重篤な有害事象の叙述

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
ニューモシスチス・イロベチイ肺炎	X	X		X

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo /P2:Upa 15 mg QD	5[redacted]	MALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
ASTHMA	19[redacted]
RHINITIS ALLERGIC	19[redacted]
DEPRESSION	20[redacted]
INSOMNIA	20[redacted]
PHLEGMONE	20[redacted]
POST INFLAMMATORY PIGMENTATION	20[redacted]
ALCOHOLIC HEPATITIS	20[redacted]
HYPOTHYROIDISM	20[redacted]
AST HIGH	20[redacted]
ESSENTIAL HYPERTENSION	20[redacted]
LONG QT SYNDROME	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED
GALLSTONES	NOT REPORTED
SPLEOMEGALY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 CIGARETTE	17	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
P1:Placebo		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 112	112
P2:ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 113	[redacted]20[redacted] / 183	71

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BETAMETHASONE	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted]
EPINASTINE	20 mg	QD	Y-M: 20[redacted]
STELAMIN	1 OTHER: TABLETS	PRN	Y-M: 20[redacted]
TACROLIMUS	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted]
BETAMETHASONE	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted]
EPINASTINE	20 mg	QD	Y-M: 20[redacted]
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted]
STELAMIN	1 OTHER: TABLETS	PRN	Y-M: 20[redacted]
TACROLIMUS	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted]
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted]
VALISONE-G	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted]
CINAL	1 OTHER: TABLETS	TID	Y-M: 20[redacted]
TACROLIMUS	APPLICATION OTHER: APPLICATION	PRN	Y-M: 20[redacted]
CLONAZEPAM	0.5 mg	QD	Y-M: 20[redacted] / -342
LEVOTHYROXINE	12.5 ug	QD	Y-M: 20[redacted] / -342
VENLAFAXINE	150 mg	QD	Y-M: 20[redacted] / -342
SUVOREXANT	20 mg	QD	Y-M: 20[redacted] / -283
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / -181
HEPARINOID	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted] / -97
WHITE SOFT PARAFFIN	PROPER DOSE OTHER: APPLICATION	BID	Y-M: 20[redacted] / -63
AMLODIPINE	2.5 mg	QD	Y-M: 20[redacted] / -51
AMLODIPINE	5 mg	QD	Y-M: 20[redacted] / -36
TRAZODONE	25 mg	QD	Y-M: 20[redacted] / -20

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
EPINASTINE	20 mg	QD	Y-M: 20[redacted]	NOT REPORTED

FEXOFENADINE	60 mg	BID	Y-M: 20[redacted]	NOT REPORTED
CINAL	1 OTHER: TABLETS	TID	Y-M: 20[redacted]	Y-M: 20[redacted] / 188
LEVOTHYROXINE	12.5 ug	QD	Y-M: 20[redacted] / - 342	NOT REPORTED
VENLAFAXINE	150 mg	QD	Y-M: 20[redacted] / - 342	NOT REPORTED
SUVOREXANT	20 mg	QD	Y-M: 20[redacted] / - 283	NOT REPORTED
HYDROXYZINE	25 mg	QD	Y-M: 20[redacted] / - 181	NOT REPORTED
HEPARINOID	PROPER DOSE OTHER: APPLICATION	PRN	Y-M: 20[redacted] / - 97	NOT REPORTED
TRAZODONE	25 mg	QD	Y-M: 20[redacted] / - 20	NOT REPORTED
CANDESAR A	1 OTHER: TABLETS	QD	Y-M: 20[redacted] / 9	NOT REPORTED
ALPRAZOLAM	0.4 mg	PRN	Y-M: 20[redacted] / 15	NOT REPORTED
HERBAL PREPARATION	3 OTHER: TABLET	TID	Y-M: 20[redacted] / 183	Y-M: 20[redacted] / 183
AMBROXOL	15 mg	TID	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 187
CEFDITOREN	100 mg	TID	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 187
DIMEMORFAN	20 mg	TID	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 187
IBUPROFEN	200 mg	TID	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 187
CEFTRIAXONE	1 g	QD	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 188
ESZOPICLONE	1 mg	QD	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 188
MINOCYCLINE	100 mg	QD	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 188
LOXOPROFEN	60 mg	QD	Y-M: 20[redacted] / 188	Y-M: 20[redacted] / 189
ASCORBIC ACID	1 OTHER: PACKAGE	TID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 189
METHYLPREDNISOLONE	500 mg	QD	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 191
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 192
MINOCYCLINE	100 mg	BID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 192
BACTRIM	3 OTHER: TABLET	TID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 197
REBAMIPIDE	100 mg	TID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 201
FAMOTIDINE	10 mg	BID	Y-M: 20[redacted] / 189	Y-M: 20[redacted] / 204

ASCORBIC ACID	1 OTHER: PACKAGE	TID	Y-M: 20[redacted]-[redacted] / 190	Y-M: 20[redacted]-[redacted] / 218
PREDNISOLONE	30 mg	BID	Y-M: 20[redacted]-[redacted] / 192	Y-M: 20[redacted]-[redacted] / 194
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted]-[redacted] / 195	Y-M: 20[redacted]-[redacted] / 197
LOXOPROFEN	60 mg	QD	Y-M: 20[redacted]-[redacted] / 197	Y-M: 20[redacted]-[redacted] / 199
BACTRIM	3 OTHER: TABLET	QD	Y-M: 20[redacted]-[redacted] / 198	Y-M: 20[redacted]-[redacted] / 198
MOXIFLOXACIN	400 mg	QD	Y-M: 20[redacted]-[redacted] / 198	Y-M: 20[redacted]-[redacted] / 201
PREDNISOLONE	15 mg	QD	Y-M: 20[redacted]-[redacted] / 198	Y-M: 20[redacted]-[redacted] / 201
TACROLIMUS	PROPER DOSE OTHER: APPLICATION	QD	Y-M: 20[redacted]-[redacted] / 211	NOT REPORTED
WHITE SOFT PARAFFIN	PROPER DOSE OTHER: APPLICATION	QD	Y-M: 20[redacted]-[redacted] / 211	NOT REPORTED
FLUOCINONIDE	PROPER DOSE OTHER: APPLICATION	QD	Y-M: 20[redacted]-[redacted] / 211	Y-M: 20[redacted]-[redacted] / 224

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 Zosters

Event Description PNEUMOCYSTIS PNEUMONIA

Preferred term ニューモシスチス・イロベチイ肺炎

AE Onset Date / Rx Day [redacted]20[redacted] / 188 (5 DAYS AFTER LAST TREATMENT)

Age at AE Onset 5[redacted]

Laboratory Testing [redacted]20[redacted] (RX DAY 174): Chloride: 102 [98 - 108] MMOL/L; [redacted]20[redacted] (RX DAY 188): Alanine Aminotransferase: 53 [5 - 35] U/L; Albumin: 38 [38 - 52] G/L; Alkaline Phosphatase: 235 [100 - 360] U/L; Aspartate Aminotransferase: 64 [10 - 35] U/L; Basophils: 0.018 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0.3 [0 - 2] %; Bilirubin: 32 [3 - 19] UMOL/L; Blood Urea Nitrogen: 4.2 [2.9 - 8.2] MMOL/L; Calcium: 2.2 [2.07 - 2.59] MMOL/L; Chloride: 99 [98 - 108] MMOL/L; Cholesterol: 4.37 [3.36 - 5.69] MMOL/L; Creatine Kinase: 109 [60 - 270] U/L; Creatinine: 83 [53 - 106] UMOL/L; Eosinophils: 0.048 [0 - 0.43] 10^9/L; Eosinophils/Leukocytes: 0.8 [0 - 5] %; Erythrocytes: 2.7 [4.3 - 5.5] 10^12/L; Glucose: 6.7 [3.9 - 6.1] MMOL/L; Glucose: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; Hematocrit: 0.27 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 91 [135 - 170] G/L; Leukocytes: 6 [4 - 8.5] 10^9/L; Lymphocytes: 1.122 [0.96 - 4.75] 10^9/L; Lymphocytes/Leukocytes: 18.7 [18 - 52] %; Monocytes: 1.074 [0.1 - 0.97] 10^9/L; Monocytes/Leukocytes: 17.9 [3 - 9] %; NPTST001-A/G: 0.97 [1.2 - 2.1] RATIO; NPTST004-AMYLASE: 67 [35 - 125] U/L; NPTST005-ANA: LESS THAN 40 [0 - 39.999] TIMES; NPTST006-ANA(CYTOPLASMIC): NOT DETECTED [NOT REPORTED - NOT REPORTED] TIMES; NPTST007-ANA(DISCRETE SP.): NOT DETECTED [NOT REPORTED - NOT REPORTED] TIMES; NPTST008-ANA(HEMOGENEOUS): NOT DETECTED [NOT REPORTED - NOT REPORTED] TIMES; NPTST009-ANA(NUCLEOLAR): NOT DETECTED [NOT REPORTED - NOT REPORTED] TIMES; NPTST010-ANA(OTHER CHROMOSOME TYPE 1): NOT DETECTED [NOT REPORTED - NOT REPORTED] TIMES; NPTST011-ANA(OTHER CHROMOSOME TYPE2): NOTO DETECTED [NOT REPORTED - NOT REPORTED] TIMES; NPTST012-ANA(SPECKLED): NOT DETECTED [NOT REPORTED - NOT REPORTED] TIMES; NPTST014-APTT(ACTIVITY): 78 [70 - 130] %; NPTST015-APTT(CONTROL): 28.7 [NOT REPORTED - NOT REPORTED] sec; NPTST016-APTT(SEC): 32.1 [NOT REPORTED - NOT REPORTED] sec; NPTST017-ATYPICAL LYMPHOCYTE: 0 [0 - 0] %; NPTST020-BETA-D-GLUCAN: 200 [0 - 20] PG/ML; NPTST021-BLOOD GAS(BE): 1 [-2 - 2] MMOL/L; NPTST022-BLOOD GAS(BODY TEMPERATURE): 37.0 [NOT REPORTED - NOT REPORTED] DEGREE; NPTST023-BLOOD GAS(HCO3): 24.7 [21 - 29] MMOL/L; NPTST024-

