Y-M: 20[redacted] / -55
PYRIDOXAL	20 mg	TID	Y-M: 20[redacted] / -56
ALENDRONIC ACID	35 mg	OTHER: ONCE A WEEK	Y: 20[redacted]
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	NOT REPORTED	OTHER: UNKNOWN	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
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted]	ONGOING
ESTRADIOL	0.5 mg	QD	Y-M: 20[redacted]	ONGOING
BETAMETHASONE	3 mg	QD	Y-M: 20[redacted]	Not reported
CLOSTRIDIUM BUTYRICUM	3 OTHER: TABLETS	TID	Y-M: 20[redacted]	ONGOING
MESALAZINE	1 g	QD	Y-M: 20[redacted]	Not reported
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted]	ONGOING
BUDESONIDE	2 mg	QD	Y-M: 20[redacted]	Not reported
LORATADINE	5 mg	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]	ONGOING
PYRIDOXAL	20 mg	TID	Y-M: 20[redacted] / -56	ONGOING
BETAMETHASONE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	QD	Y-M: 20[redacted] / 102	ONGOING
BETAMETHASONE;GENTAMICIN	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / 102	ONGOING
ACICLOVIR	250 mg	QD	Y-M: 20[redacted] / 169	Y-M: 20[redacted] / 170
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 169	Y-M: 20[redacted] / 169
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 169	Y-M: 20[redacted] / 172
HEPARIN	1000 OTHER: UNITS	QD	Y-M: 20[redacted] / 170	Y-M: 20[redacted] / 170
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 194
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	BID	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 183
GUAIAZULENE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	QD	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 171
PARACETAMOL	400 mg	QID	Y-M: 20[redacted] / 173	Y-M: 20[redacted] / 189

GUALENIC ACID;SODIUM BICARBONATE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMONT	PRN	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 194
HEPARIN	1000 OTHER: UNITS	QD	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 193
LIDOCAINE	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMONT	PRN	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 194
SUPROFEN	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	BID	Y-M: 20[redacted] / 174	ONGOING
TRAMADOL	25 mg	QID	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 184
METOCLOPRAMIDE	5 mg	QID	Y-M: 20[redacted] / 175	Y-M: 20[redacted] / 194
PREGABALIN	75 mg	BID	Y-M: 20[redacted] / 175	ONGOING
TRAMADOL	50 mg	QID	Y-M: 20[redacted] / 185	Y-M: 20[redacted] / 189
ZINC	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: THREE TIMES OR FOUR TIMES PER DAY	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 197
PARACETAMOL	400 mg	TID	Y-M: 20[redacted] / 190	Y-M: 20[redacted] / 191
TRAMADOL	25 mg	BID	Y-M: 20[redacted] / 190	Y-M: 20[redacted] / 191
TRAMADOL	50 mg	BID	Y-M: 20[redacted] / 190	Y-M: 20[redacted] / 191
PARACETAMOL	400 mg	BID	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 193
TRAMADOL	25 mg	QID	Y-M: 20[redacted] / 192	Y-M: 20[redacted] / 193
NADIFLOXACIN	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: ONCE OR TWICE PER DAY	Y-M: 20[redacted] / 194	Y-M: 20[redacted] / 225
TRAMADOL	25 mg	BID	Y-M: 20[redacted] / 194	ONGOING
BILASTINE	20 mg	QD	Y-M: 20[redacted] / 211	ONGOING
EPINASTINE	ONE OTHER: DROP	BID	Y-M: 20[redacted] / 211	ONGOING
BETAMETHASONE;GENTAMICIN	APPROPRIATE AMOUNT OTHER: APPROPRIATE AMOUNT	OTHER: ONE OR TWO TIMES A DAY	Y-M: 20[redacted] / 225	ONGOING
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	QD	Y-M: 20[redacted] / 269	Y-M: 20[redacted] / 269

HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 269	Y-M: 20[redacted] / 269
SODIUM PICOSULFATE	10 mL	QD	Y-M: 20[redacted] / 269	Y-M: 20[redacted] / 269
ALENDRONIC ACID	35 mg	OTHER: ONCE A WEEK	Y: 20[redacted]	ONGOING

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

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 225
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #2: Serious Adverse Event, AE Leading to Discontinuation of Study Drug, Event of Interest - Serious Infections, Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER MENINGITIS
Preferred term	帯状疱疹性髄膜炎
AE Onset Date / Initial Rx Day	[redacted] / 225
Age at AE Onset	5[redacted]
Laboratory Testing	
[redacted] (RX DAY 169): Leukocytes: 9.23 [3.3 - 8.6] 10^9/L; [redacted] (RX DAY 171): Leukocytes: 5.21 [3.3 - 8.6] 10^9/L; [redacted] (RX DAY 188): Leukocytes: 3.94 [3.3 - 8.6] 10^9/L	
Microbiology	
[redacted] (RX DAY 169): CEREBROSPINAL FLUID NPTST547-VZV PCR: POSITIVE-7*10^2 COPIES/ML; [redacted] (RX DAY 188): CEREBROSPINAL FLUID NPTST547-VZV PCR: NEGATIVE	
AE Stopped Initial Rx Day	250 (25 DAYS AFTER LAST TREATMENT)
Duration of AE	26 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 5[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，帯状疱疹性髄膜炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，頭痛，末梢性感覚ニューロパチー，高血圧，非喫煙者及び非飲酒者であった。

Event 2 の臨床経過：

投与225日後＊，被験者は帯状疱疹性髄膜炎を発現した。投与250日後＊　，帯状疱疹性髄膜炎は消失した。

投与225日後＊　，被験者は頭痛があり救急治療室を受診した。帯状疱疹感染が疑われたが，皮膚症状はなかった。髄膜炎も疑われたため，腰椎穿刺を受けたところ髄膜炎が確認された。投与226日後＊，被験者の顎及び右頬に皮疹が認められ，皮膚科医は複数の皮膚分節にまたがる片側性の帯状疱疹と診断した。投与227日後＊　，被験者は帯状疱疹性髄膜炎の治療のために入院し，抗ウイルス薬を投与された。投与237日後＊　，被験者は腰椎穿刺を受けたところ脳脊髄液の細胞は減少していたが，髄膜炎は回復していなかった。投与238日後＊，被験者の発疹は痂皮を形成した。投与248日後＊　，被験者の脳脊髄液を調べたところ髄膜炎は陰性であった。投与250日後＊，被験者は退院した。

被験者には，水疱及び帯状疱疹の病歴はなく，帯状疱疹ワクチンは未接種であった。

投与された薬剤は，トラマール，スレンダム軟膏，含嗽用ハチアズレ顆粒，キシロカイン含嗽液，プレガバリン，アズノール軟膏，カロナール，アシクロビル及び亜鉛華単軟膏であった。

The patient's past medications include:

RINDERON for ULCERATIVE COLITIS ([redacted])

ASACOL for ULCERATIVE COLITIS ([redacted])

LIALDA for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

HIROSHIMA KAMPO for ULCERATIVE COLITIS ([redacted])

CELLSORBA E for ULCERATIVE COLITIS ([redacted])

AZATHIOPRINE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Herpes zoster meningitis (10074259)　(Herpes zoster meningitis (10074259))　[v.23.1]　[10074259]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of HERPES ZOSTER MENINGITIS

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] COVID-19 PCR TEST:** negative

[redacted] **20[redacted] VZV PCR:** cerebrospinal fluid - cerebrospinal fluid cell count was increased; confirmed meningitis. 700 copies/mL

[redacted] **20[redacted] VZV PCR:** decrease in cerebrospinal fluid cells without recovery

[redacted] **20[redacted] VZV PCR:** cerebrospinal fluid was negative

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.23 X10**3/MCL (normal 3.30 to 8.60)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 3.94 X10**3/MCL (normal 3.30 to 8.60)

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes zoster: Meningoencephalopathic involvement and Unilateral involving multiple dermatomes (R-V2, R-V3).

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
Placebo	5[redacted]	FEMALE	ASIAN

Medical History	Onset Year
ANEMIA	20[redacted]
BEHCET'S DISEASE	19[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HEADACHE	19[redacted]
HYPERLIPIDEAMIA	20[redacted]
MENOPAUSE	20[redacted]
OSTEOPOROSIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	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	24	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 168	168

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
ALENDRONIC ACID	35 mg	QD	Y-M: 20[redacted] / -192
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -194
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -198
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / -199
BEZAFIBRATE	400 mg	BID	Y-M: 20[redacted] / -165
CLOSTRIDIUM BUTYRICUM	1 OTHER: TAB	TID	Y-M: 20[redacted] / -176
DIMETICONE	3 mL	OTHER: ONCE	Y-M: 20[redacted] / -81
LIDOCAINE	REQUIRED AMOUNT mL	OTHER: ONCE	Y-M: 20[redacted] / -81
DIMETICONE	3 mL	OTHER: ONCE	Y-M: 20[redacted] / -3
LIDOCAINE	REQUIRED AMOUNT mL	OTHER: ONCE	Y-M: 20[redacted] / -3
BCG Vaccine	NOT REPORTED	NOT REPORTED	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 / Stop Year-Month / RX Day	
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]	ONGOING
ALENDRONIC ACID	35 mg	QD	Y-M: 20[redacted] / -192	ONGOING
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -198	ONGOING
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / -199	ONGOING
BEZAFIBRATE	400 mg	BID	Y-M: 20[redacted] / -165	ONGOING
CLOSTRIDIUM BUTYRICUM	1 OTHER: TAB	TID	Y-M: 20[redacted] / -176	ONGOING
PREDNISOLONE	1 mg	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 171
ESZOPICLONE	2 mg	PRN	Y-M: 20[redacted] / 169	ONGOING
PREDNISOLONE	20 mg	BID	Y-M: 20[redacted] / 171	Y-M: 20[redacted] / 173
PREDNISOLONE	20 mg	BID	Y-M: 20[redacted] / 174	Y-M: 20[redacted] / 176
PREDNISOLONE	15 mg	BID	Y-M: 20[redacted] / 177	Y-M: 20[redacted] / 182
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TAB	QD	Y-M: 20[redacted] / 178	Y-M: 20[redacted] / 179
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 185
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TAB	QD	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 183
ZOLPIDEM	5 mg	PRN	Y-M: 20[redacted] / 184	ONGOING
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TAB	QD	Y-M: 20[redacted] / 185	Y-M: 20[redacted] / 185
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / 186	Y-M: 20[redacted] / 192
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 OTHER: TAB	QD	Y-M: 20[redacted] / 187	Y-M: 20[redacted] / 187

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

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 224
Age at AE Onset	5[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 170): NPTST165-CRP: 7.27 [NOT REPORTED - 0.14] mg/dL	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	244 (20 DAYS AFTER LAST TREATMENT)
Duration of AE	21 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	EXACERBATION OF ULCERATIVE COLITIS IS UNCREAR.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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

Event 1 の臨床経過：

投与224日後＊，被験者は潰瘍性大腸炎の悪化を発現した。投与244日後＊　，潰瘍性大腸炎の悪化は消失した。

本事象の発現前，被験者は投与から約7ヵ月目の＊上旬から便通の増加があり，投与220日後＊から血便があった。

投与224日後＊　，被験者は排便回数の増加，血便及び腹痛があり入院し，潰瘍性大腸炎の悪化と診断された。被験者は絶食し，補液を開始した。その後プレドニンを増量したところ，排便回数は減少し，被験者の状態も安定した。投与244日後＊，被験者は退院した。

本事象により治験薬の投与は中止された。

投与された薬剤は，ヒュミラ及びプレドニンであった。

The patient's past medications include:

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

BORRAZA G for BLEEDING HEMORRHOIDS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

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

Causality for UPADACITINIB (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.22.1] [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 UPADACITINIB (Blinded)

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: EXACERBATION OF ULCERATIVE COLITIS

- AbbVie: Event more likely related to pre-existing Ulcerative Colitis

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL X-RAY:** There are not Toxic megacolon and Toxic colon.

[redacted] **20[redacted] ABDOMINAL X-RAY:** Small intestinal gas is noticeable

[redacted] **20[redacted] ABDOMINAL X-RAY:** No abnormality.

[redacted] **20[redacted] ENDOSCOPY:** Large intestine: Ulcerative colitis activity is mild. lleum: Deformation of Bauhins Valve. No complications.