BLOOD GAS(HEMOGLOBIN): 9.1 [NOT REPORTED - NOT REPORTED] g/dL; NPTST025-BLOOD GAS(O2CT): 12.1 [18 - 22] ML/DL; NPTST026-BLOOD GAS(O2SAT): 93.9 [92 - 96] %; NPTST027-BLOOD GAS(PCO2): 35.5 [32 - 46] MMHG; NPTST028-BLOOD GAS(PH): 7.46 [7.38 - 7.46] N/A; NPTST029-BLOOD GAS(PO2): 65 [74 - 108] MMHG; NPTST030-BNP: 20.5 [0 - 18.4] PG/ML; NPTST033-CHOLINESTERASE: 95 [200 - 470] U/L; NPTST035-CMV IGG(EIA): 20.6 [0 - 2] N/A; NPTST037-CMV IGM(INDEX): 1.09 [0 - 0.8] N/A; NPTST040-CRP: 12.68 [0 - 0.3] MG/DL; NPTST042-D-DIMER QUANTITATIVE: 800 [0 - 1000] NG/ML; NPTST043-DIRECT BILIRUBIN: 1.1 [0 - 0.4] MG/DL; NPTST046-EGFR: 67.16 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST047-ERYTHROBLAST: 0 [0 - 0] N/A; NPTST048-FIBRINOGEN: 604 [200 - 400] MG/DL; NPTST050-GAMMA-GTP: 787 [0 - 80] U/L; NPTST051-HBS ANTIGEN(SEMIQUANTITATIVE): LESS THAN 8 [0 - 7.999] N/A; NPTST052-HCV ANTIBODY(DETERMINATION): NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; NPTST053-HCV ANTIBODY(IDX): 0.1 [0 - 0.99] N/A; NPTST056-IGA: 598 [110 - 410] MG/DL; NPTST057-IGE(IGE NON-SPECIFIC): 11500 [0 - 173] IU/ML; NPTST058-IGG: 1346 [870 - 1700] MG/DL; NPTST059-IGM: 59 [33 - 190] MG/DL; NPTST060-KL-6: 320 [0 - 500] U/ML; NPTST062-LDH: 333 [110 - 240] U/L; NPTST063-MCH: 33.6 [27 - 35] PG; NPTST064-MCHC: 34 [31 - 36] G/DL; NPTST065-MCV: 99 [83 - 98] FL; NPTST066-METAMYELOCYTE: 0 [0 - 0] %; NPTST070-MYELOBLAST: 0 [0 - 0] %; NPTST071-MYELOCYTE: 0 [0 - 0] %; NPTST075-PERIPHERAL: NOT DETECTED [NOT REPORTED - NOT REPORTED] TIMES; NPTST076-PROCALCITONIN: LESS THAN 0.5~2 [NOT REPORTED - NOT REPORTED] ng/dL; NPTST077-PROMYELOCYTE: 0 [0 - 0] %; NPTST079-PT TIME(ACTIVITY): 54 [70 - 130] %; NPTST080-PT TIME(CONTROL): 11.5 [NOT REPORTED - NOT REPORTED] sec; NPTST081-PT TIME(INR): 1.34 [NOT REPORTED - NOT REPORTED] N/A; NPTST082-PT TIME(SEC): 15.4 [NOT REPORTED - NOT REPORTED] sec; NPTST087-PULMONARY SURFACTANT PROTEIN D: 27 [0 - 110] NG/ML; NPTST089-RF(QUANTITATIVE): 13 [0 - 15] IU/ML; NPTST090-RPR: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; NPTST093-TPHA: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; NPTST096-URIN PROTEIN: +/- [NOT REPORTED - NOT REPORTED] N/A; NPTST097-URINARY OCCULT BLOOD: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; NPTST099-URINARY SEDIMENT(BACTERIA): 1+ [NOT REPORTED - NOT REPORTED] N/A; NPTST100-URINARY SEDIMENT(GLITTER CELL): 1+ [NOT REPORTED - NOT REPORTED] N/A; NPTST101-URINARY SEDIMENT(HYALINE CAST): 1 [NOT REPORTED - NOT REPORTED] /2-5 VISUAL FIELDS; NPTST102-URINARY SEDIMENT(MUCUS): 1+ [NOT REPORTED - NOT REPORTED] N/A; NPTST103-URINARY SEDIMENT(RED BLOOD CELL: BELOW 1 [NOT REPORTED - NOT REPORTED] /10 VISUAL FIELD; NPTST104-URINARY SEDIMENT(SQUAMOUS CELL): 1~4 [NOT REPORTED - NOT REPORTED] /VF; NPTST106-URINARY SEDIMENT(URINARY TRACRT: BELOW 1 [NOT REPORTED - NOT REPORTED] /10 VISUAL FIELD; NPTST108-URINARY SEDIMENT(WHITE BLOOD CE: 20~29 [NOT REPORTED - NOT REPORTED] /VF; NPTST109-URINE BILIRUBIN: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; NPTST110-URINE KETON BODY: NEGATIVE [NOT REPORTED - NOT REPORTED] N/A; NPTST115-UROBILINOGEN: 2+ [NOT REPORTED - NOT REPORTED] N/A; Neutrophils: 3.738 [2.4 - 7.56] 10^9/L; Neutrophils/Leukocytes: 62.3 [40 - 79] %; Platelets: 135 [130 - 350] 10^9/L; Potassium: 3.8 [3.5 - 5] MMOL/L; Protein: 77 [65 - 82] G/L; Sodium: 135 [137 - 147] MMOL/L; Triglycerides: 1.25 [0.34 - 1.7] MMOL/L; Urate: 345.01 [214.14 - 416.39] UMOL/L; [redacted]20[redacted] (RX DAY 191): Alanine Aminotransferase: 54 [5 - 35] U/L; Albumin: 33 [38 - 52] G/L; Aspartate Aminotransferase: 68 [10 - 35] U/L; Basophils: 0.014 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0.1 [0 - 2] %; Bilirubin: 10 [3 - 19] UMOL/L; Blood Urea Nitrogen: 6 [2.9 - 8.2] MMOL/L; Calcium: 2.1 [2.07 - 2.59] MMOL/L; Chloride: 108 [98 - 108] MMOL/L; Creatine Kinase: 62 [60 - 270] U/L; Creatinine: 57 [53 - 106] UMOL/L; Eosinophils: 0 [0 - 0.43] 10^9/L; Eosinophils/Leukocytes: 0 [0 - 5] %; Erythrocytes: 2.4 [4.3 - 5.5] 10^12/L; Glucose: 8.3 [3.9 - 6.1] MMOL/L; Hematocrit: 0.24 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 82 [135 - 170] G/L; Leukocytes: 14.4 [4 - 8.5] 10^9/L; Lymphocytes: 5.573 [0.96 - 4.75] 10^9/L; Lymphocytes/Leukocytes: 38.7 [18 - 52] %; Monocytes: 1.022 [0.1 - 0.97] 10^9/L; Monocytes/Leukocytes: 7.1 [3 - 9] %; NPTST001-A/G: 0.94 [1.2 - 2.1] RATIO; NPTST017-ATYPICAL LYMPHOCYTE: 0 [0 - 0] %; NPTST033-CHOLINESTERASE: 75 [200 - 470] U/L; NPTST040-CRP: 5.82 [0 - 0.3] MG/DL; NPTST046-EGFR: 100.55 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST047-ERYTHROBLAST: 0 [0 - 0] N/A; NPTST050-GAMMA-GTP: 530 [0 - 80] U/L; NPTST061-LD: 342 [110 - 240] U/L; NPTST063-MCH: 33.6 [27 - 35] PG; NPTST064-MCHC: 34.2 [31 - 36] G/DL; NPTST065-MCV: 98 [83 - 98] FL; NPTST066-METAMYELOCYTE: 0 [0 - 0] %; NPTST070-MYELOBLAST: 0 [0 - 0] %; NPTST071-

MYELOCYTE: 0 [0 - 0] %; NPTST077-PROMYELOCYTE: 0 [0 - 0] %; Neutrophils: 7.79 [2.4 - 7.56] 10^9/L; Neutrophils/Leukocytes: 54.1 [40 - 79] %; Platelets: 136 [130 - 350] 10^9/L; Potassium: 3.9 [3.5 - 5] MMOL/L; Protein: 68 [65 - 82] G/L; Sodium: 139 [137 - 147] MMOL/L; Urate: 208.2 [214.14 - 416.39] UMOL/L; [redacted]20[redacted] (RX DAY 196): Alanine Aminotransferase: 120 [5 - 35] U/L; Albumin: 39 [38 - 52] G/L; Alkaline Phosphatase: 256 [100 - 360] U/L; Aspartate Aminotransferase: 67 [10 - 35] U/L; Basophils: 0.062 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0.5 [0 - 2] %; Bilirubin: 14 [3 - 19] UMOL/L; Blood Urea Nitrogen: 6.3 [2.9 - 8.2] MMOL/L; Calcium: 2.32 [2.07 - 2.59] MMOL/L; Chloride: 105 [98 - 108] MMOL/L; Creatine Kinase: 32 [60 - 270] U/L; Creatinine: 92 [53 - 106] UMOL/L; Eosinophils: 0.185 [0 - 0.43] 10^9/L; Eosinophils/Leukocytes: 1.5 [0 - 5] %; Erythrocytes: 3.1 [4.3 - 5.5] 10^12/L; Glucose: 4.1 [3.9 - 6.1] MMOL/L; Hematocrit: 0.3 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 102 [135 - 170] G/L; Leukocytes: 12.3 [4 - 8.5] 10^9/L; Lymphocytes: 3.936 [0.96 - 4.75] 10^9/L; Lymphocytes/Leukocytes: 32 [18 - 52] %; Monocytes: 0.763 [0.1 - 0.97] 10^9/L; Monocytes/Leukocytes: 6.2 [3 - 9] %; NPTST001-A/G: 1.08 [1.2 - 2.1] RATIO; NPTST017-ATYPICAL LYMPHOCYTE: 0 [0 - 0] %; NPTST033-CHOLINESTERASE: 93 [200 - 470] U/L; NPTST040-CRP: 0.33 [0 - 0.3] MG/DL; NPTST046-EGFR: 60.13 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST047-ERYTHROBLAST: 0 [0 - 0] N/A; NPTST050-GAMMA-GTP: 502 [0 - 80] U/L; NPTST061-LD: 316 [110 - 240] U/L; NPTST063-MCH: 33.4 [27 - 35] PG; NPTST064-MCHC: 33.9 [31 - 36] G/DL; NPTST065-MCV: 99 [83 - 98] FL; NPTST066-METAMYELOCYTE: 0 [0 - 0] %; NPTST070-MYELOBLAST: 0 [0 - 0] %; NPTST071-MYELOCYTE: 0 [0 - 0] %; NPTST077-PROMYELOCYTE: 0 [0 - 0] %; Neutrophils: 7.355 [2.4 - 7.56] 10^9/L; Neutrophils/Leukocytes: 59.8 [40 - 79] %; Platelets: 177 [130 - 350] 10^9/L; Potassium: 4.5 [3.5 - 5] MMOL/L; Protein: 75 [65 - 82] G/L; Sodium: 135 [137 - 147] MMOL/L; Urate: 339.06 [214.14 - 416.39] UMOL/L; [redacted]20[redacted] (RX DAY 198): Alanine Aminotransferase: 73 [5 - 35] U/L; Albumin: 38 [38 - 52] G/L; Alkaline Phosphatase: 283 [100 - 360] U/L; Aspartate Aminotransferase: 29 [10 - 35] U/L; Basophils: 0.014 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0.1 [0 - 2] %; Bilirubin: 10 [3 - 19] UMOL/L; Blood Urea Nitrogen: 10.9 [2.9 - 8.2] MMOL/L; Calcium: 2.5 [2.07 - 2.59] MMOL/L; Chloride: 103 [98 - 108] MMOL/L; Creatine Kinase: 30 [60 - 270] U/L; Creatinine: 147 [53 - 106] UMOL/L; Eosinophils: 0.043 [0 - 0.43] 10^9/L; Eosinophils/Leukocytes: 0.3 [0 - 5] %; Erythrocytes: 3.1 [4.3 - 5.5] 10^12/L; Glucose: 4.4 [3.9 - 6.1] MMOL/L; Glucose: - [NOT REPORTED - NOT REPORTED] N/A; Hematocrit: 0.3 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 103 [135 - 170] G/L; Leukocytes: 14.3 [4 - 8.5] 10^9/L; Lymphocytes: 2.36 [0.96 - 4.75] 10^9/L; Lymphocytes/Leukocytes: 16.5 [18 - 52] %; Monocytes: 0.329 [0.1 - 0.97] 10^9/L; Monocytes/Leukocytes: 2.3 [3 - 9] %; NPTST001-A/G: 1.12 [1.2 - 2.1] RATIO; NPTST017-ATYPICAL LYMPHOCYTE: 0 [0 - 0] %; NPTST033-CHOLINESTERASE: 80 [200 - 470] U/L; NPTST040-CRP: 1.76 [0 - 0.3] MG/DL; NPTST046-EGFR: 36.05 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST047-ERYTHROBLAST: 0 [0 - 0] N/A; NPTST050-GAMMA-GTP: 390 [0 - 80] U/L; NPTST061-LD: 247 [110 - 240] U/L; NPTST063-MCH: 33.7 [27 - 35] PG; NPTST064-MCHC: 34.1 [31 - 36] G/DL; NPTST065-MCV: 99 [83 - 98] FL; NPTST066-METAMYELOCYTE: 0 [0 - 0] %; NPTST070-MYELOBLAST: 0 [0 - 0] %; NPTST071-MYELOCYTE: 0 [0 - 0] %; NPTST077-PROMYELOCYTE: 0 [0 - 0] %; NPTST096-URIN PROTEIN: +/- [NOT REPORTED - NOT REPORTED] N/A; NPTST097-URINARY OCCULT BLOOD: - [NOT REPORTED - NOT REPORTED] N/A; NPTST098-URINARY SEDIMANT(MUCUS): 1+ [NOT REPORTED - NOT REPORTED] N/A; NPTST099-URINARY SEDIMENT(BACTERIA): 2+ [NOT REPORTED - NOT REPORTED] N/A; NPTST101-URINARY SEDIMENT(HYALINE CAST): 1~4 [NOT REPORTED - NOT REPORTED] /VF; NPTST103-URINARY SEDIMENT(RED BLOOD CELL: BELOW 1 [NOT REPORTED - NOT REPORTED] /10 VISUAL FIELD; NPTST104-URINARY SEDIMENT(SQUAMOUS CELL): 1~4 [NOT REPORTED - NOT REPORTED] /VF; NPTST105-URINARY SEDIMENT(URIC ACID CRYS: 1+ [NOT REPORTED - NOT REPORTED] N/A; NPTST107-URINARY SEDIMENT(URINARY TRACT: 1 [NOT REPORTED - NOT REPORTED] /2-5 VISUAL FIELD; NPTST108-URINARY SEDIMENT(WHITE BLOOD CE: 1~4 [NOT REPORTED - NOT REPORTED] /VF; NPTST109-URINE BILIRUBIN: - [NOT REPORTED - NOT REPORTED] N/A; NPTST111-URINE KETONE BODY: - [NOT REPORTED - NOT REPORTED] N/A; NPTST114-URINRY SEDIMENT(TUBALAR EPITHEL: 1~4 [NOT REPORTED - NOT REPORTED] /VF; Neutrophils: 11.554 [2.4 - 7.56] 10^9/L; Neutrophils/Leukocytes: 80.8 [40 - 79] %; Platelets: 133 [130 - 350] 10^9/L; Potassium: 5.1 [3.5 - 5] MMOL/L; Protein: 72 [65 - 82] G/L; Sodium: 133 [137 - 147] MMOL/L; Urate: 345.01 [214.14 - 416.39] UMOL/L; Urobilinogen: +/- [NOT REPORTED - NOT REPORTED] N/A; [redacted]20[redacted] (RX DAY 201): Alanine Aminotransferase: 45 [5 - 35] U/L; Albumin: 35 [38 - 52] G/L; Alkaline Phosphatase: 288 [100 - 360] U/L; Aspartate Aminotransferase: 22 [10 - 35] U/L; Basophils: 0.061 [0 -

	0.22] 10^9/L; Basophils/Leukocytes: 0.4 [0 - 2] %; Bilirubin: 9 [3 - 19] UMOL/L; Blood Urea Nitrogen: 5.9 [2.9 - 8.2] MMOL/L; Calcium: 2.42 [2.07 - 2.59] MMOL/L; Chloride: 106 [98 - 108] MMOL/L; Creatinine: 84 [53 - 106] UMOL/L; Eosinophils: 0.334 [0 - 0.43] 10^9/L; Eosinophils/Leukocytes: 2.2 [0 - 5] %; Erythrocytes: 2.7 [4.3 - 5.5] 10^12/L; Glucose: 4 [3.9 - 6.1] MMOL/L; Hematocrit: 0.27 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 91 [135 - 170] G/L; Leukocytes: 15.2 [4 - 8.5] 10^9/L; Lymphocytes: 8.482 [0.96 - 4.75] 10^9/L; Lymphocytes/Leukocytes: 55.8 [18 - 52] %; Monocytes: 0.775 [0.1 - 0.97] 10^9/L; Monocytes/Leukocytes: 5.1 [3 - 9] %; NPTST001-A/G: 0.88 [1.2 - 2.1] RATIO; NPTST017-ATYPICAL LYMPHOCYTE: 0 [0 - 0] %; NPTST040-CRP: 1.55 [0 - 0.3] MG/DL; NPTST046-EGFR: 66.39 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST047-ERYTHROBLAST: 0 [0 - 0] %; NPTST050-GAMMA-GTP: 306 [0 - 80] U/L; NPTST061-LD: 240 [110 - 240] U/L; NPTST063-MCH: 33.2 [27 - 35] PG; NPTST064-MCHC: 33.3 [31 - 36] G/DL; NPTST065-MCV: 100 [83 - 98] FL; NPTST066-METAMYELOCYTE: 0 [0 - 0] %; NPTST070-MYELOBLAST: 0 [0 - 0] %; NPTST071-MYELOCYTE: 0 [0 - 0] %; NPTST077-PROMYELOCYTE: 0 [0 - 0] %; Neutrophils: 5.548 [2.4 - 7.56] 10^9/L; Neutrophils/Leukocytes: 36.5 [40 - 79] %; Platelets: 145 [130 - 350] 10^9/L; Potassium: 5 [3.5 - 5] MMOL/L; Protein: 75 [65 - 82] G/L; Sodium: 137 [137 - 147] MMOL/L; [redacted]20[redacted] (RX DAY 204): Alanine Aminotransferase: 52 [5 - 35] U/L; Albumin: 36 [38 - 52] G/L; Alkaline Phosphatase: 260 [100 - 360] U/L; Aspartate Aminotransferase: 26 [10 - 35] U/L; Basophils: 0.05 [0 - 0.22] 10^9/L; Basophils/Leukocytes: 0.6 [0 - 2] %; Bilirubin: 10 [3 - 19] UMOL/L; Blood Urea Nitrogen: 3.1 [2.9 - 8.2] MMOL/L; Calcium: 2.47 [2.07 - 2.59] MMOL/L; Creatinine: 62 [53 - 106] UMOL/L; Eosinophils: 0.299 [0 - 0.43] 10^9/L; Eosinophils/Leukocytes: 3.6 [0 - 5] %; Erythrocytes: 2.8 [4.3 - 5.5] 10^12/L; Glucose: 4.8 [3.9 - 6.1] MMOL/L; Hematocrit: 0.28 [0.4 - 0.5] FRACTION OF 1; Hemoglobin: 93 [135 - 170] G/L; Leukocytes: 8.3 [4 - 8.5] 10^9/L; Lymphocytes: 4.176 [0.96 - 4.75] 10^9/L; Lymphocytes/Leukocytes: 50.2 [18 - 52] %; Monocytes: 0.838 [0.1 - 0.97] 10^9/L; Monocytes/Leukocytes: 10.1 [3 - 9] %; NPTST001-A/G: 0.8 [1.2 - 2.1] RATIO; NPTST017-ATYPICAL LYMPHOCYTE: 0 [0 - 0] %; NPTST040-CRP: 0.51 [0 - 0.3] MG/DL; NPTST046-EGFR: 92.72 [NOT REPORTED - NOT REPORTED] mL/min/1.73m2; NPTST047-ERYTHROBLAST: 0 [0 - 0] N/A; NPTST050-GAMMA-GTP: 287 [0 - 80] U/L; NPTST061-LD: 211 [110 - 240] U/L; NPTST063-MCH: 32.9 [27 - 35] PG; NPTST064-MCHC: 33.5 [31 - 36] G/DL; NPTST065-MCV: 98 [83 - 98] FL; NPTST066-METAMYELOCYTE: 0 [0 - 0] %; NPTST070-MYELOBLAST: 0 [0 - 0] %; NPTST071-MYELOCYTE: 0 [0 - 0] %; NPTST077-PROMYELOCYTE: 0 [0 - 0] %; Neutrophils: 2.974 [2.4 - 7.56] 10^9/L; Neutrophils/Leukocytes: 35.5 [40 - 79] %; Platelets: 104 [130 - 350] 10^9/L; Potassium: 4.6 [3.5 - 5] MMOL/L; Protein: 81 [65 - 82] G/L; Sodium: 137 [137 - 147] MMOL/L
Microbiology	[redacted]20[redacted] (RX DAY 188): BLOOD NPTST019-BETA-D GLUCAN: POSITIVE-BETA-D GLUCAN 200; BLOOD NPTST034-CMV IGG(DETERMINATION): POSITIVE-CMV IGG(EIA)20.6; BLOOD NPTST036-CMV IGM(DETERMINATION): -+/-; BLOOD NPTST038-CMV PP65: NEGATIVE; BLOOD NPTST069-MYCOPLASMAL ANTIGEN: NEGATIVE; URINE NPTST112-URINE LEGIONELLA ANTIGEN: NEGATIVE; URINE NPTST113-URINE PNEUMOCOCCAL: NEGATIVE
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 188): CT: THE CONCENTRATION RISE AREA SUCH AS FROSTED GLASS WAS OBSERVED OVER LUNG UPPER. THERE IS A MILD THICKENING IN INTERLOBULAR SEPTA. IT'S LIKE A INTERSTITIAL CHANGE. SAME FINDINGS AS DRUG INDUCED LUNG INJURY. IN THE LOWER LOBE, BRONCHOPNEUMONIA LIKE BY SHADING AROUND THE BRONCHI. PNEUMOCYSTIS PNEUMONIA (PCP) WAS SUSPECTED FROM DRUG INDUCED LUNG INJURY AND PNEUMONIA CYTOMEGALOVIRAL .
AE Stopped Rx Day	212 (29 DAYS AFTER LAST TREATMENT)
Duration of AE	25 DAYS
Severity	Severe
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED

Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 5[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬，フルオシノロンアセトニド，プレドニゾロン及び tacrolimus を投与され，ニューモシスチス肺炎を発現した。被験者は元喫煙者（紙巻タバコ 20 本／日，17 年間）かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎，喘息，アレルギー性鼻炎，甲状腺機能低下症及び本態性高血圧症であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者はニューモシスチス肺炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，ニューモシスチス肺炎は消失した。

本事象の発現前，被験者は 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで続いた発熱を報告し，感冒（非重篤）と診断された。その後，治験薬の投与は中断された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は発熱，倦怠感，咳嗽，頭痛，呼吸困難及び食欲不振のため入院した。同日の好中球絶対数は 3738/μL，リンパ球絶対数は 1122/μL であった。20[redacted] 年 [redacted] 月 [redacted] 日，気管支鏡検査が予定されたが，酸素 5 L/分が必要な状態となったため実施しなかった。20[redacted] 年 [redacted] 月 [redacted] 日，呼吸不全は持続しており，酸素 7 L/分が必要であった。また，β-D-グルカン増加も認められ，ニューモシスチス肺炎と判断された。20[redacted] 年 [redacted] 月 [redacted] 日，酸素の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，発熱していたが他の症状はなく，Avelox の投与により改善した。20[redacted] 年 [redacted] 月 [redacted] 日，クレアチニン値上昇のため Bactramin は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は呼吸不全から回復していたため退院した。20[redacted] 年 [redacted] 月 [redacted] 日，受診時に微熱（36.9°C）が認められた以外に症状はなく，被験者は回復したと判断された。

被験者は本試験を中止した。

プレドニゾロン，ファモチジン，レバミピド，AVELOX，LOXOPROFEN SODIUM，CEFTRIAXONE NA，ミノサイクリン塩酸塩，SOL-MELCORT 及び BACTRAMIN が投与された。

The patient's past medications include:

ANFLAVATE LOTION for ATOPIC DERMATITIS ([redacted])

ANFLAVATE OINTMENT for ATOPIC DERMATITIS ([redacted])

CELESTANA for ATOPIC DERMATITIS ([redacted])

EPINASTINE HYDROCHLORIDE for ATOPIC DERMATITIS ([redacted])

TACROLIMUS for ATOPIC DERMATITIS ([redacted])

HYDROXYZINE PAMOATE for ATOPIC DERMATITIS ([redacted])

RINDERON-VG for ATOPIC DERMATITIS ([redacted])

PROTOPIC for ATOPIC DERMATITIS ([redacted])

PROPETO for EMOLLIENT THERAPY ([redacted])

FLUOCINONIDE for ATOPIC DERMATITIS RESCUE THERAPY ([redacted])

AMBROXOL for COMMON COLD ([redacted])

ASTOMIN for COMMON COLD ([redacted])

CEFDITOREN PIVOXIL for COMMON COLD ([redacted])

IBUPROFEN for COMMON COLD ([redacted])

Causality for UPADACITINIB (Blinded)

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

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

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

Dechallenge: Not Applicable

Causality for FLUOCINOLONE ACETONIDE (Open Label)

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

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

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

Dechallenge: Not Applicable

Causality for PREDNISOLONE (Open Label)

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

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

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

Dechallenge: Not Applicable

Causality for TACROLIMUS (Open Label)

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

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 PNEUMOCYTIS PNEUMONIA

- Investigator: Not applicable

- AbbVie: Not applicable.

Alternative Etiology for FLUOCINOLONE ACETONIDE (Open Label)

Event of PNEUMOCYTIS PNEUMONIA

- Investigator: More likely related to Upadacitinib/Placebo.

- AbbVie: Weak temporal association. Last dose prior to event onset was approximately five and a half months prior to event onset.

Alternative Etiology for PREDNISOLONE (Open Label)

Event of PNEUMOCYTIS PNEUMONIA

- Investigator: More likely related to Upadacitinib/Placebo.

- AbbVie: Weak temporal association. Last dose prior to event onset was approximately five months prior to event onset.

Alternative Etiology for TACROLIMUS (Open Label)

Event of PNEUMOCYTIS PNEUMONIA

- Investigator: More likely related to Upadacitinib/Placebo.

- AbbVie: Weak temporal association. Last dose prior to event onset was approximately three months prior to event onset.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANA(HEMOGENEOUS):** Not detected.

[redacted] **20[redacted] A/G RATIO:** 0.97 no unit (normal 1.20 to 2.10)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 53 U/L (normal 5 to 35)

[redacted] **20[redacted] ALANINE AMINO TRANSFERASE:** 120 U/L (normal 5 to 35)

[redacted] **20[redacted] ALBUMIN:** 3.3 G/DL (normal 3.8 to 5.2)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 98 U/L (normal 40 to 129)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 235 U/L (normal 100 to 360)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 256 U/L (normal 100 to 360)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 88 U/L (normal 40 to 129)

[redacted] 20[redacted] **ALT:** 28 U/L (normal 6 to 43)

[redacted] 20[redacted] **ALT:** 21 U/L (normal 6 to 43)

[redacted] 20[redacted] **ANA:** LESS THAN 40.

[redacted] 20[redacted] **ANA(CYTOPLASMIC):** Not detected.

[redacted] 20[redacted] **ANA(DISCRETE SP):** Not detected.

[redacted] 20[redacted] **ANA(NUCLEOLAR):** Not detected.

[redacted] 20[redacted] **ANA(OTHER CHROMOSOME TYPE 1):** Not detected.

[redacted] 20[redacted] **ANA(OTHER CHROMOSOME TYPE2):** Not detected.

[redacted] 20[redacted] **ANA(SPECKLED):** Not detected.

[redacted] 20[redacted] **APTT(ACTIVITY):** 78 % (normal 70 to 130)

[redacted] 20[redacted] **APTT(CONTROL):** 11.5 SEC

[redacted] 20[redacted] **APTT(SEC):** 32.1 SEC

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 64 U/L (normal 10 to 35)

[redacted] 20[redacted] **ASPARTATE AMINO TRANSFERASE:** 7.5 U/L (normal 10 to 35)

[redacted] 20[redacted] **AST:** 87 U/L (normal 11 to 36)

[redacted] 20[redacted] **AST:** 44 U/L (normal 11 to 36)

[redacted] 20[redacted] **AST:** 28 U/L (normal 11 to 36)

[redacted] 20[redacted] **ATYPICAL LYMPHOCYTE:** 0 % (normal 0 to 0)

[redacted] 20[redacted] **BASOPHILS %:** 0.3 % (normal 0 to 2)

[redacted] 20[redacted] **BASOPHILS ABS:** 62 /UL (normal 0 to 0.3)

[redacted] 20[redacted] **BILIRUBIN:** 1.1 mg/dL (normal 0.0 to 0.4)

[redacted] 20[redacted] **BILIRUBIN:** 0.6 mg/dL (normal 0.2 to 1.1)

[redacted] 20[redacted] **BLOOD GAS(BE):** 1.0 MMOL/L (normal -2 to 2)

[redacted] 20[redacted] **BLOOD GAS(BODY TEMPERATURE):** 37.0 Degrees C

[redacted] 20[redacted] **BLOOD GAS(HCO3):** 24.7 MMOL/L (normal 21 to 29)

[redacted] 20[redacted] **BLOOD GAS(HEMOGLOBIN):** 9.1 G/DL

[redacted] 20[redacted] **BLOOD GAS(O2CT):** 12.1 ml/dl (normal 18 to 22)

[redacted] 20[redacted] **BLOOD GAS(O2SAT):** 93.9 % (normal 92 to 96)

[redacted] 20[redacted] **BLOOD GAS(PCO2):** 35.5 mmHg (normal 32 to 46)

[redacted] 20[redacted] **BLOOD GAS(PH):** 7.460 no unit (normal 7.38 to 7.46)

[redacted] 20[redacted] **BLOOD GAS(PO2):** 65.0 mmHg (normal 74 to 108)

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 11.7 mg/dL (normal 8 to 23)

[redacted] 20[redacted] **BNP:** 20.5 PG/ML (normal 0 to 18.4)

[redacted] 20[redacted] **BODY TEMPERATURE:** 38.3 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 38.8 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 40 Degrees C

[redacted] 20[redacted] **BODY TEMPERATURE:** 36.9 Degrees C

[redacted] 20[redacted] **CALCIUM:** 8.8 mg/dL (normal 8.3 to 10.4)

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

[redacted] 20[redacted] **CHOLESTEROL:** 169 mg/dL (normal 130 to 220)

[redacted] 20[redacted] **CHOLINESTERASE:** 95 U/L (normal 200 to 470)

[redacted] 20[redacted] **CHOLINESTERASE:** 93 U/L (normal 200 to 470)

[redacted] 20[redacted] **CL:** 99 MEQ/L (normal 98 to 108)

[redacted] 20[redacted] **CMV IGG(DETERMINATION):** Positive.