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

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	3[redacted]	MALE	ASIAN

Medical History	Onset Year
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	19[redacted]
ATOPIC DERMATITIS	19[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
IRON DEFICIENCY ANEMIA	20[redacted]
KAWASAKI DISEASE	NOT REPORTED

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.1 PACK	5	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 8	8

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]
CLOSTRIDIUM BUTYRICUM	3.000 g	TID	Y-M: 20[redacted]
ENTEROCOCCUS FAECALIS	6.000 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted]
RAMOSETRON	5.000 ug	QD	Y-M: 20[redacted]
INFLIXIMAB	300.000 UNKNOWN	UNKNOWN	Y-M: 20[redacted]
PREDNISOLONE	4 mg	QD	Y-M: 20[redacted]
LACTOMIN	1 g	TID	Y-M: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: 10 TIMES	Y-M: 20[redacted]
TACROLIMUS	9 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
THEOPHYLLINE	200 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
IRON	100 mg	QD	Y-M: 20[redacted] / -218
HYOSCINE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / -70
MAGNESIUM CITRATE	100 g	OTHER: ONCE	Y-M: 20[redacted] / -70
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / -71
MESALAZINE	2000 mg	BID	Y-M: 20[redacted] / -85
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / -1
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: ABOUT 10 TIMES	Y: 20[redacted]
ALL OTHER NON-THERAPEUTIC PRODUCTS	1.000 OTHER: KIT	OTHER: ABOUT 10 TIMES	Y: 20[redacted]
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM INFANTIS	1 g	TID	Y: 20[redacted]
MESALAZINE	2000 mg	BID	Y: 20[redacted]
BETAMETHASONE	NOT REPORTED	PRN	Y: 20[redacted]
CLOBETASOL	NOT REPORTED	PRN	Y: 20[redacted]
HEPARINOID	NOT REPORTED	PRN	Y: 20[redacted]
PROCATEROL	1 OTHER: PUFFS	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	
LACTOMIN	1 g	TID	Y-M: 20[redacted]	ONGOING
THEOPHYLLINE	200 mg	BID	Y-M: 20[redacted]	ONGOING
IRON	100 mg	QD	Y-M: 20[redacted] / -218	ONGOING
MESALAZINE	2000 mg	BID	Y-M: 20[redacted] / -85	ONGOING
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
CLOSTRIDIUM BUTYRICUM	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
HYOSCINE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
MAGNESIUM CITRATE	100 g	PRN	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 1
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 14
HYOSCINE	20 mg	OTHER: ONCE	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
MAGNESIUM CITRATE	100 g	OTHER: ONCE	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 15
BIFIDOBACTERIUM BIFIDUM;BIFIDOBACTERIUM INFANTIS	1 g	TID	Y: 20[redacted]	Y-M: 20[redacted] / -1
BETAMETHASONE	NOT REPORTED	PRN	Y: 20[redacted]	ONGOING
CLOBETASOL	NOT REPORTED	PRN	Y: 20[redacted]	ONGOING
HEPARINOID	NOT REPORTED	PRN	Y: 20[redacted]	ONGOING
PROCATEROL	1 OTHER: PUFFS	BID	Y: 20[redacted]	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	ADENOCARCINOMA(SIGMOID COLON)STAGE 0
Preferred term	結腸腺癌
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 65 (1 DAY AFTER LAST TREATMENT)
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	THIS MALIGNANT LESION DEVELOPED ON ASSOCIATION WITH ULCERATIVE COLITIS. MALIGNANT LESIONS ARE NOT DIRECTLY ASSOCIATION WITH DRUGS.
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION, IMPORTANT MEDICAL EVENT REQUIRING MEDICAL OR SURGICAL INTERVENTION

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，腺癌（S 状結腸）ステージ 0 の事象を発現した。関連する病歴は，アトピー性皮膚炎，鉄欠乏性貧血，潰瘍性大腸炎（全大腸炎型），現喫煙者（1 日 0.1 箱を 5 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65日後＊，被験者は腺癌（S 状結腸）ステージ 0 を発現した。

投与57日後＊（導入療法期の投与 8 週時），被験者は臨床反応を示したと判断された。投与65日後＊，導入療法期の投与 8 週時のびらんより生検された病理組織から，腺癌が疑われた。治験薬の投与は一時的に中止された。投与68日後＊，被験者は結腸内視鏡検査を再び受けた。投与79日後＊　　，新たな組織を病理検査した結果，腺癌と診断された。治験実施計画書の規定に従い，被験者の治験は中止された。

大腸炎関連発癌（CAC）であったため，結腸切除が必要と考えられた。投与101日後＊　，被験者は入院した。入院は潰瘍性大腸炎のためであった。投与103日後＊　，被験者は腹腔鏡下の結腸全摘術及び J 型回腸嚢肛門吻合術を受けた。投与124日後＊，被験者は退院した。

投与228日後＊　，被験者は回腸瘻閉鎖術のために入院した。投与229日後＊　　，被験者は回腸瘻閉鎖術を受けた。投与236日後＊，被験者は退院した。

The patient's past medications include:

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

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

MIYA-BM 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])

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

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

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1)　Adenocarcinoma of sigmoid colon (10075432)　(Adenocarcinoma of colon (10001167))　[v.24.0] [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 (Blinded)

Event of ADENOCARCINOMA (SIGMOID COLON) STAGE 0

- Investigator: This malignant lesion developed on association with ulcerative colitis. Malignant lesions are not directly association with drugs.

- AbbVie: risk factors include pre-existing history of ulcerative colitis and current smoking status.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BIOPSY:** ADENOCARCINOMA

[redacted] **20[redacted] COLONOSCOPY:** Week 8: Clear demarcation between normal and inflamed colonic mucosa seen at 25 from anal verge.

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
大腸感染	X			X

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

Medical History	Onset Year
HEADACHE	20[redacted]
LEFT SIDED UC	20[redacted]
PERIOD PAIN	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): FLEXIBLE SIGMOIDOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 366	366

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	3600 mg	TID	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
BUDESONIDE	4 mg	BID	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
MESALAZINE	4000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -126
MESALAZINE	1200 mg	TID	Y-M: 20[redacted] / -98
FLUMAZENIL	0.5 mg	QD	Y-M: 20[redacted] / -70
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / -70
LIDOCAINE	5 mL	QD	Y-M: 20[redacted] / -70
MIDAZOLAM	10 mg	QD	Y-M: 20[redacted] / -70
SODIUM PHOSPHATE	50 OTHER: TABLETS	QD	Y-M: 20[redacted] / -70
CEFTRIAXONE	1 OTHER: BOTTLE	QD	Y-M: 20[redacted] / -40
CELLULASE;DIASTASE;LIPASE;NEWLASE;PANCREATIN	1 OTHER: CAPSULE	TID	Y-M: 20[redacted] / -40
DIFENIDOL	25 mg	TID	Y-M: 20[redacted] / -40
DOMPERIDONE	10 mg	TID	Y-M: 20[redacted] / -40
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / -40
ISOSORBIDE DINITRATE	20 mL	TID	Y-M: 20[redacted] / -40
LOPERAMIDE	1 mg	BID	Y-M: 20[redacted] / -40
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted] / -40
TIQUIZIUM	10 mg	TID	Y-M: 20[redacted] / -40
BIFIDOBACTERIUM NOS	1 OTHER: TABLET	TID	Y-M: 20[redacted] / -41
CAMPHOR;MENTHOL;SALICYLIC ACID;THYMOL	PROPER DOSE OTHER: PROPER DOSE	QD	Y-M: 20[redacted] / -41
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / -41
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / -45
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / -45
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / -45
PARACETAMOL	300 mg	QD	Y-M: 20[redacted] / -45
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / -45
FLUMAZENIL	0.5 mg	QD	Y-M: 20[redacted] / -2
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / -2

LIDOCAINE	5 mL	QD	Y-M: 20[redacted] / -2
MIDAZOLAM	10 mg	QD	Y-M: 20[redacted] / -2
SODIUM PHOSPHATE	50 OTHER: TABLETS	QD	Y-M: 20[redacted] / -2
BCG Vaccine	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 / Stop Year-Month / RX Day	
MESALAZINE	1200 mg	TID	Y-M: 20[redacted] / -98	ONGOING
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 6
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 30
CLOSTRIDIUM BUTYRICUM	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 41
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 30
ASCORBIC ACID	500 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 37
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 31
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 35
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 31
GLUCOSE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 31
MENATETRENONE	10 mg	QD	Y-M: 20[redacted] / 31	Y-M: 20[redacted] / 31
ALANINE;ARGININE;ASPARTIC ACID;CALCIUM GLUCONATE;CYSTEINE;GLUCOSE;GLUTAMIC ACID;GLYCINE;HISTIDINE;ISOLEUCINE;LEUCINE;LYSINE;MAGNESIUM SULFATE;METHIONINE;PHENYLALANINE;POTASSIUM PHOSPHATE DIBASIC;PROL	500 mL	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 37
CARBOHYDRATES NOS;POTASSIUM;SODIUM CHLORIDE;SODIUM LACTATE	500 mL	BID	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 37
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 37
MENATETRENONE	10 mg	BID	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 37
HEPARIN	100 mL	PRN	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 41
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 35

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

Event Description	INFECTIOUS COLITIS
Preferred term	大腸感染
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 87
Age at AE Onset	2[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 30): Leukocytes: 14.3 [3 - 9] 10^9/L; [redacted]20[redacted] (RX DAY 31): Leukocytes: 11.1 [3 - 9] 10^9/L; [redacted]20[redacted] (RX DAY 34): Leukocytes: 5 [3 - 9] 10^9/L; [redacted]20[redacted] (RX DAY 37): Leukocytes: 5.1 [3 - 9] 10^9/L; [redacted]20[redacted] (RX DAY 40): Leukocytes: 4.8 [3 - 9] 10^9/L

Microbiology	

NOT REPORTED

AE Stopped Initial Rx Day	98
Duration of AE	12 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，感染性大腸炎の事象を発現した。関連する病歴は，潰瘍性大腸炎（左側），非喫煙者及び現飲酒者（1 日 2–4 杯）であった。

Event 1 の臨床経過：

投与87日後＊　，被験者は感染性大腸炎を発現した。投与98日後＊　　，感染性大腸炎は消失した。

被験者は 投与12日後＊　から 投与22日後＊　　まで感染性胃腸炎（非重篤）を発現していた。

投与87日後＊　　，被験者は下痢，腹痛，頭痛及び摂氏 39°C までの発熱があり入院した。被験者は抗菌薬及び補液の注入で治療され，経口では何も摂取しないよう指示された。被験者の症状は消失し，経口摂取が再開された。投与98日後＊，被験者は退院した。

投与された薬剤は，ツインパル，ミヤ BM，カロナール，ソルアセト F 輸液，セフトリアキソン Na，ソルデム 3A 輸液，ケイツーN 静注，ビタミン C 及びファモチジンであった。

The patient's past medications include:

BUSCOPAN for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

CALONAL for HEADACHE and INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

METOCLOPRAMIDE for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SOLDEM 3A for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BIOFERMIN for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALONPAS for UNKNOWN INDICATION ([redacted] 20[redacted] - [redacted] 20[redacted])

CEFTRIAXONE SODIUM for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CEPHADOL for UNKNOWN INDICATION ([redacted] 20[redacted] - [redacted] 20[redacted])

FELTASE for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ISOBIDE for UNKNOWN INDICATION ([redacted] 20[redacted] - [redacted] 20[redacted])

LOPEMIN for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

NAUZELIN for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PARIET for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

THIATON for INFECTIVE GASTROENTERITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1)　Infectious colitis (10021905)　(Large intestine infection (10081959))　[v.22.1]　[10021905]

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 INFECTIOUS COLITIS

- Investigator: Infection

- AbbVie: Event is common in the general population. Additional risk factor includes pre-existing ulcerative colitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] COLONOSCOPY:** There was a clear demarcation between normal and inflamed colonic mucosa seen. The distance of demarcation from the anal verge 15. Central Reader Endoscopy Subscore 2.

[redacted] **20[redacted] CT SCAN:** CT scan showed inflammatory reaction from ileocecum to transverse colon.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 14.3 X10**3/MCL (normal 3 to 9)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 11.1 X10**3/MCL (normal 3 to 9)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5 X10**3/MCL (normal 3 to 9)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 5.1 X10**3/MCL (normal 3 to 9)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 4.8 X10**3/MCL (normal 3 to 9)

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
帯状疱疹	X			X
ヘルペス後神経痛				X

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

Medical History	Onset Year
CHICKEN POX	19[redacted]
GASTRO ESOPHAGEAL REFLUX DISEASE	20[redacted]
HERPES ZOSTER	20[redacted]
HYPERLIPIDAEMIA	20[redacted]
LEFT SIDED UC	20[redacted]
LEFT) PAIN IN THE FOURTH TOE	20[redacted]
RINGWORM	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	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	42	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted] / 1	[redacted] / 57	57
M14-234 SS2 ABT-494 (OL)	45 mg	ORAL	QD	[redacted] / 58	[redacted] / 111	54
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted] / 1	[redacted] / 364	364

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	20 mg	BID	Y-M: [redacted]
MESALAZINE	1 mg	QD	Y-M: [redacted]
AZATHIOPRINE	50 mg	QD	Y-M: [redacted]
PREDNISOLONE	15 mg	BID	Y-M: [redacted]
PREDNISOLONE	20 mg	QD	Y-M: [redacted]
MERCAPTOPURINE	40 mg	QD	Y-M: [redacted]
ADALIMUMAB	160.000 mg	ONCE EVERY TWO WEEKS	Y-M: [redacted]
INFLIXIMAB	325.000 mg	WEEK0,2,6	Y-M: [redacted]
MESALAZINE	4800 mg	QD	Y-M: [redacted]
VALGANCICLOVIR	1800 mg	BID	Y-M: [redacted]
ESCHERICHIA COLI;HYDROCORTISONE	2 g	QD	Y-M: [redacted]
VALGANCICLOVIR	900 mg	BID	Y-M: [redacted] / -153
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACKET	PRN	Y-M: [redacted] / -119
SENNOSIDE A+B	48 mg	QD	Y-M: [redacted] / -120
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACKET	PRN	Y-M: [redacted] / -54
SENNOSIDE A+B	48 mg	QD	Y-M: [redacted] / -55
SENNOSIDE A+B	48 mg	QD	Y-M: [redacted] / -1
BETAMETHASONE	1 mg	QD	Y: [redacted]
LULICONAZOLE	1 OTHER: APPLICATION	PRN	Y: [redacted]
MESALAZINE	1200 mg	TID	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	4800 mg	QD	Y-M: 20[redacted]	ONGOING
GENTAMICIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 244	Y-M: 20[redacted] / 281
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / 251	Y-M: 20[redacted] / 252
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 252	Y-M: 20[redacted] / 253
PARACETAMOL	600 mg	PRN	Y-M: 20[redacted] / 253	Y-M: 20[redacted] / 257
ACICLOVIR	PRN OTHER: TOPICAL	QD	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 264
HYALURONIC ACID	PRN OTHER: TOPICAL	QID	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 269
MOXIFLOXACIN	PRN OTHER: TOPICAL	QID	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 265
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 258
VALACICLOVIR	1000 mg	TID	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 258
ACICLOVIR	250 mg	BID	Y-M: 20[redacted] / 258	Y-M: 20[redacted] / 258
PARACETAMOL;TRAMADOL	1 OTHER: TABLET	QD	Y-M: 20[redacted] / 258	Y-M: 20[redacted] / 258
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 260
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 259
PARACETAMOL;TRAMADOL	1 OTHER: TAB	QID	Y-M: 20[redacted] / 259	Y-M: 20[redacted] / 261
PARACETAMOL	400 mg	QID	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 261
SENNOSIDE A+B	24 mg	PRN	Y-M: 20[redacted] / 260	Y-M: 20[redacted] / 260
FAMCICLOVIR	500 mg	TID	Y-M: 20[redacted] / 261	Y-M: 20[redacted] / 263
PARACETAMOL	400 mg	TID	Y-M: 20[redacted] / 262	Y-M: 20[redacted] / 262
PARACETAMOL;TRAMADOL	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 262	Y-M: 20[redacted] / 274
PREDNISOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 262	Y-M: 20[redacted] / 267
PREGABALIN	25 mg	BID	Y-M: 20[redacted] / 262	Y-M: 20[redacted] / 264
PARACETAMOL	400 mg	QID	Y-M: 20[redacted] / 263	Y-M: 20[redacted] / 265
PREGABALIN	25 mg	TID	Y-M: 20[redacted] / 265	Y-M: 20[redacted] / 273
PARACETAMOL	400 mg	BID	Y-M: 20[redacted] / 274	Y-M: 20[redacted] / 281
PREGABALIN	25 mg	BID	Y-M: 20[redacted] / 274	Y-M: 20[redacted] / 310
DEXAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 281	Y-M: 20[redacted] / 310
LULICONAZOLE	1 OTHER: APPLICATION	PRN	Y: 20[redacted]	ONGOING