[redacted] 20[redacted] **CMV IGG(EIA):** 20.6 no unit (normal 0 to 1.999)

[redacted] 20[redacted] **CMV IGM(DETERMINATION):** ±.

[redacted] 20[redacted] **CMV IGM(INDEX):** 1.09 no unit (normal 0 to 0.799)

[redacted] 20[redacted] **CMV PP65:** Negative.

[redacted] 20[redacted] **CREATINE KINASE:** 109 U/L (normal 60 to 270)

[redacted] 20[redacted] **CREATININE:** 0.65 mg/dL (normal 0.6 to 1.2)

[redacted] 20[redacted] **CRP:** 5.82 mg/dL (normal 0 to 0.3)

[redacted] 20[redacted] **CRP:** 0.33 mg/dL (normal 0 to 0.3)

[redacted] 20[redacted] **CRP QUANTITATIVE:** 12.68 mg/dL (normal 0 to 0.3)

[redacted] 20[redacted] **CT:** THE CONCENTRATION RISE AREA SUCH AS FROSTED GLASS WAS OBSERVED OVER LUNG UPPER. THERE IS A MILD THICKENING IN INTERLOBULAR SEPTA. IT'S LIKE A INTERSTITIAL CHANGE. SAME FINDINGS AS DRUG INDUCED LUNG INJURY. IN THE LOWER LOBE, BRONCHOPNEUMONIA LIKE BY SHADING AROUND THE BRONCHI. PNEUMOCYSTIS PNEUMONIA (PCP) WAS SUSPECTED FROM DRUG INDUCED LUNG INJURY AND PNEUMONIA CYTOMEGALOVIRAL.

[redacted] 20[redacted] **D-DIMER QUANTITATIVE:** 800 NG/ML (normal 0 to 1000)

[redacted] 20[redacted] **EGFR:** 67.16 ML/MIN/1.73M*2

[redacted] 20[redacted] **EGFR:** 100.55 ML/MIN/1.73M^2

[redacted] 20[redacted] **EOSINOPHILS %:** 1.5 % (normal 0 to 5)

[redacted] 20[redacted] **EOSINOPHILS ABS:** 48000 10^3/uL

[redacted] 20[redacted] **EOSINOPHILS ABS:** 0

[redacted] 20[redacted] **EOSINOPHILS ABS:** 185 /UL (normal 0 to 0.3)

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

[redacted] 20[redacted] **GLUCOSE:** 120 mg/dL (normal 70 to 110)

[redacted] 20[redacted] **GLUCOSE:** 150 mg/dL (normal 70 to 110)

[redacted] 20[redacted] **GLUCOSE:** 74 mg/dL (normal 70 to 110)

[redacted] 20[redacted] **HBS ANTIGEN (SEMIQUANTITATIVE):** Less than 8. Normal value low: 0, Normal value high: 7.999.

[redacted] 20[redacted] **HCV ANTIBODY(DETERMINATION):** Negative.

Unknown date HCV ANTIBODY(IDX): 0.1 no unit (normal 0 to 0.99)

[redacted] 20[redacted] **HEMATOCRIT:** 24.0 % (normal 40 to 50)

[redacted] 20[redacted] **HEMOGLOBIN:** 10.2 G/DL (normal 13.5 to 17)

[redacted] 20[redacted] **IGA:** 598 mg/dL (normal 110 to 410)

[redacted] 20[redacted] **IGE(IGE NON-SPECIFIC):** 11500 IU/mL (normal 0 to 173)

[redacted] 20[redacted] **IGG:** 1346 mg/dL (normal 870 to 1700)

[redacted] 20[redacted] **IGM:** 59 mg/dL (normal 33 to 190)

[redacted] 20[redacted] **KL-6:** 320 U/ML (normal 0 to 499.999)

[redacted] 20[redacted] **LD:** 316 U/L (normal 110 to 240)

[redacted] 20[redacted] **LDH:** 333 U/L (normal 110 to 240)

[redacted] 20[redacted] **LYMPHOCYTES %:** 32.0 % (normal 18 to 52)

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 1122 10^3/uL

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 5.573 10^3/uL

[redacted] 20[redacted] **LYMPHOCYTES ABS:** 3936 /UL (normal 0 to 0.3)

[redacted] 20[redacted] **MCH:** 33.6 PG (normal 27 to 35)

[redacted] 20[redacted] **MCHC:** 34.2 G/DL (normal 31 to 36)

[redacted] 20[redacted] **MCV:** 99 FL (normal 83 to 98)

[redacted] 20[redacted] **METAMYELOCYTE:** 0 % (normal0 to 0)

[redacted] 20[redacted] **MONOCYTES %:** 17.9 % (normal 3 to 9)

[redacted] 20[redacted] **MONOCYTES %:** 6.2 % (normal 3 to 9)

[redacted] 20[redacted] **MONOCYTES ABS:** 1074000 10^3/uL

[redacted] 20[redacted] **MONOCYTES ABS:** 1.022 10^3/uL

[redacted] 20[redacted] **MYCOPLASMAL ANTIGEN:** Negative.

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

[redacted] 20[redacted] **NEUTROPHILS %:** 62.3 % (normal 40 to 79)

[redacted] 20[redacted] **NEUTROPHILS ABS:** 3738 10^3/uL

[redacted] 20[redacted] **NEUTROPHILS ABS:** 7.79 10^3/uL

[redacted] 20[redacted] **NEUTROPHILS ABS:** 763 /UL

[redacted] 20[redacted] **NEUTROPHILS ABS:** 7355 /UL (normal 0 to 0.3)

[redacted] 20[redacted] **PLATELET COUNT:** 1350 10^3/uL (normal 130 to 350)

[redacted] 20[redacted] **PLATELET COUNT:** 136 10^3/uL (normal 130 to 350)

[redacted] 20[redacted] **PLATELET COUNT:** 177 10^3/uL (normal 13 to 35)

[redacted] 20[redacted] **POTASSIUM:** 3.8 MEQ/L (normal 3.5 to 5.0)

[redacted] 20[redacted] **PROCALCITONIN:** LESS THAN 0.5~2 NG/DL.

[redacted] 20[redacted] **RED BLOOD CELLS:** 2710 10^3/uL (normal 4300 to 5500)

[redacted] 20[redacted] **RED BLOOD CELLS:** 305 no units (normal 430 to 550)

[redacted] 20[redacted] **RPR:** Negative.

[redacted] 20[redacted] **SUGAR URINARY:** Negative.

[redacted] 20[redacted] **TOTAL BILIRUBIN:** 1.1 mg/dL (normal 0.2 to 1.2)

[redacted] 20[redacted] **TOTAL PROTEIN:** 7.7 G/DL (normal 6.5 to 8.2)

[redacted] 20[redacted] **TPHA:** Negative.

[redacted] 20[redacted] **UEIN LEGIONELLA ANTIGEN:** Negative.

[redacted] 20[redacted] **URINARY OCCULATE BLOOD:** Negative.

[redacted] 20[redacted] **URINARY SEDIMENT(BACTERIA):** 1+.

[redacted] 20[redacted] **URINARY SEDIMENT(GLITTER CELL):** 1+.

[redacted] 20[redacted] **URINARY SEDIMENT(HYALINE CAST):** 1.

[redacted] 20[redacted] **URINARY SEDIMENT(MUCUS):** 1+.

[redacted] 20[redacted] **URINARY SEDIMENT(RED BLOOD CELL):** Below 1.

[redacted] 20[redacted] **URINARY SEDIMENT(SQUAMOUS CELL):** 1-4.

[redacted] 20[redacted] **URINARY SEDIMENT(URINARY TRACRT CELL):** Below 1.

[redacted] 20[redacted] **URINARY SEDIMENT(WHITE BLOOD CELL):** 20-29.

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

[redacted] 20[redacted] **URINE KETONE BODY:** Negative.

[redacted] 20[redacted] **URINE PNEUMOCOCCAL:** Negative.

[redacted] 20[redacted] **URINE PROTEIN:** ±.

[redacted] 20[redacted] **UROBILINOGEN:** 2+.

[redacted] **20[redacted] WHITE BLOOD CELLS:** 6000 U/L (normal 4000 to 8500)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 123000 /UL (normal 4000 to 8500)

[redacted] **20[redacted] Y-GTP:** 502 U/L (normal 0 to 80)

[redacted] **20[redacted] Y-GTP:** 530 U/L (normal 0 to 80)

[redacted] **20[redacted] B-D GLUCAN:** 200 PG/ML (normal 0 to 20)

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
カポジ水痘様発疹				X
小脳出血	X	X		X

Treatment Group	Age at Study Start	Sex	Race
P1:Upa 15 mg QD	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
FOOD ALLERGY(BUCKWHEAT)	20[redacted]
FOOD ALLERGY(CRUSTACEAN)	20[redacted]
FOOD ALLERGY(EGG)	20[redacted]
FOOD ALLERGY(WALNUT)	20[redacted]
ASTHAMA	20[redacted]
CATARACT	20[redacted]
ACNE COMEDONAL	20[redacted]
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
PRIOR PROCEDURES: CATARACT SURGERY	20[redacted]

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
P1:ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 65	65

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BETAMETHASONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -135
CLINDAMYCIN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -135
CLOBETASOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -135
KETOCONAZOLE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -135
MINOCYCLINE	100 mg	QD	Y-M: 20[redacted] / -135
TACROLIMUS	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -135
UREA	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -135
ZINC	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -135
CETIRIZINE	10 mg	QD	Y-M: 20[redacted] / -125
NADIFLOXACIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -122
VALISONE-G	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -122
BYAKKOKANINJINTO	3 g	BID	Y-M: 20[redacted] / -119
HERBAL PREPARATION	2.5 g	BID	Y-M: 20[redacted] / -119
RUPATADINE	10 mg	QD	Y-M: 20[redacted] / -119
CEFDINIR	100 mg	TID	Y-M: 20[redacted] / -103
ENTEROCOCCUS FAECALIS	1 mg	TID	Y-M: 20[redacted] / -103
HEPARINOID	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -103
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	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
CLINDAMYCIN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -135	Y-M: 20[redacted] / 65
HEPARINOID	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -103	Y-M: 20[redacted] / 65
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -7	Y-M: 20[redacted] / 158
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 15	Y-M: 20[redacted] / 19
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 33	Y-M: 20[redacted] / 37
ATROPINE	0.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
EPHEDRINE	28 mg	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66

FLURBIPROFEN	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
HYDROCORTISONE	1000 mg	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
MANNITOL	300 mL	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
PHENYLEPHRINE	0.7 mg	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
PROPOFOL	80 mg	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
REMIFENTANIL	8 mg	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
ROCURONIUM	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
SUGAMMADEX	200 mL	OTHER: ONCE	Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 66
CEFAZOLIN	1 g		Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 67
DEXMEDETOMIDINE	400 ug		Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 67
ACTIT	500 mL		Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 69
GLYCEOL	200 mL		Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 69
FAMOTIDINE	20 mg		Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 71
METOCLOPRAMIDE	10 mg		Y-M: 20[redacted] / 66	Y-M: 20[redacted] / 75
HYDROXYZINE	25 mg		Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 70
AMINO ACIDS NOS W/ELECTROLYTES NOS/GLUCOSE/TH	500 mL		Y-M: 20[redacted] / 70	Y-M: 20[redacted] / 79
ASCORBIC ACID	500 ug		Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 99
FLAVINE ADENINE DINUCLEOTIDE	10 mg		Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 99
HAITAMIN	30 mg		Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 99
THIAMINE	50 mg		Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 99
FAMOTIDINE	20 mg	QD	Y-M: 20[redacted] / 71	Y-M: 20[redacted] / 130
CEFTRIAXONE	2 g	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 93
VANCOMYCIN	1 g	OTHER: EVERY 12 HOURS	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 104
MEROPENEM	2 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 91	Y-M: 20[redacted] / 130
ACTIT	500 mg	PRN	Y-M: 20[redacted] / 93	Y-M: 20[redacted] / 101
ATROPINE	0.5 mg	OTHER: ONCE	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97

FLURBIPROFEN	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
HYDROCORTISONE	100 mg	OTHER: ONCE	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
METOCLOPRAMIDE	10 mg	OTHER: ONCE	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
PROPOFOL	120 ng	OTHER: ONCE	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
REMIFENTANIL	8 mg	OTHER: ONCE	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
ROCURONIUM	50 mg	OTHER: ONCE	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
SUGAMMADEX	200 mg	OTHER: ONCE	Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 97
FAMOTIDINE	20 mg		Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 98
IMMUNOGLOBULIN HUMAN NORMAL	2.5 g		Y-M: 20[redacted] / 97	Y-M: 20[redacted] / 99
METOCLOPRAMIDE	50 mL	OTHER: ONCE	Y-M: 20[redacted] / 100	Y-M: 20[redacted] / 100
ACTIT	500 mL		Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
BETAHISTINE	1 OTHER: TAB	PRN	Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
CLOSTRIDIUM BUTYRICUM	1 OTHER: TAB	PRN	Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
ESZOPICLONE	1 mg	PRN	Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
MEROPENEM	0.5 g		Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
METOCLOPRAMIDE	10 mg		Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
SODIUM CHLORIDE	100 mL		Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
SODIUM CHLORIDE	50 mL		Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
VANCOMYCIN	0.5 g		Y-M: 20[redacted] / 101	Y-M: 20[redacted] / 122
BETAHISTINE	1 OTHER: TAB	BID	Y-M: 20[redacted] / 104	Y-M: 20[redacted] / 122
VANCOMYCIN	1 g	OTHER: EVERY 8 HOURS	Y-M: 20[redacted] / 105	Y-M: 20[redacted] / 122
CLOSTRIDIUM BUTYRICUM	1 OTHER: TAB	TID	Y-M: 20[redacted] / 106	Y-M: 20[redacted] / 122
CLOSTRIDIUM BUTYRICUM			Y-M: 20[redacted] / 122	NOT REPORTED

Event #1: Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zosters

Event Description	KAPOSI'S VARICELLIFORM ERUPTION (AROUND THE FACE AND MOUTH)
Preferred term	カポジ水痘様発疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 31

Age at AE Onset	2[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	43
Duration of AE	13 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	CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

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

Event Description	CEREBELLAR HAEMORRHAGE
Preferred term	小脳出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 65
Age at AE Onset	2[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 65): MRI,CT: CEREBELLAR HAEMORRHAGE CEREBRAL HAEMORRHAGE IN THE CENTER OF THE RIGHT CEREBELLUM; [redacted]20[redacted] (RX DAY 89): MRI:; [redacted]20[redacted] (RX DAY 91): CT:; [redacted]20[redacted] (RX DAY 94): CT:; [redacted]20[redacted] (RX DAY 96): CT:; [redacted]20[redacted] (RX DAY 97): CT:; [redacted]20[redacted] (RX DAY 98): CT:; [redacted]20[redacted] (RX DAY 101): CT:; [redacted]20[redacted] (RX DAY 104): CT:; [redacted]20[redacted] (RX DAY 107): CT:
AE Stopped Rx Day	123 (58 DAYS AFTER LAST TREATMENT)
Duration of AE	59 DAYS
Severity	Severe
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, OTHER MEDICALLY IMPORTANT SERIOUS EVENT, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 2[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬，プレドニゾロン及びトリアムシノロンアセトニドを投与され，小脳出血を発現した。被験者は非喫煙者か

つ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎及び喘息であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は小脳出血を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，小脳出血は消失した。

本事象の発現前，2[redacted]9 年 [redacted] 月 [redacted] 日から同年 [redacted] 月 [redacted] 日まで発現していたヘルペス感染（非重篤）のため，プレドニゾロン及びトリアムシノロンアセトニドの投与が中断された。20[redacted] 年 [redacted] 月 [redacted] 日から同年 [redacted] 月 [redacted] 日まで，カポジ水痘様発疹（非重篤）が発現していた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は頭痛，嘔吐及び転倒のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は小脳出血と診断された。血腫が増大し，続いて意識レベルが低下した。開頭術が行われた。術後，意識レベル，頭痛及び運動失調は改善した。

20[redacted] 年 [redacted] 月 [redacted] 日，微熱があり，右後頭下に自発痛及び圧痛があった。コンピュータ断層撮影（以下「CT」）検査の結果，筋肉下に体液貯留が認められ，穿刺により排膿が認められた。CEFXONE + バンコマイシン塩酸塩が投与された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は同患部の圧痛を自覚した。CT 検査の結果，膿瘍が認められ，穿刺が実施された。治療は meropenem + VENILON I に変更された。20[redacted] 年 [redacted] 月 [redacted] 日，デブリードマンで洗浄した際，筋肉下及び皮下からの排膿が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，ドレーンが抜去された。ドレーン抜去以降，感染はコントロールされた状態であった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は核磁気共鳴画像検査を受けた。長期にわたる後遺症は認められず，20[redacted] 年 [redacted] 月 [redacted] 日に被験者は退院した。

治験責任医師の記述：被験者の病歴に頭部損傷はなく，本人の病歴及び家族歴に不正薬剤の使用又は高血圧などの小脳出血の交絡因子，若しくは動脈瘤もなかった。

ceftriaxone，バンコマイシン塩酸塩，meropenem，VENILON I，ROPION，LUNESTA，ファモチジン，mannitol，GASTER，GLYCEOL 及び塩酸メトクロプラミドが投与された。

The patient's past medications include:

ACETYLOL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ANFLAVATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DERMOVATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MINOMYCIN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

NITRAZEN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

PROTOPIC for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON DP for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ZINC OXIDE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CETIRIZINE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ACUATIM for ATOPIC DERMATITIS ([redacted])

RINDERON-VG for ATOPIC DERMATITIS ([redacted])

BYAKKOKANINJINTO for ATOPIC DERMATITIS ([redacted])

JIZUSOIPPO for ATOPIC DERMATITIS ([redacted])

RUPAFIN for ATOPIC DERMATITIS ([redacted])

BIOFERMIN R for ATOPIC DERMATITIS ([redacted])

CEFZON for ATOPIC DERMATITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Cerebellar haemorrhage (10008030) (Cerebellar haemorrhage (10008030)) [v.22.1] [10008030]

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

Causality for PREDNISOLONE (Open Label)

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1) Cerebellar haemorrhage (10008030) (Cerebellar haemorrhage (10008030)) [v.22.1] [10008030]

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

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

Dechallenge: Not Applicable

Causality for TRIAMCINOLONE ACETONIDE (Open Label)

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1) Cerebellar haemorrhage (10008030) (Cerebellar haemorrhage (10008030)) [v.22.1] [10008030]

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 CEREBELLAR HAEMORRHAGE

- Investigator: Not applicable

- AbbVie: Event's etiology is not consistent with study drug's mechanism of action. Additional risk factors include recent herpes infection and Kaposi's varicelliform eruption.

Alternative Etiology for PREDNISOLONE (Open Label)

Event of CEREBELLAR HAEMORRHAGE

- Investigator: Not reported

- AbbVie: Event's etiology is not consistent with study drug's mechanism of action. Additional risk factors include recent herpes infection and Kaposi's varicelliform eruption.