Event #1: 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	[redacted]20[redacted] / 368
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 198): Leukocytes: 5.47 [3.6 - 9.2] 10^9/L; NPTST469-SEGMENTAL NUCLEUS NEUTROPHIL: 73.3 [40 - 73] %; [redacted]20[redacted] (RX DAY 253): Leukocytes: 5.62 [3.6 - 9.2] 10^9/L; Neutrophils/Leukocytes: 75.3 [40 - 73] %; [redacted]20[redacted] (RX DAY 258): Leukocytes: 7.19 [3.6 - 9.2] 10^9/L; Neutrophils/Leukocytes: 83.1 [40 - 73] %; [redacted]20[redacted] (RX DAY 262): Leukocytes: 5.49 [3.6 - 9.2] 10^9/L; NPTST451-ROD-SHAPED NEUTROPHIL: 11.0 [2 - 8] %; NPTST469-SEGMENTAL NUCLEUS NEUTROPHIL: 60.0 [29 - 64] %; [redacted]20[redacted] (RX DAY 274): Leukocytes: 5.29 [3.6 - 9.2] 10^9/L; Neutrophils/Leukocytes: 67 [40 - 73] %

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	392
Duration of AE	25 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: Event of Interest - Herpes Zoster

Event Description	POSTHERPETIC NEURALGIA
Preferred term	ヘルペス後神経痛
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 392
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	427
Duration of AE	36 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]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 6[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬及び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，帯状疱疹，元喫煙者（1 日 1 箱を 42 年間）及び現飲酒者（1 日 2 杯未満）であった。

被験者は本治験のサブスタディ 2 パート 1 に参加し，盲検化された治験薬を投与された。投与58日後＊，被験者はサブスタディ 2 パート 2 に入り，非盲検の治験薬を投与された。投与113日後＊，被験者はサブスタディ 3 に入り，盲検化された治験薬を投与された。

Event 1 の臨床経過：

投与368日後＊，被験者は帯状疱疹を経験した。投与392日後＊，帯状疱疹は消失した。

投与359日後＊，被験者は発疹を伴わない左側の頭痛（非重篤）を経験した。投与366日後＊，被験者は左目の周りに水疱を生じた。投与367日後＊，被験者は左眼瞼に腫脹を呈した。投与368日後＊，被験者は救急科を受診し，帯状疱疹と診断された。帯状疱疹は 1 つの皮膚分節に限局されていた。発疹は三叉神経の第一領域にあった。診断は病歴及び身体検査により行われた。被験者は抗ウイルス薬及び鎮痛薬で治療された。投与373日後＊　，帯状疱疹による痛みのためにリリカが治療レジメンに追加された。投与378日後＊　，被験者の症状は緩和され，退院した。

被験者には水疱及び帯状疱疹の病歴があった。

投与された薬剤は，バラシクロビル，アシクロビル眼軟膏 3%，ベガモックス点眼液 0.5%，ヒアルロン酸ナトリウム点眼液 0.1%，ファムビル，ゲンタマイシン硫酸塩，ボアラ，アセトアミノフェン，トアラセット，ビクロックス及びリリカであった。

The patient's past medications include:

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

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

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

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

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

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

MERCAPTOPURINE HYDRATE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

INFLIXIMAB BS FOR I.V for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

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

POSTERISAN FORTE 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.23.0]　[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

Causality for UPADACITINIB (Open Label)

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

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of HERPES ZOSTER

- Investigator: Not reported

- AbbVie: Not applicable

Alternative Etiology for UPADACITINIB (Open Label)

Event of HERPES ZOSTER

- Investigator: Not reported

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] NEUTROPHILS %:** 75.3 % (normal 40 to 73)

[redacted] **20[redacted] NEUTROPHILS %:** 83.1 % (normal 40 to 73)

[redacted] **20[redacted] NEUTROPHILS %:** 67 % (normal 40 to 73)

[redacted] **20[redacted] WBC:** 5620 /MM**3 (normal 3600 to 9200)

[redacted] **20[redacted] WBC:** 7190 /MM**3 (normal 3600 to 9200)

[redacted] **20[redacted] WBC:** 5490 /MM**3 (normal 3600 to 9200)

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
Placebo	2[redacted]	FEMALE	ASIAN

Medical History	Onset Year
ANEMIA	20[redacted]
ATOPIC DEREMATITIS	20[redacted]
DRUG INDUCEL PANCEATITIS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HAEMORRHOIDS	20[redacted]
THIOPRINE INTOLERANCE	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
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	2	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 28	28

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
CLOSTRIDIUM BUTYRICUM	2 g	TID	Y-M: 20[redacted]
INFLIXIMAB	300.000 mg	NOT REPORTED	Y-M: 20[redacted]
SULFASALAZINE	1000 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
POLYCARBOPHIL	500.000 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -272
INFLIXIMAB	300.000 mg	NOT REPORTED	Y-M: 20[redacted] / -204
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -128
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -121
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	PRN	Y-M: 20[redacted] / -69
DIMETICONE	10 mL	PRN	Y-M: 20[redacted] / -69
GLUCOSE;SODIUM CHLORIDE	500 mL	PRN	Y-M: 20[redacted] / -69
HYOSCINE	UNK OTHER: UNK	PRN	Y-M: 20[redacted] / -69
LIDOCAINE	10 mL	PRN	Y-M: 20[redacted] / -69
MIDAZOLAM	2.5 mg	PRN	Y-M: 20[redacted] / -69
PETHIDINE	35 mg	PRN	Y-M: 20[redacted] / -69
MAGNESIUM CITRATE	1 OTHER: PACK	PRN	Y-M: 20[redacted] / -70
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted] / -78
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted] / -91
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
MESALAZINE	3600 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	
CLOSTRIDIUM BUTYRICUM	2 g	TID	Y-M: 20[redacted]	ONGOING
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]	ONGOING
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -272	Y: 20[redacted] / 90
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted] / -78	Y-M: 20[redacted] / -1
PREDNISOLONE	7.5 mg	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 14
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 26
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted] / 27	Y-M: 20[redacted] / 28
ASCORBIC ACID	500 mL	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 40
CALCIUM GLUCONATE;GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE;SODIUM CHLORIDE	500 mL	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 44
HYDROXOCOBALAMIN;PYRIDOXAL;THIAMINE	10 mg	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 40
HYDROXYZINE	25 mg	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 38
METOCLOPRAMIDE	2 mL	PRN	Y-M: 20[redacted] / 29	Y-M: 20[redacted] / 38
FAMOTIDINE	20 mg	PRN	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 38
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / 30	Y-M: 20[redacted] / 35
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: PACK	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
DIMETICONE	10 mL	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
GLYCEROL	60 mL	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
HYOSCINE	20 mg	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
LIDOCAINE	10 mL	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
LIDOCAINE	5 mL	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
MIDAZOLAM	2.5 mg	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
PETHIDINE	35 mg	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 34
PARACETAMOL	50-100 mL	PRN	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 40
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 42
GLYCINE MAX	100 mL	PRN	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 37
VONOPRAZAN	10 mg	QD	Y-M: 20[redacted] / 39	ONGOING
PREDNISOLONE	10 mg	TID	Y-M: 20[redacted] / 43	Y-M: 20[redacted] / 49
VEDOLIZUMAB	300 mg	PRN	Y-M: 20[redacted] / 43	ONGOING

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

Event Description	COLITIS ULCERATIVE AGGRAVATED
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 68
Age at AE Onset	2[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	105 (19 DAYS AFTER LAST TREATMENT)
Duration of AE	38 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	BECAUSE THE ACTIVE INGREDIENT WAS REDUCED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 2[redacted] 歳女性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，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，貧血，現喫煙者（1 日 0.25 箱を 2 年間）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68日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与105日後＊　　，潰瘍性大腸炎の悪化は消失した。

入院前の 投与59日後＊　　，被験者は結腸内視鏡検査を受け，肛門縁から約 70 cm のところの正常な大腸粘膜と炎症を起こした大腸粘膜の間に明確な境界があることが確認された。

投与87日後＊，被験者は定期的な診察を受けた。胸部 X 線検査及び血液検査を受けた（結果は報告されていない）。同日，被験者は潰瘍性大腸炎の悪化のエピソードが認められたため，緊急入院した。被験者は何も飲食できず，悪心もあった。被験者の症状はわずかに改善した。投与93日後＊　，被験者は悪心があった。投与94日後＊　，この被験者の治験は中止された。投与105日後＊，被験者の症状は改善したが，まだわずかな症状があった。投与105日後＊，被験者は退院した。

投与された薬剤は，フィジオ35，ネオラミン・スリービー液，ビタ C，アセリオ，アタラックス–P，ファモチジン，プレドニン，イントラリポス，エンタイビオ及びプリンペランであった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS ([redacted])

PREDONIN for ULCERATIVE COLITIS ([redacted])

SALAZOPYRIN for ULCERATIVE COLITIS ([redacted])

AZANIN for ULCERATIVE COLITIS ([redacted])

COLONEL for ULCERATIVE COLITIS ([redacted])

REMICADE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1)　Colitis ulcerative aggravated (10009901)　(Colitis ulcerative (10009900))　[v.22.1]　[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 UPADACITINIB (Blinded)

Event of COLITIS ULCERATIVE AGGRAVATED

- Investigator: Because the active ingredient was reduced.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST X-RAY:** No clinical objection.

[redacted] **20[redacted] CHEST X-RAY:** No clinical objection.

[redacted] **20[redacted] COLONOSCOPY:** A clear demarcation between normal and inflamed colonic mucosa was seen ; 70 cm from the anal verge

[redacted] **20[redacted] COLONOSCOPY:** ULCERATIVE COLITIS AGGRAVATED.

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

Reason for Narrative

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

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

Medical History	Onset Year
ALCOHOLIC FATTY LIVER	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
HYPERLIPIDEMIA	NOT REPORTED
HYPERTENSION	20[redacted]
HYPERURICEMIA	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	1 PACK	35	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 53	53
M14-675 ABT-494 (OL)	45 mg	ORAL	QD	[redacted]20[redacted] / 54	[redacted]20[redacted] / 112	59
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 83	83

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	2000 mg	BID	Y-M: 20[redacted] / -201
PREDNISOLONE	10 mg	BID	Y-M: 20[redacted] / -175
PREDNISOLONE	10 mg	TID	Y-M: 20[redacted] / -180
BERBERINE	100 mg	TID	Y-M: 20[redacted] / -187
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -187
CLOSTRIDIUM BUTYRICUM	1 OTHER: TABLET	TID	Y-M: 20[redacted] / -190
PREDNISOLONE	5 mg	BID	Y-M: 20[redacted] / -161
FEBUXOSTAT	40 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
CLOSTRIDIUM BUTYRICUM	1 OTHER: TABLET	TID	Y-M: 20[redacted] / -190	ONGOING
FEBUXOSTAT	40 mg	QD	Y-M: 20[redacted] / -45	ONGOING
CEFTRIAXONE	2 g	QD	Y-M: 20[redacted] / 103	Y-M: 20[redacted] / 111
CLINDAMYCIN	600 mg	QD	Y-M: 20[redacted] / 103	Y-M: 20[redacted] / 103
DIPHENHYDRAMINE	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 103	ONGOING
PIPERACILLIN	4 g	QD	Y-M: 20[redacted] / 103	Y-M: 20[redacted] / 103
CLINDAMYCIN	600 mg	BID	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 111
ASCORBIC ACID	500 mg	PRN	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 84
CALCIUM GLUCONATE;GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE;SODIUM CHLORIDE	500 mg	PRN	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 84
HYDROXYZINE	50 mg	PRN	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 83
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 84
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 83
PENTAZOCINE	15 mg	PRN	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 83
THIAMINE	10 mL	PRN	Y-M: 20[redacted] / 83	Y-M: 20[redacted] / 84
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84
GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84
KETOCONAZOLE	APPLICATION OTHER: APPLICATION	QD	Y-M: 20[redacted] / 84	ONGOING
LIDOCAINE	100 mg	QD	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 88
PIPERACILLIN;TAZOBACTAM	100 mL	BID	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84

REBAMIPIDE	100 mg	BID	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 84
ATROPINE	0.5 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	BID	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
EPHEDRINE	40 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
FENTANYL	0.9 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 89
GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	BID	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 92
LANDIOLOL	50 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
NICARDIPINE	10 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
PHENYLEPHRINE	1 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
PIPERACILLIN;TAZOBACTAM	100 mL	TID	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 96
PIPERACILLIN;TAZOBACTAM	4.5 g	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
PROPOFOL	UNK OTHER: UNK	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
ROCURONIUM	150 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
ROPIVACAINE	4 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 89
SEVOFLURANE	35 mL	OTHER: PUFFS	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
SUGAMMADEX	200 mg	QD	Y-M: 20[redacted] / 85	Y-M: 20[redacted] / 85
CALCIUM CHLORIDE;POTASSIUM;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 88
PARACETAMOL	1000 mg	TID	Y-M: 20[redacted] / 86	Y-M: 20[redacted] / 86
ZOLPIDEM	5 mg	QD	Y-M: 20[redacted] / 86	ONGOING
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / 87	Y-M: 20[redacted] / 88
LOXOPROFEN	60 mg	TID	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 106
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 89
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 106
ROPIVACAINE	4 mg	PRN	Y-M: 20[redacted] / 89	Y-M: 20[redacted] / 91
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 90	ONGOING