Alternative Etiology for TRIAMCINOLONE ACETONIDE (Open Label)

Event of CEREBELLAR HAEMORRHAGE

- Investigator: Not reported

- AbbVie: Event's etiology is not consistent with study drug's mechanism of action. Additional risk factors include recent herpes infection and Kaposi's varicelliform eruption.

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] **20[redacted] CT:** Cerebellar haemorrha

[redacted] **20[redacted] CT:** Showed submuscular fluid retention, pustular retention with puncture.

[redacted] **20[redacted] CT:** Showed pustular puncture

[redacted] **20[redacted] MRI:** Cerebellar hemorrhage in the center of the right cerebullum

非重篤な有害事象

被験者は顔面（両眼及び口の周囲）に広がるカポジ水痘様発疹を発現し，抗ウイルス薬が投与された。カポジ水痘様発疹の特性及び推定罹患面積は不明である。本事象の原因は単純ヘルペスウイルス（血清型不明）であった。細菌性の重複感染はなかった。本事象のため治験薬の投与は中断された。本事象は消失した。

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:Upa 15 mg QD /P2:Upa 15 mg QD	2[redacted]	MALE	ASIAN

Medical History	Onset Year
ALLERGIC RHINITIS	19[redacted]
ASTHMA	19[redacted]
ATOPIC DERMATITIS	19[redacted]
FOOD ALLERGY	19[redacted]
CHICKEN POX	19[redacted]
ATTENTION DEFICIT HYPERACTIVITY DISORDER	20[redacted]
SOCIAL ANXIETY DISORDER	20[redacted]
INFLUENZA VIRAL INFECTION	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
P1:ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 109	109
P2:ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 110	[redacted]20[redacted] / 368	259

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]
ARIPIPRAZOLE	3 mg	QD	Y-M: 20[redacted]
MEQUITAZINE	3 mg	BID	Y-M: 20[redacted]
OLOPATADINE	5 mg	BID	Y-M: 20[redacted]
STELAMIN	1 OTHER: TABLET	BID	Y-M: 20[redacted]
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
VALISONE-G	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
BETAMETHASONE	1 OTHER: APPLICATION	TID	Y-M: 20[redacted]
CICLOSPORIN	50 mg	QD	Y-M: 20[redacted]
SUPLATAST TOSILATE	100 mg	TID	Y-M: 20[redacted]
TACROLIMUS	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
OLOPATADINE	5 mg	BID	Y-M: 20[redacted]
LEVOCETIRIZINE	5 mg	QD	Y-M: 20[redacted]
BEPOTASTINE	10 mg	BID	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
SALICYLIC ACID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
METHYLPHENIDATE	36 mg	QD	Y-M: 20[redacted]
CLOBETASOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -332
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -255
OLEA EUROPAEA	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -199
OLOPATADINE	5 mg	BID	Y-M: 20[redacted] / -171
UNSEIIN	7.5 g	TID	Y-M: 20[redacted] / -128
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -101
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -88
AUGMENTIN	1 OTHER: TABLETS	BID	Y-M: 20[redacted] / -49
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -49

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ARIPIPRAZOLE	3 mg	QD	Y-M: 20[redacted]	NOT REPORTED
BEPOTASTINE	10 mg	BID	Y-M: 20[redacted]	NOT REPORTED
METHYLPHENIDATE	36 mg	QD	Y-M: 20[redacted]	NOT REPORTED

OLOPATADINE	5 mg	BID	Y-M: 20[redacted] / - 171	NOT REPORTED
FAMOTIDINE	20 mg	BID	Y-M: 20[redacted] / 6	NOT REPORTED
CLOBETASOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 47	NOT REPORTED
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 110	NOT REPORTED
PREDNISOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 153	NOT REPORTED
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 153	NOT REPORTED
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 263
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 257	Y-M: 20[redacted] / 264
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 262	NOT REPORTED

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 / Rx Day	[redacted]20[redacted] / 254
Age at AE Onset	2[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 257): Leukocytes: 6.1 [3.5 - 9] 10^9/L; Lymphocytes/Leukocytes: 18 [30 - 45] %
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	265
Duration of AE	12 DAYS
Severity	Severe
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 2[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬，プレドニゾロン及びフルオシノロンアセトニドを投与され，帯状疱疹を発現した。被験者は非喫煙者かつ

飲酒者（2 杯未満／日）であり，関連する病歴はアレルギー性鼻炎，アトピー性皮膚炎，食物アレルギー，水痘及びインフルエンザウイルス感染であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は自宅で発熱して体温 37°C となり，殿部のリンパ節腫脹が認められた。20[redacted] 年 [redacted] 月 [redacted] 日，右腹部から背部にかけて小水疱が発生した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は病院の皮膚科を受診した。右腹部から背部にかけて，複数の小水疱集簇及び環状紅斑が認められた。また被験者は，昼夜を通して疼痛があると訴えた。帯状疱疹と診断され，被験者は入院した。

被験者の免疫力低下が疑われ，点滴注入療法が必要と判断された。右腹部から背部にかけて，痂皮形成が始まった。20[redacted] 年 [redacted] 月 [redacted] 日，発疹が痂皮化して疼痛が改善し，被験者は退院した。

この帯状疱疹は病歴及び身体的診察所見に基づいて診断されたものであり，症状は単一の皮膚分節に限局していた。

被験者には水痘の病歴があり，帯状疱疹の病歴又は帯状疱疹ワクチンの接種歴はなかった。

LOXONIN TABLETS 及び acyclovir が投与された。

The patient's past medications include:

ZESULAN TABLETS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ALLELOCK TABLETS for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

EMPERACIN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DIFLAL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON-VG for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ANTBATE LOTION for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

NEORAL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

IPD CAPSULE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PROTOPIC for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DERMOVATE SCALP LOTION for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

OLOPATADINE HYDRCHLORIDE OD for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

XYZAL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

SALICYLIC ACID OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

COMCLO SHAMPOO for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

OLIVE OIL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

UNSEIIN for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

CLOBETASOL PROPIONATE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Causality for PREDNISOLONE (Open Label)

---

1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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

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

Dechallenge: Not Applicable

Causality for FLUOCINOLONE ACETONIDE (Open Label)

---

1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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 HERPES ZOSTER

- Investigator: Not applicable

- AbbVie: Not applicable

Alternative Etiology for PREDNISOLONE (Open Label)

Event of HERPES ZOSTER

- Investigator: More likely related to ABT-494/Placebo

- AbbVie: Weak temporal association. Last dose of suspect drug was more than 4.5 months prior to event onset.

Alternative Etiology for FLUOCINOLONE ACETONIDE (Open Label)

Event of HERPES ZOSTER

- Investigator: More likely due to ABT-494/Placebo

- AbbVie: Weak temporal association. Last dose was approximately 7 months prior to event onset.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY TEMPERATURE:** 37 Degrees C

[redacted] **20[redacted] WBC:** 6.1 10^3/ul (normal 3.5 to 9.0)

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo /P2:Upa 30 mg QD	5[redacted]	MALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
ALLERGIC RHINITIS	19[redacted]
CONJINCTIVITS ALLERGIC	19[redacted]
ASTHMA	20[redacted]
HYPER TENSION	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
P1:Placebo		ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 110	110
P2:ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 111	[redacted]20[redacted] / 369	259

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
SERETIDE	1 OTHER: INHALATION	BID	Y-M: 20[redacted]-[redacted]

AMLODIPINE	5 mg	QD	Y-M: 20[redacted]
BILASTINE	20 mg	QD	Y-M: 20[redacted]
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
PREDNISOLONE	5 mg	TID	Y-M: 20[redacted]
BYAKKOKANINJINTO	3 g	TID	Y-M: 20[redacted]
ORENGEDOKUTO	2.5 mg	TID	Y-M: 20[redacted]
CICLOSPORIN	150 mg	QD	Y-M: 20[redacted]
OLOPATADINE	5 mg	TID	Y-M: 20[redacted]
PREDNISOLONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
TACROLIMUS	1 OTHER: APPLICATION	QD	Y-M: 20[redacted]
OLOPATADINE	5 mg	BID	Y-M: 20[redacted]
CICLOSPORIN	150 mg	OTHER: ONCE TWO DAYS	Y-M: 20[redacted]
HYDROXYZINE	10 mg	QD	Y-M: 20[redacted] / -296
CICLOSPORIN	150 mg	QD	Y-M: 20[redacted] / -135
DEXCHLORPHENIRAMINE	6 mg	QD	Y-M: 20[redacted] / -65
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -33
CLOBETASOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -21

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
SERETIDE	1 OTHER: INHALATION	BID	Y-M: 20[redacted]	NOT REPORTED
AMLODIPINE	5 mg	QD	Y-M: 20[redacted]	NOT REPORTED
OLOPATADINE	5 mg	BID	Y-M: 20[redacted]	NOT REPORTED
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -33	NOT REPORTED
MOMETASONE	2 OTHER: SPRAY	QD	Y-M: 20[redacted] / 13	NOT REPORTED
OLOPATADINE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 13	NOT REPORTED
DEXCHLORPHENIRAMINE	6 mg	QD	Y-M: 20[redacted] / 111	NOT REPORTED
ACICLOVIR	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 271	Y-M: 20[redacted] / 272
VALACICLOVIR	500 mg	TID	Y-M: 20[redacted] / 271	Y-M: 20[redacted] / 272
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 272	Y-M: 20[redacted] / 274
AMOXICILLIN	250 mg	TID	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 284
AUGMENTIN	1 OTHER: TABLETS	TID	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 284

ACICLOVIR	1 OTHER: APPKICATION	QID	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 285
BETAMETHASONE	0.1 %	QID	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 285
LEVOFLOXACIN	0.5 %	QID	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 285
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 273	Y-M: 20[redacted] / 285
DIFLORASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 275	NOT REPORTED
PREDNISOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 275	NOT REPORTED
GENTAMICIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 279	Y-M: 20[redacted] / 285