LIDOCAINE	100 mg	QD	Y-M: 20[redacted] / 92	Y-M: 20[redacted] / 92
GLUCOSE;MAGNESIUM CHLORIDE;POTASSIUM;POTASSIUM PHOSPHATE MONOBASIC;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 97
LIDOCAINE	100 mg	QD	Y-M: 20[redacted] / 96	Y-M: 20[redacted] / 96
PIPERACILLIN	4 g	QD	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
PIPERACILLIN;TAZOBACTAM	100 mL	QD	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
PIPERACILLIN	4 g	BID	Y-M: 20[redacted] / 98	Y-M: 20[redacted] / 102
LOXOPROFEN	60 mg	BID	Y-M: 20[redacted] / 107	ONGOING
REBAMIPIDE	100 mg	BID	Y-M: 20[redacted] / 107	ONGOING
AMOXICILLIN	250 mg	TID	Y-M: 20[redacted] / 112	ONGOING

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

Event Description	PNEUMONIA
Preferred term	肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 184
Age at AE Onset	4[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 83): NPTST087-C-REACTIVE PROTEIN: 3.41 [0 - 0.3] MG/DL	
Microbiology	
NOT REPORTED	
AE Stopped Initial 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]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 1 箱を 35 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184日後＊，被験者は肺炎を発現した。

投与184日後＊　，被験者は発熱した。投与194日後＊　，被験者は外来を受診し，CT スキャン検査及び胸部 X 線検査を受けたところ，肺炎が確認された。投与195日後＊　，被験者は高熱があり入院し，胸痛もあった。被験者は解熱薬及び鎮痛薬で治療された。投与196日後＊　，被験者は別の病院に転院した。

投与197日後＊　，被験者は膿胸の切開掻爬術を受けた。病理検査の結果，放線菌症と診断された。手術後に，被験者はアンピシリンナトリウム（ABPC）の点滴による 2 週間の治療を受けた。投与224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。

投与された薬剤は，ロキソプロフェン，アセリオ，アタラックス–P，ソセゴン，パセトシン，タゾピペ，ピペラシリン Na，クリンダマイシンリン酸エステル，セフトリアキソン Na 及びカロナールであった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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

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

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

Dechallenge: No

Alternative Etiology for UPADACITINIB (Blinded)----------

Event of PNEUMONIA

- Investigator: Not applicable.

- AbbVie: Risk factor includes subject's extensive smoking history (1 PPD for 35 years).

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] C-REACTIVE PROTEIN:** 3.41 mg/dL (normal 0.00 to 0.30)

[redacted] **20[redacted] CHEST X-RAY:** A nodule in S6 area of left lower lobe with pleural effusion.

[redacted] **20[redacted] CT SCAN:** A nodule in S6 area of left lower lobe with pleural effusion.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肝機能異常		X		X
好中球数減少				X
くも膜下出血	X			X

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

Medical History	Onset Year
ANAEMIA	20[redacted]
BLOOD BETA D-GLUCAN INCREASED	20[redacted]
DYSLIPIDAEMIA	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
GGTP INCREASE	20[redacted]
HYPERURICAEMIA	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 318	318

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DEXAMETHASONE	3.3 mg	QD	Y-M: 20[redacted] / -210
CLOSTRIDIUM BUTYRICUM	1 OTHER: TABLET	TID	Y-M: 20[redacted] / -214
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -215
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -216
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -235
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted] / -185
DEXAMETHASONE	2 mg	BID	Y-M: 20[redacted] / -207
TACROLIMUS	8 mg	BID	Y-M: 20[redacted] / -208
PREDNISOLONE	2.5 mg	BID	Y-M: 20[redacted] / -130
BUDESONIDE	4 mg	BID	Y-M: 20[redacted] / -103
RAMOSETRON	5 ug	QD	Y-M: 20[redacted] / -34
GUALENIC ACID;LEVOGLUTAMIDE	0.67 g	TID	Y-M: 20[redacted] / -44

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 OTHER: TABLET	TID	Y-M: 20[redacted] / -214	ONGOING
MESALAZINE	4800 mg	QD	Y-M: 20[redacted] / -215	ONGOING
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted] / -185	Y-M: 20[redacted] / 31
RAMOSETRON	5 ug	QD	Y-M: 20[redacted] / -34	ONGOING
GUALENIC ACID;LEVOGLUTAMIDE	0.67 g	TID	Y-M: 20[redacted] / -44	Y-M: 20[redacted] / 141
NADIFLOXACIN	ADEQUATE DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 76
PREDNISOLONE	12.5 mg	QD	Y-M: 20[redacted] / 1	Y-M: 20[redacted] / 27
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 28	Y-M: 20[redacted] / 31
GLUCOSE;SODIUM CHLORIDE;SODIUM LACTATE	200 mL	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 32

HYDROCORTISONE	100 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 32
LANSOPRAZOLE	30 mg	BID	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 34
METOCLOPRAMIDE	10 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 38
NICARDIPINE	20 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 32
PARACETAMOL	1000 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 32
PENTAZOCINE	15 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 33
PARACETAMOL	500 mg	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 40
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 34
PARACETAMOL	300 mg	PRN	Y-M: 20[redacted] / 34	Y-M: 20[redacted] / 47
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 61
LANSOPRAZOLE	15 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 48
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 37
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 41
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 42	Y-M: 20[redacted] / 55
ROSUVASTATIN	2.5 mg	QD	Y-M: 20[redacted] / 49	ONGOING
PREDNISOLONE	7.5 mg	QD	Y-M: 20[redacted] / 56	Y-M: 20[redacted] / 83
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted] / 62	ONGOING
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / 84	Y-M: 20[redacted] / 113
PREDNISOLONE	2.5 mg	QD	Y-M: 20[redacted] / 114	Y-M: 20[redacted] / 141
SERTRALINE	25 mg	QD	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 141
PREDNISOLONE	1 mg	QD	Y-M: 20[redacted] / 142	Y-M: 20[redacted] / 253
ETIZOLAM	0.5 mg	PRN	Y-M: 20[redacted] / 246	Y-M: 20[redacted] / 252
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 330
LIDOCAINE	10 mg	QD	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 330
SODIUM PHOSPHATE	5 OTHER: TABLET	PRN	Y-M: 20[redacted] / 330	Y-M: 20[redacted] / 330

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

Event Description	HEPATIC FUNCTION ABNORMAL
Preferred term	肝機能異常
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 15
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial 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 - Adjudicated MACE *

Event Description	SUBARACHNOID HAEMORRHAGE
Preferred term	くも膜下出血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 90
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	106
Duration of AE	17 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	IT WAS CONSIDERED THAT THERE WAS NO CAUSAL RELATIONSHIP TO THE INVESTIGATIONAL DRUG, AS IT WAS CONSIDERED THAT THE INCREASE IN TEMPERATURE AND EXCESSIVE DRINKING WERE THE CAUSES.
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 - Neutropenia

Event Description	NEUTROPHOL COUNT DECREASED
Preferred term	好中球数減少
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 360
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	

AE Stopped Initial 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]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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，くも膜下出血の事象を発現した。関連する病歴は，広範囲な潰瘍性大腸炎（全大腸炎型），貧血，脂質異常症，非喫煙者及び現飲酒者（1 日 2–4 杯）であった。

Event 2 の臨床経過：

投与90日後＊　，被験者はくも膜下出血を発現した。投与106日後＊　，くも膜下出血は消失した。

投与90日後＊　，被験者は朝 5 時に目覚めてから激しい後頭部の頭痛及び嘔吐があり，入院した。バイタルサインは，血圧が 158/91 mmHg，脈拍が 81 回/分であった。被験者は，意識ははっきりしており，麻痺もなく，眼振もなかった。被験者は CT スキャン検査によりくも膜下出血と診断された。被験者は援助を必要とする中等度の障害があったが，歩行は介助なしで可能であった。被験者は他の病院に移った。被験者の悪心及び頭痛の症状は，薬物療法で管理された。投与103日後＊，カテーテルによる脳血管造影が行われた。動脈や静脈の基部に異常は認められず，典型的なくも膜下出血とは異なる出血と考えられ，原因は不明と判断された。投与106日後＊，被験者は症状が回復し，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アルコール摂取であった。

投与された薬剤は，プリンペラン，ニカルジピン塩酸塩，acello，ソルデム 1 輸液及び hydrocortisone phosphate であった。

The patient's past medications include:

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

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

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Subarachnoid haemorrhage (10042316) (Subarachnoid haemorrhage (10042316)) [v.23.0] [10042316]

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 SUBARACHNOID HAEMORRHAGE

- Investigator: It was considered that there was no casual relationship to the investigational drug, as it was considered that the increase in temperature and excessive drinking were the causes.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BLOOD PRESSURE:** 158/91 mmHg

[redacted] **20[redacted] CEREBAL ANGIOGRAPHY BY A CATHETER:** No abnormality in the arterial or venous system were shown.

[redacted] **20[redacted] CT:** No abnormality in the arterial or venous system were shown.

[redacted] **20[redacted] CT SCAN HEAD:** subarachnoid hemorrhage

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

[redacted] **20[redacted] MRI:** No abnormality in the arterial or venous system were shown.

[redacted] **20[redacted] MRI:** No abnormality in the arterial or venous system were shown.

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Hepatic function abnormal: 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
肺挫傷	X			
胸椎骨折	X			

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

Medical History	Onset Year
ALLERGIC RHINITIS	20[redacted]
COMMON COLD	20[redacted]
DUODENITIS	20[redacted]
EXTENSIVE UC/PANCOLITIS	20[redacted]
NASH	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	3	20[redacted]
CIGARS	FORMER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-675 ABT-494 (OL)	45 mg	ORAL	QD	[redacted]20[redacted] / 58	[redacted]20[redacted] / 113	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 358	358

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CLOSTRIDIUM BUTYRICUM	3 OTHER: TAB.	BID	Y-M: 20[redacted]
MESALAZINE	3600 mg	QD	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
MESALAZINE	2000 mg	BID	Y-M: 20[redacted]
MESALAZINE	3600 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	BID	Y-M: 20[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]
MESALAZINE	2000 mg	QD	Y-M: 20[redacted]
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted]
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / -197
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / -198
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -161

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	3 OTHER: TAB.	BID	Y-M: 20[redacted]	ONGOING
MESALAZINE	1000 mg	QD	Y-M: 20[redacted]	ONGOING
MESALAZINE	2000 mg	QD	Y-M: 20[redacted]	ONGOING
RABEPRAZOLE	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 358
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / -197	ONGOING
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -161	Y-M: 20[redacted] / 1
ESZOPICLONE	1 mg	PRN	Y-M: 20[redacted] / 14	Y-M: 20[redacted] / 93
CEFCAPENE	100 mg	TID	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 17
PREDNISOLONE	5 mg	QD	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 54
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 39
PARACETAMOL;TRAMADOL	1 OTHER: TAB.	QID	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 174
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / 17	Y-M: 20[redacted] / 17
DOMPERIDONE	10 mg	TID	Y-M: 20[redacted] / 19	Y-M: 20[redacted] / 56

PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / 2	Y-M: 20[redacted] / 15
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / 20	Y-M: 20[redacted] / 20
CAMPHOR;ENOXOLONE;MENTHOL;SALICYLIC ACID	UNK OTHER: UNK	PRN	Y-M: 20[redacted] / 44	ONGOING
PREDNISOLONE	2 mg	QD	Y-M: 20[redacted] / 55	Y-M: 20[redacted] / 68
PREDNISOLONE	1 mg	QD	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 82
PARACETAMOL	100 mL	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 110
PARACETAMOL;TRAMADOL	1 OTHER: TAB.	PRN	Y-M: 20[redacted] / 175	ONGOING
CROTAMITON;HYDROCORTISONE	UNK OTHER: UNK	PRN	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 246
IVERMECTIN	3 mg	QD	Y-M: 20[redacted] / 197	Y-M: 20[redacted] / 202
IVERMECTIN	18 mg	QD	Y-M: 20[redacted] / 211	Y-M: 20[redacted] / 211
AMOXICILLIN	250 mg	TID	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 224
DEQUALINIUM	0.25 mg	PRN	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 224
TRANEXAMIC ACID	250 mg	TID	Y-M: 20[redacted] / 220	Y-M: 20[redacted] / 224
MOSAPRIDE	1.5 g	QD	Y-M: 20[redacted] / 358	Y-M: 20[redacted] / 358
SENNOSIDE A+B	24 mg	QD	Y-M: 20[redacted] / 358	Y-M: 20[redacted] / 358
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	244.212 g	QD	Y-M: 20[redacted] / 359	Y-M: 20[redacted] / 359
DIMETICONE	5 mL	QD	Y-M: 20[redacted] / 359	Y-M: 20[redacted] / 359
HYOSCINE	20 mg	QD	Y-M: 20[redacted] / 359	Y-M: 20[redacted] / 359
MIDAZOLAM	4 mg	QD	Y-M: 20[redacted] / 359	Y-M: 20[redacted] / 359
OTHER EMOLLIENTS AND PROTECTIVES	10 g	QD	Y-M: 20[redacted] / 359	Y-M: 20[redacted] / 359

Event #1: Serious Adverse Event

Event Description	PULMONARY CONTUSION
Preferred term	肺挫傷
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 127
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FALL FROM HIGH PLACE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Event #2: Serious Adverse Event

Event Description	THORACIC VERTEBRAL FRACTURE (TH2-6)
Preferred term	胸椎骨折
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 127
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	FALL FROM HIGH PLACE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，肺挫傷及び胸椎骨折（TH2-6）の事象を発現した。

Event 1 及び 2 の臨床経過：

投与127日後＊ ，被験者は肺挫傷及び胸椎骨折（TH2-6）を発現した。投与545日後＊ ，肺挫傷及び胸椎骨折（TH2-6）は消失した。

被験者は 4 m の高さから転落した。投与127日後＊ ，被験者は入院した。被験者は胸椎骨折及び肺挫傷の治療を受けた。投与139日後＊，被験者は別の病院に移され，手術が予定された。投与141日後＊ ，被験者は骨折（T6）の脊椎後方固定術を受けた。被験者は，疼痛コントロールのためにロキソプロフェン Na で治療された。投与164日後＊ ，手術部位は治癒し，感染の徴候は認められなかった。手術前，被験者は痛みがあった。投与206日後＊ ，被験者は退院した。

投与された薬剤は，スチックゼノール A，ルネスタ，アセリオ，セフカペン，ロキソプロフェン及びトアラセットであった。

The patient's past medications include:

ASACOL for ULCERATIVE COLITIS ([redacted])

PENTASA for ULCERATIVE COLITIS ([redacted])

PREDNISOLONE for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Pulmonary contusion (10037370) (Pulmonary contusion (10037370)) [v.24.0] [10037370]

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) Thoracic vertebral fracture (10049948) (Thoracic vertebral fracture (10049948)) [v.24.0] [10049948]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of PULMONARY CONTUSION

- Investigator: Fall from high place

- AbbVie: Event is more likely an unexpected and unintentional incident (fall from 4 meters, per PI).

Event of THORACIC VERTEBRAL FRACTURE (TH2-6)

- Investigator: Fall from high place

- AbbVie: Event is more likely an unexpected and unintentional incident (fall from 4 meters, per PI).

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

Reason for Narrative

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

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

Medical History	Onset Year
CHEST PAIN	20[redacted]
CHRONIC GASTRITIS	20[redacted]
HEADACHES	20[redacted]
INSOMNIA	20[redacted]
LEFT SIDED UC	20[redacted]
REFLUX OESOPHAGITIS	20[redacted]

Prior Procedures	Procedure Year
SAE SUPPLEMENTAL PROCEDURE: ATHEROSCLEROSIS TESTS	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: CHEST X-RAYS	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: CORONARY ANGIOGRAPHY	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: ECHOCARDIOGRAPHY	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: ELECTROCARDIOGRAMS	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: LABORATORY VALUES	20[redacted]
SAE SUPPLEMENTAL PROCEDURE: THE TEST FOR INDUCTION OF CORONARY SPASM	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	20	20[redacted]
CIGARS	FORMER			
E-CIGARETTES	CURRENT	0.5 SESSIONS	1	
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 378	378

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	4000 mg	BID	Y-M: 20[redacted]
BIFIDOBACTERIUM NOS	2.000 OTHER: TABLETS	BID	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
BROTIZOLAM	0.25 mg	PRN	Y-M: 20[redacted] / -71
ESOMEPRAZOLE	20 mg	PRN	Y-M: 20[redacted] / -71
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -84
RIZATRIPTAN	10 mg	PRN	Y-M: 20[redacted] / -84
GLYCERYL TRINITRATE	0.3 mg	PRN	Y-M: 20[redacted] / -13

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	4800 mg	QD	Y-M: 20[redacted]	ONGOING
BROTIZOLAM	0.25 mg	PRN	Y-M: 20[redacted] / -71	Y-M: 20[redacted] / 30
ESOMEPRAZOLE	20 mg	PRN	Y-M: 20[redacted] / -71	Y-M: 20[redacted] / 253
PARACETAMOL	500 mg	PRN	Y-M: 20[redacted] / -84	ONGOING
RIZATRIPTAN	10 mg	PRN	Y-M: 20[redacted] / -84	ONGOING
GLYCERYL TRINITRATE	0.3 mg	PRN	Y-M: 20[redacted] / -13	ONGOING
ESZOPICLONE	2 mg	PRN	Y-M: 20[redacted] / 1	ONGOING
CARBOCISTEINE	500 mg	TID	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 15
CHLORPHENAMINE;DIHYDROCODEINE;METHYLEPHEDRINE	2 OTHER: TABLETS	TID	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 15
LANINAMIVIR	40 mg	OTHER: ONCE	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 11

PARACETAMOL	200 mg	BID	Y-M: 20[redacted] / 11	Y-M: 20[redacted] / 15
BETAMETHASONE	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 152	Y-M: 20[redacted] / 291
CLOBETASONE	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 152	Y-M: 20[redacted] / 291
DIAZEPAM	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
DIMETICONE	5 mL	OTHER: ONCE	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
PRONASE	20000 OTHER: UNIT	OTHER: ONCE	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 233
ACOTIAMIDE	100 mg	TID	Y-M: 20[redacted] / 254	ONGOING
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted] / 254	Y-M: 20[redacted] / 288
VONOPRAZAN	10 mg	QD	Y-M: 20[redacted] / 289	Y-M: 20[redacted] / 300
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / 292	ONGOING
NADIFLOXACIN	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 292	Y-M: 20[redacted] / 299
DIAZEPAM	5 mg	OTHER: ONCE	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 301
DIMETICONE	5 mL	OTHER: ONCE	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 301
PRONASE	20000 OTHER: UNIT	OTHER: ONCE	Y-M: 20[redacted] / 301	Y-M: 20[redacted] / 301
VONOPRAZAN	20 mg	QD	Y-M: 20[redacted] / 301	ONGOING
MAGNESIUM CITRATE	50 g	OTHER: ONCE	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 365
SENNA ALEXANDRINA	24 mg	OTHER: ONCE	Y-M: 20[redacted] / 365	Y-M: 20[redacted] / 365
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: BAG	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
CALCIUM CHLORIDE;GLUCOSE;POTASSIUM;SODIUM ACETATE;SODIUM CHLORIDE	500 mL	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
DIMETICONE	5 mL	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
GLUCAGON	1 mg	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
LIDOCAINE	30 mL	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
MIDAZOLAM	2 mL	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
SODIUM CHLORIDE	20 mL	OTHER: ONCE	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366

Event #1: Serious Adverse Event

Event Description	CHEST PAIN
Preferred term	胸痛
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 45

Age at AE Onset	4[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY -12): Aspartate Aminotransferase: 27 [13 - 30] U/L; Creatine Kinase: 115 [59 - 248] U/L; Leukocytes: 4.73 [3.3 - 8.6] 10^9/L; NPTST316-LACTIC DEHYDROGENAGE: 160 [124 - 222] U/L; NPTST357-N-TERMINAL PRO-BRAIN NATRIURETI: 5 [0 - 125] PG/ML; NPTST523-TROPONIN T: 0.005 [0.01 - 0.1] NG/ML

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	HE OCCASIONALLY HAD CHEST PAIN BEFORE THE STUDY DRUG ADMINISTRATION AND WAS ADMITTED FOR SCRUTINY.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-675

治験責任医師からの報告。本被験者は日本の 4[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，胸痛の事象を発現した。関連する病歴は，潰瘍性大腸炎，元喫煙者（1 日 1 箱を 20 年間），不眠症，慢性胃炎，逆流性食道炎，電子タバコの現喫煙者（1 日 0.5 回を 1 年間）及び現飲酒者（1 日 4 杯以上）であった。

Event 1 の臨床経過：

投与45日後＊，被験者は胸痛を発現した。

投与45日後＊　　，被験者は胸痛を発現した。ニトロペンを服用し，症状が鎮まった。同日，専門医によりアンギナの疑いがあると診断された。投与46日後＊　　，被験者は精査のために入院した。同日，心臓カテーテル検査を行った。検体検査及び診断は，全て正常であった。被験者は，病歴から冠攣縮性狭心症の疑いがあると診断された。被験者は，治療の必要性はなく，胸痛に対してニトロペンを服用した。投与48日後＊，被験者は退院した。

投与された薬剤は，ニトロペンであった。

The patient's past medications include:

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

BIOFERMIN ([redacted] 20[redacted] - [redacted] 20[redacted])

INFLUENZA VACCINE HA for PREVENTION OF INFLUENZA ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Chest pain (10008479) (Chest pain (10008479)) [v.22.1] [10008479]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of CHEST PAIN

- Investigator: He occasionally had chest pain before the study drug administration and was admitted for scrutiny.

- AbbVie: Event is common in the general population. The mean annual prevalence of non-cardiac chest pain in 6 population-based studies was approximately 25%. Risk factors for cardiac chest pain include chronic gastritis and reflux esophagitis.

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 27 U/L (normal 13 to 30)

[redacted] 20[redacted] **ATHEROSCLEROSIS TESTS:** No abnormalities.

[redacted] 20[redacted] **CHEST X-RAYS:** No abnormalities.

[redacted] 20[redacted] **CORONARY ANGIOGRAPHY:** No significant stenosis.

[redacted] 20[redacted] **CREATINE KINASE:** 115 U/L (normal 59 to 248)

[redacted] 20[redacted] **ECHOCARDIOGRAPHY:** No abnormalities.

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

[redacted] 20[redacted] **ELECTROCARDIOGRAM:** No abnormalities.

[redacted] 20[redacted] **LACTIC DEHYDROGENASE:** 160 U/L (normal 124 to 222)

[redacted] 20[redacted] **N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE:** 5 PG/ML (normal 0 to 125)

[redacted] 20[redacted] **THE TEST FOR INDUCTION OF CORONARY SPASM:** Borderline type.

[redacted] 20[redacted] **TROPONIN T:** 0.0005 NG/ML (normal 0.01 to 0.1)

[redacted] 20[redacted] **WHITE BLOOD CELLS:** 4.73 10^3/uL (normal 3.3 to 8.6)

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			

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	7[redacted]	MALE	ASIAN

Medical History	Onset Year
ABDOMINAL PAIN	20[redacted]
CARDIAC ARRHYTHMIAS	20[redacted]
CATARACT	NOT REPORTED
CERVICAL SPONDYLOSIS	20[redacted]
CHRONIC GASTRITIS	20[redacted]
CHRONIC URTICARIA	20[redacted]
DRY EYE	NOT REPORTED
ESSENTIAL TREMOR	20[redacted]
GASTRIC POLYPS	20[redacted]
GLAUCOMA	NOT REPORTED
LEFT SIDED UC	20[redacted]
LUMBER SPIAL STENOSIS	20[redacted]
POLLINOSIS	NOT REPORTED
REFLUX ESOPHAGITIS	20[redacted]
TUBERCULOSIS TEST POSITIVE	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	28	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[redacted] / 1	[redacted] / 54	54
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted] / 1	[redacted] / 364	364

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
INFLIXIMAB	5.000 mg/kg	WEEK0,2,6	Y-M: [redacted]
FEXOFENADINE	60 mg	BID	Y-M: [redacted]
ADALIMUMAB	40.000 mg	EVERY 2 WEEKS	Y-M: [redacted]
MESALAZINE	2 g	BID	Y-M: [redacted]
MESALAZINE	3200 mg	BID	Y-M: [redacted]
MESALAZINE	1 g	PRN	Y-M: [redacted]
GOLIMUMAB	200.000 mg	EVERY 2 WEEKS	Y-M: [redacted]
GOLIMUMAB	100.000 mg	ONCE	Y-M: [redacted]
MESALAZINE	4800 mg	QD	Y-M: [redacted]
ADALIMUMAB	160.000 mg	EVERY 2 WEEKS	Y-M: [redacted]
PILSICAINIDE	25 mg	PRN	Y-M: [redacted]
MESALAZINE	2000 mg	QD	Y-M: [redacted]
BUDESONIDE	4 mg	BID	Y-M: [redacted]
MESALAZINE	4800 mg	QD	Y-M: [redacted]
ZONISAMIDE	50 mg	QD	Y-M: [redacted] / -269
ESOMEPRAZOLE	20 mg	QD	Y-M: [redacted] / -126
HYOSCINE	20 mg	PRN	Y-M: [redacted] / -96
ISONIAZID	300 mg	QD	Y-M: [redacted] / -75
LEMBOREXANT	5 mg	PRN	Y-M: [redacted] / -28
MESALAZINE	3200 mg	BID	Y: [redacted]
AZATHIOPRINE	50 mg	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 / Stop Year-Month / RX Day	RX Day
ANTIDIARRHEAL MICROORGANISMS	2 OTHER: TABLETS	BID	Not reported	ONGOING
HYALURONIC ACID	1 OTHER: DROP	PRN	Not reported	ONGOING
KETOPROFEN	40 mg	PRN	Not reported	ONGOING
MECOBALAMIN	0.5 mg	TID	Not reported	ONGOING
OFLOXACIN	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Not reported	ONGOING
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted]	ONGOING
PILSICAINIDE	25 mg	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	4800 mg	QD	Y-M: 20[redacted]	ONGOING
ZONISAMIDE	50 mg	QD	Y-M: 20[redacted] / -269	ONGOING
ESOMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / -126	Y-M: 20[redacted] / 140
HYOSCINE	20 mg	PRN	Y-M: 20[redacted] / -96	ONGOING
LEMBOREXANT	5 mg	PRN	Y-M: 20[redacted] / -28	ONGOING
DEQUALINIUM	0.25 mg	PRN	Y-M: 20[redacted] / 1	ONGOING
HYALURONIC ACID	UNKNOWN OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / 18	ONGOING
BETAMETHASONE;GENTAMICIN	PROPER AMOUNT OTHER: PROPER AMOUNT	PRN	Y-M: 20[redacted] / 113	ONGOING
PYRIDOXAL	20 mg	TID	Y-M: 20[redacted] / 141	Y-M: 20[redacted] / 168

Event #1: Serious Adverse Event

Event Description	EXACERBATION OF CARPAL TUNNEL SYNDROME[RIGHT]
Preferred term	手根管症候群
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 202
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	210
Duration of AE	9 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

Investigator Alternative Etiology	OVERUSE OF HANDS.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は日本の 7[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，手根管症候群（右）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 28 年間），潰瘍性大腸炎，腰部脊柱管狭窄症及び非飲酒者であった。

被験者は，本試験の投与 0 週時から投与 8 週時までは盲検期間であった。投与111日後＊，被験者は本試験の非盲検期間に入った。

Event 1 の臨床経過：

投与202日後＊，被験者は手根管症候群（右）の悪化を発現した。投与210日後＊，手根管症候群（右）の悪化は消失した。

本事象発現前の 投与129日後＊　　，被験者は手根管症候群（右）（非重篤）と診断された。末梢神経障害性疼痛を緩和するためにタリージェでの治療を開始した。

投与202日後＊，被験者は手根管の手術のために入院した。投与203日後＊　，治験薬を休薬した。同日，手根管の手術が行われた。投与210日後＊，被験者は退院した。被験者の症状が改善したため，治験薬の投与を再開した。

The patient's past medications include:

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

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

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

HUMIRA 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])

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

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

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

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

Causality for UPADACITINIB (Blinded)

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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: Yes

Rechallenge: rechallenge was done, reaction did not recur

Alternative Etiology for UPADACITINIB (Blinded)

Event of EXACERBATION OF CARPAL TUNNEL SYNDROME [RIGHT]

- Investigator: Overuse of hands

- AbbVie: Event is more likely related to repetitive use of the hands as noted by PI.

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
小細胞癌	X	X		X

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

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
HEMORRHOID	20[redacted]
INSOMNIA	20[redacted]
PERITONSILLAR ABSCESS	20[redacted]
PLUMONARY TBC	19[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	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	28	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 356	356

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AZATHIOPRINE	50 mg	QD	Y-M: 20[redacted]
MESALAZINE	NOT REPORTED	BID	Y-M: 20[redacted]
AZATHIOPRINE	25 mg	QD	Y-M: 20[redacted]
ZOLPIDEM	3.125 mg	PRN	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted]
MESALAZINE	2 g	BID	Y-M: 20[redacted]
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -291
MESALAZINE	2.4 g	BID	Y-M: 20[redacted] / -189
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -199
INFLIXIMAB	5.000 mg/kg	WEEK 0, WEEK 2, WEEK 6	Y-M: 20[redacted] / -162
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted] / -83
CALCIUM CARBONATE;COLECALCIFEROL	1000 mg	QD	Y-M: 20[redacted] / -94
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted] / -94
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / -94
PREDNISOLONE	20 mg	QD	Y-M: 20[redacted] / -94
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -72
CIMETROPIUM	5 mg	QD	Y-M: 20[redacted] / -73
MIDAZOLAM	4 mg	QD	Y-M: 20[redacted] / -73
PETHIDINE	25 mg	QD	Y-M: 20[redacted] / -73
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 L	QD	Y-M: 20[redacted] / -74
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 L	QD	Y-M: 20[redacted] / -1
BCG Vaccine	NOT REPORTED	NOT REPORTED	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
ZOLPIDEM	3.125 mg	PRN	Y-M: 20[redacted]	ONGOING
MESALAZINE	2.4 g	BID	Y-M: 20[redacted] / -189	ONGOING

CALCIUM CARBONATE;COLECALCIFEROL	1000 mg	QD	Y-M: 20[redacted] / -94	ONGOING
PREDNISOLONE	10 mg	QD	Y-M: 20[redacted] / -72	ONGOING
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted] / 106	ONGOING
ALMAGATE	1 OTHER: TABLET	TID	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 318
CALAMINE	1 OTHER: ENOUGH	BID	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 317
DEXAMETHASONE	5 mg	QD	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 314
FAMCICLOVIR	250 mg	TID	Y-M: 20[redacted] / 312	Y-M: 20[redacted] / 318
DEXAMETHASONE	5 mg	QD	Y-M: 20[redacted] / 316	Y-M: 20[redacted] / 316
GENTAMICIN	1 OTHER: ENOUGH	QD	Y-M: 20[redacted] / 318	Y-M: 20[redacted] / 356
ESOMEPRAZOLE	40 mg	QD	Y-M: 20[redacted] / 341	Y-M: 20[redacted] / 356
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted] / 341	Y-M: 20[redacted] / 356
MIRABEGRON	50 mg	QD	Y-M: 20[redacted] / 347	ONGOING
TAMSULOSIN	0.4 mg	QD	Y-M: 20[redacted] / 347	ONGOING
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 L	QD	Y-M: 20[redacted] / 356	Y-M: 20[redacted] / 357
MIDAZOLAM	4 mg	QD	Y-M: 20[redacted] / 357	Y-M: 20[redacted] / 357
PETHIDINE	25 mg	QD	Y-M: 20[redacted] / 357	Y-M: 20[redacted] / 357

Event #1: Event of Interest - Herpes Zoster

Event Description	HERPES ZOSTER
Preferred term	帯状疱疹
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 369
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	374
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, AE Leading to Discontinuation of Study Drug, Event of Interest-Possible Malignancies, Event of Interest-Malignancy, Event of Interest-Malignancies Excl NMSC

Event Description	PROSTATE CANCER,SMALL CELL CARCINOMA
Preferred term	小細胞癌
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 390
Age at AE Onset	5[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 358): NPTST113-CEA: 85.5 [0 - 6] NG/ML; NPTST427-PSA: 1.2 [0 - 3] NG/ML	
Microbiology	
NOT REPORTED	
AE Stopped Initial 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]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者は韓国の 5[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，前立腺癌（小細胞癌）の事象を発現した。関連する病歴は，痔核，元喫煙者（1 日 1 箱を 28 年間），潰瘍性大腸炎及び元飲酒者（1 日 2–4 杯）であった。

Event 2 の臨床経過：

投与390日後＊，被験者は前立腺癌（小細胞癌）を発現した 。

入院前，被験者は潰瘍性大腸炎の悪化（投与の約13ヵ月後＊発症，非重篤）及び排尿困難（非重篤）を経験していた。

投与414日後＊，被験者は肛門痛及び潰瘍性大腸炎の症状の悪化のために入院した。投与414日後＊，被験者は治験中止時の結腸内視鏡検査を受けた。被験者は前立腺癌（小細胞癌）と診断され，化学療法を開始するために腫瘍科に移された。投与425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])

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

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

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Small cell carcinoma (10041056) (Small cell carcinoma (10041056)) [v.24.0] [10041056]

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 PROSTATE CANCER, SMALL CELL CARCINOMA

- Investigator: Unknown

- AbbVie: Per pathology more likely a neuroendocrine small cell cancer, etiology of which is unclear in medical literature at this time, additionally this is a rare type of aggressive cancer associated with multiple genomic alterations.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] BONE SCAN WHOLE BODY:** Multiple bone metastases in C-T-L-S spine, bilateral pelvic bones, bilateral ribs, sternum and bilateral scapulae

[redacted] **20[redacted] CEA:** 85.5 NG/ML (normal 0 to 6)

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

[redacted] **20[redacted] COLONOSCOPY:** No normal mucosa (pancolitis). No dysplasia or malignancy seen on biopsy.

[redacted] **20[redacted] COLONOSCOPY:** No inflammation seen (normal mucosa). Biopsy showed evidence of dysplasia/malignancy.

[redacted] **20[redacted] CT ABDOMEN AND PELVIS:** 1) ABOUT 10-CM PELVIC CAVITY MASS WITH MULTIPLE ORGAN INVASION. - INVOLVEMENT: ENTIRE PROSTATE, SEMINAL VESICLE, URINARY BLADDER, RECTUM, AND RIGHT PELVIC FLOOR. 2) MULTIPLE LYMPH NODE METASTASES IN BILATERAL PELVIC WALL, MESORECTAL, AND SUPERIOR RECTAL AREA. 3) MULTIPLE HEPATIC METASTASES IN BOTH HEPATIC LOBES. 4) SUSPICIOUS PERITONEAL SEEDING. 5) DISSEMINATED OSTEOBLASTIC BONE METASTASES. ==> PRIMARY PELVIC CAVITY TUMOR WITH LN, BONE, LIVER METASTASES, SUGGESTED. - DDX. PROSTATE CANCER, MOST LIKELY.

[redacted] **20[redacted] LARGE INTESTINE BIOPSY HISTOCHEMISTORY:** A) Large intestine, (rectum, AV 5cm), endoscopic biopsy: - NEUROENDOCRINE CARCINOMA, POORLY DIFFERENTIATED, SMALL CELL TYPE. (See note) NOTE:Please refer to the result(s) of the immunohistochemical/histochemical staining below. *Chromogranin : negative *Cytokeratin 20 : negative *Cytokeratin 7 : positive *PSA : negative *Synaptophysin : positive *KI-67 : > 90 % GROSS : A. Ten (up to 0.3 cm) piece(s), 1 cassette(s), entirely

[redacted] **20[redacted] PROSTATE MRI WITH ENHANCEMENT:** 1. A 10 cm lobulating enhancing mass in the pelvic cavity. - Invasion of bladder posterior wall, prostate, seminal vesicle, and rectum. Focal protruding to the rectum and bladder. Multiple metastatic lymph nodes in both pelvic walls and mesorectum. Multifocal bone and liver metastases. --> R/O pelvic sarcoma with multiple metastases. R/O atypical prostate cancer such as small cell carcinoma or neuroendocrine tumor. R/O all metastases from unknown primary.

[redacted] **20[redacted] PSA:** 1.2 NG/ML (normal 0 to 3)

[redacted] **20[redacted] SCREENING BODY WEIGHT:** 6[redacted].[redacted] KG

[redacted] **20[redacted] TORSO PET CT:** 1) Hypermetabolic mass involvement in prostate, bladder posterior wall, rectum; - C/W Malignant tumor 2) Multiple metastatic lymph nodes in both external iliac, bilateral pelvic side wall, presacral area 3) Multiple hepatic metastases 4) Multiple bone metastases in C-T-L-S spine, both pelvic bones, bilateral ribs, sterum, both scapulae

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Herpes Zoster: Unilateral involving multiple dermatomes(Rt arm, back, Rt. flank). 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
鉄欠乏性貧血	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	3[redacted]	MALE	WHITE

Medical History	Onset Year
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	CURRENT	0.3 PACK	15	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 363	363

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	800 mg	QID	Y-M: 20[redacted] / -345
MESALAZINE	1600 mg	TID	Y-M: 20[redacted] / -218
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted] / -218

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	TID	Y-M: 20[redacted] / -218	ONGOING
BLOOD AND RELATED PRODUCTS	3 OTHER: UNITS	QD	Y-M: 20[redacted] / 356	Y-M: 20[redacted] / 356
BLOOD PLASMA	2 OTHER: UNITS	QD	Y-M: 20[redacted] / 356	Y-M: 20[redacted] / 356
POTASSIUM	500 mL	QD	Y-M: 20[redacted] / 356	Y-M: 20[redacted] / 356
BLOOD AND RELATED PRODUCTS	2 OTHER: UNITS	QD	Y-M: 20[redacted] / 357	Y-M: 20[redacted] / 357
BLOOD PLASMA	2 OTHER: UNITS	QD	Y-M: 20[redacted] / 357	Y-M: 20[redacted] / 357
IRON	80 mg	BID	Y-M: 20[redacted] / 357	ONGOING
MACROGOL 4000;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	264 g	QD	Y-M: 20[redacted] / 363	Y-M: 20[redacted] / 363

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

Event Description	IRON DEFFICIENT ANAEMIA
Preferred term	鉄欠乏性貧血
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 413
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 310): Hemoglobin: 120 [127 - 181] G/L; [redacted]20[redacted] (RX DAY 356): Hemoglobin: 46 [135 - 169] G/L; [redacted]20[redacted] (RX DAY 357): Hemoglobin: 66 [135 - 169] G/L; [redacted]20[redacted] (RX DAY 358): Hemoglobin: 86 [135 - 169] G/L; [redacted]20[redacted] (RX DAY 393): Hemoglobin: 124 [127 - 181] G/L

Microbiology

NOT REPORTED

AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	RECTAL BLEEDING

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]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はリトアニアの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，鉄欠乏性貧血の事象を発現した。関連する病歴は，潰瘍性大腸炎，現喫煙者（1 日 0.3 箱を 15 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413日後＊　，被験者は鉄欠乏性貧血を発現した。投与593日後＊　　に鉄欠乏性貧血は消失した。

被験者は運動時に脱力及び疲労を経験していた。鉄欠乏性貧血と診断され，投与414日後＊　，被験者は入院した。ヘモグロビンが低値であり，被験者は投与414日後＊及び 投与415日後＊に輸血及び血漿の投与を受けた。輸血後，被験者は気分が良くなったと報告した。投与416日後＊　，被験者の状態が改善し，ヘモグロビンの値が上昇したため，被験者は退院した。

投与された薬剤及び処置は，tardyferon，血漿，塩化カリウム 0.9%及び輸血であった。

The patient's past medications include:

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

Causality for UPADACITINIB (Blinded)

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1)　Iron deficiency anemia (10022974)　(Iron deficiency anaemia (10022972))　[v.24.1]　[10022974]

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 IRON DEFFICIENT ANAEMIA

- Investigator: It could be chronic iron deficiency due to previous rectal bleedings.

- AbbVie: event is more likely a complication of pre-existing Ulcerative colitis and its related rectal bleeding as reported by PI.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] BASELINE HEMOGLOBIN:** 9.5 G/DL (normal 12.7 to 18.1)

[redacted] **20[redacted] BODY WEIGHT:** 6[redacted] KG

[redacted] **20[redacted] HEMOGLOBIN:** 120 G/L (normal 135 to 169)

[redacted] **20[redacted] HEMOGLOBIN:** 46 G/L (normal 135 to 169)

[redacted] **20[redacted] HEMOGLOBIN:** 66 G/L (normal 135 to 169)

[redacted] **20[redacted] HEMOGLOBIN:** 86 G/L (normal 135 to 169)

[redacted] **20[redacted] HEMOGLOBIN:** 124 G/L (normal 135 to 169)

[redacted] **20[redacted] SCREENING HEMOGLOBIN:** 9.9 G/DL (normal 12.7 to 18.1)

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
ANEMIA	20[redacted]
LEFT SIDED UC	20[redacted]
POST-MENOPAUSAL	20[redacted]

Prior Procedures	Procedure Year
PRIOR PROCEDURES: COLONOSCOPY / BIOPSY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 Placebo (IND)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 59	59
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 151	151

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
IRON	80.000 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 OTHER: 4G/60ML	QD	Y-M: 20[redacted]
MESALAZINE	1 g	TID	Y-M: 20[redacted]
MESALAZINE	1 g	QID	Y-M: 20[redacted]
AZATHIOPRINE	150 mg	QD	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted]
CIPROFLOXACIN	500 mg	BID	Y-M: 20[redacted]
METHYLPREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	30 mg	QD	Y-M: 20[redacted]
MESALAZINE	1 g	QD	Y-M: 20[redacted] / -109
IRON	10 mL	QD	Y-M: 20[redacted] / -41

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]	ONGOING
IRON	10 mL	QD	Y-M: 20[redacted] / -41	ONGOING
CEFUROXIME	1.5 g	TID	Y-M: 20[redacted] / 152	ONGOING
METHYLPREDNISOLONE	60 mg	QD	Y-M: 20[redacted] / 152	ONGOING
METRONIDAZOLE	500 mg	TID	Y-M: 20[redacted] / 152	ONGOING
RED BLOOD CELLS	230 mL	QD	Y-M: 20[redacted] / 158	Y-M: 20[redacted] / 158

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

Event Description	EXACERBATION OF ULCERATIVE COLITIS
Preferred term	潰瘍性大腸炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 210
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 151): Hemoglobin: 98 [123 - 153] G/L; NPTST084-C REACTIVE PROTEIN: 58.50 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 152): STOOL NPTST122-CL DIFFICILE TOXIN: NEGATIVE

AE Stopped Initial Rx Day	218 (8 DAYS AFTER LAST TREATMENT)
Duration of AE	9 DAYS
Severity	SEVERE

Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はリトアニアの 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，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，非喫煙者及び元飲酒者（1 日 2 杯未満）であった。

Event 1 の臨床経過：

投与210日後＊　，被験者は潰瘍性大腸炎の悪化を発現した。投与218日後＊　，潰瘍性大腸炎の悪化は消失した。

投与211日後＊　，被験者は入院した。被験者は，潰瘍性大腸炎の悪化，出血，腹痛，脱力及びしぶりを呈していた。被験者は治療の変更が必要であり，治験を中止した。画像診断及び検体検査が行われた。投与218日後＊，被験者は退院した。

投与された薬剤は，ソル・メドロール，メトロニダゾール及びセフロキシムであった。

The patient's past medications include:

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

CIPROFLOXACIN for ULCERATIVE COLITIS EXACERBATION ([redacted]20[redacted] - [redacted]20[redacted], [redacted]20[redacted] - [redacted]20[redacted])

METRONIDAZOL for ULCERATIVE COLITIS EXACERBATION ([redacted]20[redacted] - [redacted]20[redacted])

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

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

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

Causality for UPADACITINIB (Blinded)

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1) Colitis ulcerative aggravated (10009901) (Colitis ulcerative (10009900)) [v.23.0] [10009901]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of EXACERBATION OF ULCERATIVE COLITIS

- Investigator: Not applicable.

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] 20[redacted] **ABDOMINAL CT:** SPLENOMEGALY

[redacted] 20[redacted] **C REACTIVE PROTEIN:** 58.50 MG/L (normal 0.00 to 5.0)

[redacted] 20[redacted] **HEMOGLOBIN:** 98 G/L (normal 123 to 153)

[redacted] 20[redacted] **STOOL C DIFF TOXIN:** 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		X
好中球減少症				X

Treatment Group	Age at Induction Study Start	Sex	Race
ABT-494 30 mg	3[redacted]	MALE	WHITE

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
ULCERATIVE COLITIS	NOT REPORTED

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): COLONOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	3 PACK	11	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 60	60
M14-234 SS3 ABT-494 (MAIN)	30 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 109	109

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HYOSCINE	10 mg	OTHER: INTERMITTENT USE WHEN REQUIRED	Y-M: 20[redacted] / -107
LOPERAMIDE	2 mg	OTHER: INTERMITTENT USE WHEN REQUIRED	Y-M: 20[redacted] / -107
ERYTHROMYCIN	500 mg	TID	Y-M: 20[redacted] / -4
LORATADINE	10 mg	BID	Y-M: 20[redacted] / -4
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y: 20[redacted]
HYDROCORTISONE	100 mg	QID	Y: 20[redacted]
MESALAZINE	1.0 g	TID	Y: 20[redacted]
PREDNISONE	5 mg	QD	Y: 20[redacted]
INFLIXIMAB	400.000 mg	400	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
HYOSCINE	10 mg	OTHER: INTERMITTENT USE WHEN REQUIRED	Y-M: 20[redacted] / -107	ONGOING
LOPERAMIDE	2 mg	OTHER: INTERMITTENT USE WHEN REQUIRED	Y-M: 20[redacted] / -107	ONGOING
ERYTHROMYCIN	500 mg	TID	Y-M: 20[redacted] / -4	Y-M: 20[redacted] / 1
LORATADINE	10 mg	BID	Y-M: 20[redacted] / -4	Y-M: 20[redacted] / 1
DEXTROMETHORPHAN	0.3 g	TID	Y-M: 20[redacted] / 110	ONGOING
ERYTHROMYCIN	500 mg	TID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 118
GUAIFENESIN	2 g	TID	Y-M: 20[redacted] / 110	ONGOING
HYOSCINE	1 g	TID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 118
LEVOFLOXACIN	750 mg	QD	Y-M: 20[redacted] / 110	ONGOING
LORATADINE	10 mg	BID	Y-M: 20[redacted] / 110	ONGOING
ENOXAPARIN	60 mg	QD	Y-M: 20[redacted] / 119	Y-M: 20[redacted] / 125
OMEPRAZOLE	20 mg	QD	Y-M: 20[redacted] / 119	ONGOING
PARACETAMOL	500 mg	TID	Y-M: 20[redacted] / 119	ONGOING
MESALAZINE	1.0 g	TID	Y: 20[redacted]	ONGOING

Event #1: Event of Interest - Neutropenia

Event Description	NEUTROPENIA
Preferred term	好中球減少症
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 30
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
AE Stopped Initial Rx Day	ONGOING
Duration of AE	ONGOING
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 of Interest - Serious Infections

Event Description	COVID-19 PNEUMONIA INFECTION
Preferred term	COVID-19 肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 169
Age at AE Onset	3[redacted]
Laboratory Testing	
[redacted]20[redacted] (RX DAY 114): NPTST463-SARS.COV-2: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED	
Microbiology	
[redacted]20[redacted] (RX DAY 114): OTHER PHARYNGEAL EXUDATE NPTST461-SARS COV-2: POSITIVE-POSITIVE TO SARS COV-2	
AE Stopped Initial Rx Day	178 (9 DAYS AFTER LAST TREATMENT)
Duration of AE	10 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はメキシコの 3[redacted] 歳男性であり，ABT-494（ウパダシチニブ）の治験で盲検化された治験薬が投与され，COVID-19 肺炎の感染症の事象を発現した。関連する病歴は，元喫煙者（1 日 3 箱を 11 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169日後＊，被験者はCOVID-19肺炎の感染症を発現した。投与178日後＊，COVID-19肺炎の感染症は消失した。

本事象発現前の 投与から約1ヵ月後＊，被験者は好中球減少症（非重篤）と診断された。

投与174日後＊　，被験者は COVID-19 感染の可能性があるため病院に行き，陽性と確認された。被験者は発熱，咳嗽，筋肉痛及び咽頭痛を呈していた。同日，被験者は酸素飽和度が低値（90%以下）であり，入院した。被験者の症状は継続していたが，酸素飽和度は改善していた。投与178日後＊，被験者は退院した。

治験責任医師は，感染症の経過中は合併症を引き起こすリスクが高まるため，好中球減少症は本事象の関連する危険因子と考えた。

本事象により，治験薬の投与は早期に中止された。

投与された薬剤は，paracetamol，デキストロメトルファン，guaifenesina，levofloxacino，エリスロマイシン，ロラタジン及び butylhyoscine であった。

The patient's past medications include:

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

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

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

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

Causality for UPADACITINIB (Blinded)

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1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.24.1] [10084380]

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

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

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of COVID-19 PNEUMONIA INFECTION

- Investigator: Not applicable

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

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 31.85 kg/m2

[redacted] **20[redacted] COVID-19 VIRUS TEST:** nasopharyngeal swab: positive

[redacted] **20[redacted] OXYGEN SATURATION:** below 90%.

[redacted] **20[redacted] SARS COV-2:** PHARYNGEAL EXUDATE; POSITIVE

NON SERIOUS EVENTS AND **OTHER AREAS OF SAFETY INTEREST

Neutropenia: Study drug was 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
乳房膿瘍	X			X
乳腺炎	X			X

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

Medical History	Onset Year
DIABETES TYPE 1	19[redacted]
LEFT SIDED UC	20[redacted]
ULCERATIVE COLITIS	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC) (2): FLEXIBLE SIGMOIDOSCOPY	20[redacted]
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
ULCERATIVE COLITIS DISEASE HISTORY: COLONOSCOPY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	0.01 PACK	20	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 57	57

M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 378

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BECLOMETASONE	3 mg	QD	Y-M: 20[redacted]
PREDNISONE	30 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
MESALAZINE	1000 mg	QD	Y-M: 20[redacted] / -331
MESALAZINE	4 g	QD	Y-M: 20[redacted] / -127
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -70
FENTANYL	50 ug	QD	Y-M: 20[redacted] / -62
MIDAZOLAM	2.5 mg	QD	Y-M: 20[redacted] / -62
ASCORBIC ACID;MACROGOL 3350;POTASSIUM;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -63
BISACODYL	10 mg	QD	Y-M: 20[redacted] / -64
FENTANYL	25 ug	QD	Y-M: 20[redacted] / -1
MIDAZOLAM	2.5 mg	QD	Y-M: 20[redacted] / -1
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -2
BISACODYL	10 mg	QD	Y-M: 20[redacted] / -3
INSULIN ASPART	100 OTHER: UNITS PER ML	PRN	Y: 19[redacted]
INSULIN DETEMIR	18 IU	QD	Y: 19[redacted]
MESALAZINE	4 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	4 g	QD	Y-M: 20[redacted] / -127	Y-M: 20[redacted] / 1
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -70	Y-M: 20[redacted] / 1
FENTANYL	25 ug	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
MIDAZOLAM	2.5 mg	QD	Y-M: 20[redacted] / -1	Y-M: 20[redacted] / -1
MACROGOL;POTASSIUM;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE	1 OTHER: SACHET	QD	Y-M: 20[redacted] / -2	Y-M: 20[redacted] / -1
BISACODYL	10 mg	QD	Y-M: 20[redacted] / -3	Y-M: 20[redacted] / -3

FLUCLOXACILLIN	500 mg	TID	Y-M: 20[redacted] / 13	Y-M: 20[redacted] / 23
FLUCLOXACILLIN	500 mg	QID	Y-M: 20[redacted] / 6	Y-M: 20[redacted] / 11
SULFAMETHOXAZOLE;TRIMETHOPRIM	960 mg	BID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 81
NAPROXEN	500 mg	BID	Y-M: 20[redacted] / 69	Y-M: 20[redacted] / 80
INSULIN ASPART	100 OTHER: UNITS PER ML	PRN	Y: 19[redacted]	ONGOING
INSULIN DETEMIR	18 IU	QD	Y: 19[redacted]	ONGOING

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

Event Description	MASTITIS LEFT BREAST
Preferred term	乳腺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 60
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 63): NPTST055-BACTERIA CULTURE: CITROBACTER KOSERI [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST176-CYTOLOGY: NO MALIGANCY [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 68): NPTST165-CRP: 21 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 70): NPTST280-HISTOLOGY: NO MALIGANCY [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 63): WOUND NPTST187-DRAINAGE CULTURE: POSITIVE-CITROBACTER KOSERI

AE Stopped Initial Rx Day	127
Duration of AE	68 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	BACTERIAL INFECTION WITH DIABETES
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	ABSCESS LEFT BREAST
Preferred term	乳房膿瘍
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 71
Age at AE Onset	3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 63): NPTST055-BACTERIA CULTURE: CITROBACTER KOSERI [NOT REPORTED - NOT

REPORTED] UNIT NOT REPORTED; NPTST176-CYTOLOGY: NO MALIGANCY [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 68): NPTST165-CRP: 21 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 70): NPTST280-HISTOLOGY: NO MALIGANCY [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED

Microbiology

[redacted]20[redacted] (RX DAY 63): WOUND NPTST187-DRAINAGE CULTURE: POSITIVE-CITROBACTER KOSERI

AE Stopped Initial Rx Day	127
Duration of AE	57 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	MASTITIS
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]:11:02

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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）の治験で盲検化された治験薬が投与され，左乳房の乳腺炎及び左乳房の膿瘍の事象を発現した。関連する病歴は，1 型糖尿病，潰瘍性大腸炎，現喫煙者（1 日 0.01 箱を 20 年間）及び現飲酒者（1 日 2 杯未満）であった。投与126日後＊　，被験者は左乳房の膿瘍の切開及び排膿の併用療法を受けていた。

Event 1 及び 2 の臨床経過：

投与60日後＊　，被験者は左乳房の乳腺炎を発現した。投与71日後＊　，被験者は左乳房の膿瘍を発現した。投与127日後＊，左乳房の乳腺炎及び左乳房の膿瘍は消失した。

投与122日後＊　，被験者は抗生物質の投与を開始した。投与125日後＊　，被験者は膿瘍のドレナージを受けたが成功しなかった。投与126日後＊　，被験者は午前中に左乳房の発熱，腫脹及び皮膚の赤みがあり来院し，入院した。乳房超音波検査が行われた。投与127日後＊，被

験者は左乳房の膿瘍切除術を受けた。投与128日後＊，被験者は退院した。

投与された薬剤は，ナプロキセン，オキノーム，floxapen 及び co-trimoxazol であった。

The patient's past medications include:

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

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

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

0MESALAZINE for ULCERATIVE COLITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Mastitis (10026883) (Mastitis (10026883)) [v.23.0] [10026883]

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) Abscess breast (10000275) (Breast abscess (10006171)) [v.23.0] [10000275]

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 MASTITIS LEFT BREAST

- Investigator: Bacterial infection with diabetes.

- AbbVie: Mastitis is most common in younger females. Current smoking (past 20 years) and pre-existing diabetes type 1 are additional risk factors for development of this event.

Event of ABSCESS LEFT BREAST

- Investigator: Mastitis

- AbbVie: Event more likely related to concurrent mastitis and diabetes mellitus.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BACTERIAL CULTURE:** CITROBACTER KOSERI

[redacted] **20[redacted] CRP:** 21 MG/L (normal 0 to 5)

[redacted] **20[redacted] CYTOLOGY:** no malignancy

[redacted] **20[redacted] DRAINAGE CULTURE:** positive for CITROBACTER KOSERI

[redacted] **20[redacted] HISTOLOGY:** no 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
尿閉	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
ENDOSCOPY (UC): COLONOSCOPY	20[redacted]
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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

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

M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 258	258

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	40 mg	QD	Y-M: 20[redacted]
PREDNISONE	20 mg	BID	Y-M: 20[redacted]
PREDNISOLONE	15 mg	BID	Y-M: 20[redacted]
MESALAZINE	1.5 g	QD	Y-M: 20[redacted] / -181
PREDNISONE	40 mg	QD	Y-M: 20[redacted] / -181
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: BAG	BID	Y-M: 20[redacted] / -85
ALFENTANIL	1.75 ug	PRN	Y-M: 20[redacted] / -62
FLUMAZENIL	0.1 mg	OTHER: ONCE	Y-M: 20[redacted] / -62
MIDAZOLAM	5 mg	PRN	Y-M: 20[redacted] / -62
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	1 OTHER: BAG	BID	Y-M: 20[redacted] / -63
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / -17
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 20[redacted]
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] / -181	ONGOING
PARACETAMOL	1 g	PRN	Y-M: 20[redacted] / -17	ONGOING
ATROPINE	0.6 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
BUPIVACAINE	100 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
DEXAMETHASONE	16 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104

FENTANYL	300 ug	OTHER: TOTAL AMOUNT	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
ONDANSETRON	4 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
OXYCODONE	5 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
OXYMETAZOLINE	0.5 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
PROPOFOL	939 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
REMIFENTANIL	2.635 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
TRAMADOL	50 mg	PRN	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 104
ETHINYLESTRADIOL;LEVONORGESTREL	1 ug	QD	Y: 20[redacted]	ONGOING

Event #1: Serious Adverse Event

Event Description	URINARY RETENTION
Preferred term	尿閉
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 160
Age at AE Onset	3[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	161
Duration of AE	2 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	PASIENT HAD A URINARY CATHETER DURING SURGERY. WHEN THEY REMOVED THE CATHETER THE SUBJECT WERE NOT ABLE TO URINATE, AND SUBJECT HAD TO STAY THE NIGHT OVER IN THE HOSPITAL TILL SUBJECT URINATED.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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）の治験で盲検化された治験薬が投与され，尿閉の事象を発現した。関連する病歴は，広範囲な潰瘍性大腸炎（全大腸炎型），虫垂切除術，右側の皮様嚢腫，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160日後＊，被験者は尿閉を発現した。投与161日後＊，尿閉は消失した。

被験者は，成長する右卵巣類皮嚢胞腫（非重篤）を有していた。投与160日後＊ ，被験者は予定された腹腔鏡下での嚢胞切除術のために入院した。被験者は手術中に尿道カテーテルを使用した。カテーテルを外した時，被験者は排尿できず，排尿できるようになるまで病院で一晩過ごさなければならなかった。被験者は排尿困難を経験した。投与161日後＊ ，尿閉は消失し，被験者は退院した。尿路感染症（非重篤）は 投与163日後＊ に診断され，セレキシド及びトリメトプリムで治療され，投与の約6ヵ月後＊に消失した。検査結果は正常で，他の処置も行われた。

投与された薬剤は，トラマドールであった。

Causality for ABT-494 (Blinded)

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1) Urinary retention (10046555) (Urinary retention (10046555)) [v.21.0] [10046555]

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

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

Dechallenge: Not Applicable

Alternative Etiology for ABT-494 (Blinded)

Event of URINARY RETENTION

- Investigator: Patient had a urinary catheter during surgery. When they removed the catheter the subject was not able to urinate, and the subject had to stay the night over in the hospital until the subject urinated.

- AbbVie: Event is more likely related to recent surgery and use of urinary catheter during the surgery.

Relevant Laboratory & Other Diagnostic Tests

Unknown date HISTOLOGY: Benign cystic teratomy

Unknown date VAGINAL ULTRASOUND: Showed classic dermoid at 60mm

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

Reason for Narrative

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

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	3[redacted]	FEMALE	WHITE

Medical History	Onset Year
EXTENSIVE UC/PANCOLITIS	20[redacted]
ULCERATIVE COLITIES	20[redacted]

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS2 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 62	62
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 364	364

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
MESALAZINE	1.5 mg	QD	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted]
MESALAZINE	2.4 g	BID	Y-M: 20[redacted]
PREDNISONE	40 mg	QD	Y-M: 20[redacted]
MESALAZINE	4.8 g	QD	Y-M: 20[redacted] / -181
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -175
ALFENTANIL	25 ug	OTHER: ONCE	Y-M: 20[redacted] / -69
MIDAZOLAM	2.5 mg	OTHER: ONCE	Y-M: 20[redacted] / -69
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: DOSE-BAGS	OTHER: ONCE	Y-M: 20[redacted] / -70
CITRIC ACID;MAGNESIUM OXIDE;SODIUM PICOSULFATE	2 OTHER: DOSE-BAGS	OTHER: ONCE	Y-M: 20[redacted] / -1
BCG Vaccine	NOT REPORTED	NOT REPORTED	Y: 19[redacted]
ETHINYLESTRADIOL;LEVONORGESTREL	100 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	4.8 g	QD	Y-M: 20[redacted] / -181	ONGOING
BENZYLPENICILLIN	1.2 g	QID	Y-M: 20[redacted] / 125	Y-M: 20[redacted] / 128
PHENOXYMETHYLPENICILLIN	660 mg	QID	Y-M: 20[redacted] / 128	Y-M: 20[redacted] / 134
ETHINYLESTRADIOL;LEVONORGESTREL	100 ug	QD	Y: 20[redacted]	ONGOING

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

Event Description TONSILLITIS

Preferred term 扁桃炎

AE Onset Date / Initial Rx Day [redacted]20[redacted] / 176

Age at AE Onset 3[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 125): Leukocytes: 16.5 [3.5 - 8.8] 10^9/L; NPTST165-CRP: 190 [0 - 5] MG/L; NPTST345-MICROBIOLOGY: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 126): Leukocytes: 10.7 [3.5 - 8.8] 10^9/L; NPTST165-CRP: 130 [0 - 5] MG/L; [redacted]20[redacted] (RX DAY 128): Leukocytes: 8.8 [3.5 - 8.8] 10^9/L; NPTST165-CRP: 32 [0 - 5] MG/L

Microbiology

[redacted]20[redacted] (RX DAY 125): URINE NPTST346-MICROBIOLOGY TEST: NEGATIVE; SPUTUM NPTST493-STREP-A RAPID TEST: POSITIVE-GROUP A STREPTOCOCCUS; [redacted]20[redacted] (RX DAY 126): STOOL NPTST123-

CLOSTRIDIUM: NEGATIVE; STOOL NPTST491-STOOL CULTURE: NEGATIVE

AE Stopped Initial Rx Day	208
Duration of AE	33 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	INFECTION
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted] 20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

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）の治験で盲検化された治験薬が投与され，扁桃炎の事象を発現した。関連する病歴は，潰瘍性大腸炎（全大腸炎型），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176日後＊，被験者は扁桃炎を発現した。投与208日後＊，扁桃炎は消失した。

入院前，被験者は 投与176日後＊から胃部不快感及び排便回数の増加があり，また，投与182日後＊から咽頭痛及び発熱があった。

投与182日後＊　　，被験者は入院した。被験者は抗生物質の静脈内投与を開始した。糞便検査では，A 群レンサ球菌迅速検査で A 群レンサ球菌が陽性であった以外は，全て陰性であった。被験者は排便回数が減少し，咽頭痛もなく，臨床的に改善した。投与190日後＊，被験者は抗生物質を経口投与され，退院した。

投与された薬剤は，ベンジルペニシリン及び apocillin であった。

The patient's past medications include:

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

ENTOCORT for ULCERATIVE COLITIS ([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 (Blinded)

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1) Tonsillitis (10044008) (Tonsillitis (10044008)) [v.22.1] [10044008]

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 TONSILLITIS

- Investigator: Infection.

- AbbVie: Event is due to Strep A Streptococcus species which is estimated to cause 5%-15% of all pharyngitis/tonsillitis infections in adults. Additionally, incidence of Strep A pharyngitis/tonsillitis increases in winter.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CRP:** 190 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 130 MG/L (normal 0 to 5)

[redacted] **20[redacted] CRP:** 32 MG/L (normal 0 to 5)

[redacted] **20[redacted] STOOL CULTURE:** CLOSTRIDIUM: NEGATIVE

[redacted] **20[redacted] STREP A RAPID TEST:** POSITIVE: GROUP A STREPTOCOCCUS

[redacted] **20[redacted] URINE TEST:** MICROBIOLOGY: NEGATIVE

[redacted] **20[redacted] WBC:** 16.5 X10**9/L (normal 3.5 to 8.8)

[redacted] **20[redacted] WBC:** 8.8 X10**9/L (normal 3.5 to 8.8)

[redacted] **20[redacted] X-RAY:** THORAX: 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
肺炎	X			X

Treatment Group	Age at Induction Study Start	Sex	Race
Placebo	5[redacted]	FEMALE	WHITE

Medical History	Onset Year
ALLERGY	19[redacted]
ASTHMA	20[redacted]
CHRONIC BRONCHITIS	20[redacted]
EXTENSIVE UC/PANCOLITIS	19[redacted]
OPERATED COLOVESICAL FISTULA	20[redacted]
PERIODONTITIS	20[redacted]
TRANSURETHRAL RESECTION OFF BLADDERTUMOR	20[redacted]

Prior Procedures	Procedure Year
SAE SUPPLEMENTAL PROCEDURE: X-RAY THORAX	20[redacted]
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	36	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

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

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-675 ABT-494 (IND)	45 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 58	58
M14-234 SS3 Placebo (MAIN)		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 266	266

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PREDNISOLONE	31.25 mg	QD	Y-M: 20[redacted]
AZATHIOPRINE	100 mg	QD	Y-M: 20[redacted]
INFLIXIMAB	5.000 mg/kg	EVERY 8 WEEKS	Y-M: 20[redacted]
MESALAZINE	4.5 g	QD	Y-M: 20[redacted]
PREDNISOLONE	40 mg	QD	Y-M: 20[redacted]
FLUTICASONE;VILANTEROL	184/22 mg	QD	Y-M: 20[redacted]
PREDNISOLONE	20 mg	BID	Y-M: 20[redacted]
VEDOLIZUMAB	300.000 mg	EVERY 8 WEEKS	Y-M: 20[redacted]
BUDESONIDE	9 mg	QD	Y-M: 20[redacted] / -149
DESLORATADINE	5 mg	QD	Y: 20[redacted]
AZELASTINE;FLUTICASONE	1 OTHER: DOSE SPRAY	PRN	Y: 20[redacted]
IPRATROPIUM	250 OTHER: MG/1ML	PRN	Y: 20[redacted]
SALBUTAMOL	1 OTHER: MG/ML	PRN	Y: 20[redacted]
MONTELUKAST	10 mg	QD	Y: 20[redacted]
TIOTROPIUM	2.5 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
MESALAZINE	4.5 g	QD	Y-M: 20[redacted]	ONGOING
FLUTICASONE;VILANTEROL	184/22 mg	QD	Y-M: 20[redacted]	ONGOING
AMOXICILLIN	500 mg	TID	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 117
PREDNISONE	30 mg	QD	Y-M: 20[redacted] / 110	Y-M: 20[redacted] / 114
DESLORATADINE	5 mg	QD	Y: 20[redacted]	ONGOING
AZELASTINE;FLUTICASONE	1 OTHER: DOSE SPRAY	PRN	Y: 20[redacted]	ONGOING
IPRATROPIUM	250 OTHER: MG/1ML	PRN	Y: 20[redacted]	ONGOING
SALBUTAMOL	1 OTHER: MG/ML	PRN	Y: 20[redacted]	ONGOING

MONTELUKAST	10 mg	QD	Y: 20[redacted]	ONGOING
TIOTROPIUM	2.5 mg	BID	Y: 20[redacted]	ONGOING

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

Event Description	PNEUMONI
Preferred term	肺炎
AE Onset Date / Initial Rx Day	[redacted]20[redacted] / 165
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
AE Stopped Initial Rx Day	182
Duration of AE	18 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
Investigator Alternative Etiology	UNKNOWN
Discontinued Study Drug Due to the Event	NO
SAE Criteria	HOSPITALIZATION OR PROLONGED HOSPITALIZATION

Generated: [redacted]20[redacted]:11:02
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M14-234

治験責任医師からの報告。本被験者はノルウェーの 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，肺炎の事象を発現した。関連する病歴は，潰瘍性大腸炎，喘息，慢性気管支炎，現喫煙者（1 日 0.25 箱を 36 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165日後＊，被験者は肺炎を発現した。投与182日後＊，肺炎は消失した。

投与168日後＊　，被験者は緑色の喀痰を伴う咳嗽，発熱，呼吸困難及び胸部不快感があり，入院した。被験者は，治療後に気分が良くなった。投与170日後＊，被験者は退院した。

投与された薬剤は，アモキシシリン，アトロベント，ventoline 及び prednisone であった。

The patient's past medications include:

PRED-CLYSMA for ULCERATIVE COLITIS ([redacted])

PREDNISOLON for ULCERATIVE COLITIS ([redacted])

IMUREL for ULCERATIVE COLITIS ([redacted])

INFLIXIMAB for ULCERATIVE COLITIS ([redacted])

ENTYVIO for ULCERATIVE COLITIS ([redacted])

CORTIMENT for ULCERATIVE COLITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of PNEUMONI

- Investigator: Unknown

- AbbVie: Risk factors include pre-existing asthma, chronic bronchitis, current and long term smoking history of 0.25 packs per day for 36 years.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] X-RAY THORAX:** Two small atelectasis embossed stripe-shaped densities basolaterally right side. Pneumonia? No signs of pleural fluid.

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

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
肝炎				X
伝染性単核症	X			X

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

Medical History	Onset Year
LEFT SIDED UC	20[redacted]
OTHER: GILBERT SYNDROM	NOT REPORTED

Prior Procedures	Procedure Year
ENDOSCOPY (UC): COLONOSCOPY	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			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route of Administration	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
M14-234 SS1 ABT-494 (IND)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 56	56
M14-234 SS3 ABT-494 (MAIN)	15 mg	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 307	307