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 / Rx Day	[redacted] / 266
Age at AE Onset	5[redacted]
Laboratory Testing	[redacted] (RX DAY 272): Leukocytes: 9.5 [3.5 - 9] 10^9/L; Lymphocytes/Leukocytes: 16 [30 - 45] %
Microbiology	NOT REPORTED
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	286
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	REQUIRES OR PROLONGS HOSPITALIZATION, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 5[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬，フルオシノロンアセトニド及びプレドニゾロンを投与され，帯状疱疹を発現した。被験者は非喫煙者かつ元飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎及び帯状疱疹であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹は消失した。

本事象の発現前である 20[redacted] 年[redacted] 月，単純ヘルペス（非重篤）が発現し，同月中に消失した。

20[redacted] 年[redacted] 月[redacted] 日，左眼瞼及び顔面が腫脹し，小水疱が出現した。20[redacted] 年[redacted] 月[redacted] 日，皮膚科で帯状疱疹と診断され，薬物療法が開始された。20[redacted] 年[redacted] 月[redacted] 日，症状継続を理由に，被験者は入院した。被験者は夜間の発熱，疼痛，アトピー性皮膚炎によるそう痒及び左上眼瞼の二次感染（非重篤）を発現した。左上眼瞼の腫脹，水疱，びらん及び紅斑のため，入院期間は延長した。その後，左上眼瞼には痂皮が形成され，浮腫は改善した。20[redacted] 年[redacted] 月[redacted] 日，被験者は退院した。

発症したのは単一の皮膚分節であった。眼科の診察で，角膜表面の異常や眼病変はないと確認された。被験者には帯状疱疹ワクチン接種歴及び水痘の病歴がなく，帯状疱疹の病歴があった。

COCARL，VALTREX，アセトアミノフェン及び acyclovir が投与された。

The patient's past medications include:

BILANOA for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DIFLAL OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PREDNISOLONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

BYAKKO KA NINJINTO for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

OREN GEDOKUTO for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

LIDMEX KOWA OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

NEORAL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

OLOPATADINE HYDROCHLORIDE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

PROTOPIC OINTMENT for CONJUCTIVITS ALLERGIC ([redacted] 20[redacted] - [redacted] 20[redacted])

ATARAX for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

NEOMALLERMIN-TR for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

DERMOVATE OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

---

1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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

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

Dechallenge: Yes

Rechallenge: rechallenge was done, reaction did not recur

Causality for FLUOCINOLONE ACETONIDE (Open Label)

---

1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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

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

Dechallenge: Not Applicable

Causality for PREDNISOLONE (Open Label)

---

1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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 HERPES ZOSTER

- Investigator: Not applicable

- AbbVie: Not applicable

Alternative Etiology for FLUOCINOLONE ACETONIDE (Open Label)

Event of HERPES ZOSTER

- Investigator: More likely related to ABT-494/Placebo

- AbbVie: Week temporal association, last dose received 6 months prior to event onset.

Alternative Etiology for PREDNISOLONE (Open Label)

Event of HERPES ZOSTER

- Investigator: More likely related to ABT-494/Placebo

- AbbVie: Week temporal association, last dose received 6 months prior to event onset.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BODY TEMPERATURE:** 38.5 F

[redacted] **20[redacted] BODY TEMPERATURE:** 37.4 F

[redacted] **20[redacted] LYMPHOCTYE PERCENTAGE:** 16 % (normal 30 to 45)

[redacted] **20[redacted] WHITE BLOOD CELLS:** 9.5 X10**3/MCL (normal 3.5 to 9.0)

Subject [redacted] ([redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
単純ヘルペス	X			X

Treatment Group	Age at Study Start	Sex	Race
P1:Upa 30 mg QD /P2:Upa 30 mg QD	3[redacted]	MALE	ASIAN

Medical History	Onset Year
ASTHMA	20[redacted]
ATOPIC DERMATITIS	20[redacted]
HERPES SIMPLEX	20[redacted]
ASTHMA	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
P1:ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 115	115
P2:ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 116	[redacted]20[redacted] / 367	252

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LORATADINE	10 mg	QD	Y: 20[redacted]
MEQUITAZINE	3 mg	PRN	Y: 20[redacted]
OLOPATADINE	5 mg	BID	Y: 20[redacted]
TACROLIMUS	1 OTHER: APPLICATION	QD	Y: 20[redacted]

CICLOSPORIN	100 mg	BID	Y-M: 20[redacted] / -298
DIFLUPREDNATE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -298
DIFLUPREDNATE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -298
FEXOFENADINE	120 mg	BID	Y-M: 20[redacted] / -298
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -298
CICLOSPORIN	75 mg	BID	Y-M: 20[redacted] / -291
CICLOSPORIN	100 mg	QD	Y-M: 20[redacted] / -277
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / -277
CICLOSPORIN	75 mg	QD	Y-M: 20[redacted] / -256
CICLOSPORIN	100 mg	QD	Y-M: 20[redacted] / -244
DEXAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -239
CICLOSPORIN	50 mg	QD	Y-M: 20[redacted] / -195
CICLOSPORIN	75 mg	QD	Y-M: 20[redacted] / -193
CICLOSPORIN	75 mg	QD	Y-M: 20[redacted] / -137
CICLOSPORIN	75 mg	QD	Y-M: 20[redacted] / -73
TACROLIMUS	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / -46
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -18

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

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -298	NOT REPORTED
FEXOFENADINE	60 mg	BID	Y-M: 20[redacted] / -277	NOT REPORTED
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -18	NOT REPORTED
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 31
VIDARABINE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 16	Y-M: 20[redacted] / 45
PENCICLOVIR	1000 mg	QD	Y-M: 20[redacted] / 32	Y-M: 20[redacted] / 33
ACICLOVIR	250 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 36
PARACETAMOL	500 mg	TID	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 36
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 35	Y-M: 20[redacted] / 39
GUAIAZULENE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 42
PARACETAMOL	1000 mg	TID	Y-M: 20[redacted] / 36	Y-M: 20[redacted] / 42
ESZOPICLONE	2 mg	QD	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 41
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 42
PREGABALIN	75 mg	QD	Y-M: 20[redacted] / 37	Y-M: 20[redacted] / 44
PREGABALIN	25 mg	QD	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 44
CEFDITOREN	100 mg	TID	Y-M: 20[redacted] / 45	Y-M: 20[redacted] / 55

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

Event Description	HERPES SIMPLEX AGGRAVATED
Preferred term	単純ヘルペス
AE Onset Date / Rx Day	[redacted]20[redacted] / 34
Age at AE Onset	3[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 35): Lymphocytes: 1.36 [0.96 - 4.75] 10^9/L; NPTST054-HERPES SIMPLEX TYPE 1 ANTIGEN: POSITIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED
Microbiology	[redacted]20[redacted] (RX DAY 35): WOUND NPTST095-TZANCK TEST: POSITIVE-GIANT VIRAL CELLS ARE DETECTED.
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	45
Duration of AE	12 DAYS
Severity	Severe
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 3[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬，プレドニゾロン，フルオシノロンアセトニド及び tacrolimus を投与され，単純ヘルペス増悪を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴はアトピー性皮膚炎及び単純ヘルペスであった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は単純ヘルペス増悪を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，単純ヘルペス増悪は消失した。

本事象の発現前である 20[redacted] 年 [redacted] 月 [redacted] 日，有害事象である単純ヘルペス（非重篤）と初めて診断され，valaciclovir 及びビダラビン軟膏の投与が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，Famvir の投与が開始された。プレドニゾロン外用薬の投与は中止された。

本事象発現前，被験者は顔面に tacrolimus を使用していた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者が発熱した（体温の報告なし）。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は治験責任医師の診察を受けた。顔面全体の発赤及びそう痒とともに，右前額部及び左頬部の小さなびらん，紅斑及び小水疱が認められた。Tzanck 試験でウイルス性巨細胞が確認されたため，アシクロビルの点滴投与が開始された。体温は平熱であった。20[redacted] 年 [redacted] 月 [redacted] 日，症状の改善に乏しかったため，治験責任医師は被験者の入院が必要と判断した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はヘルペスに対する加療のため入院した。20[redacted] 年 [redacted] 月 [redacted] 日，アシクロビルの点滴投与が完了し，被験者は退院した。退院後の 20[redacted] 年 [redacted] 月 [redacted] 日，顔面にあった小さなびらんの消失が診察で確認された。

被験者は本事象発現前に帯状疱疹の予防接種を受けていなかった。本事象は眼病変を伴わなかった。

AZUNOL，LYRICA，LUNESTA，levofloxacin，アシクロビル，FAMVIR，ビダラビン，valaciclovir 及び CALONAL，が投与された。

The patient's past medications include:

LORATADINE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

MEQUITAZINE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

OLOPATADINE HYDROCHLORIDE for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

PROTOPIC for ATOPIC DERMATITIS (20[redacted] - [redacted] 20[redacted])

FEXOFENADINE HCL for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

MYSER for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

NEORAL for ATOPIC DERMATITIS [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

METHADERM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes simplex aggravated (10048418) (Herpes simplex (10019948)) [v.22.1] [10048418]

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 PREDNISOLONE (Open Label)

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1) Herpes simplex aggravated (10048418) (Herpes simplex (10019948)) [v.22.1] [10048418]

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

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

Dechallenge: Not Applicable

Causality for FLUOCINOLONE ACETONIDE (Open Label)

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1) Herpes simplex aggravated (10048418) (Herpes simplex (10019948)) [v.22.1] [10048418]

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

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

Dechallenge: Not Applicable

Causality for TACROLIMUS (Open Label)

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1) Herpes simplex aggravated (10048418) (Herpes simplex (10019948)) [v.22.1] [10048418]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of HERPES SIMPLEX AGGRAVATED

- Investigator: Not applicable

- AbbVie: Not applicable

Alternative Etiology for PREDNISOLONE (Open Label)

Event of HERPES SIMPLEX AGGRAVATED

- Investigator: More likely related to ABT-494/placebo

- AbbVie: Event more likely related to non-serious event of herpes simplex, which occurred prior to start of suspect drug.

Alternative Etiology for FLUOCINOLONE ACETONIDE (Open Label)

Event of HERPES SIMPLEX AGGRAVATED

- Investigator: More likely related to ABT-494/placebo

- AbbVie: Study drug is a low potency topical medication and unlikely to have significant local or systemic immunosupressive effects.

Alternative Etiology for TACROLIMUS (Open Label)

Event of HERPES SIMPLEX AGGRAVATED

- Investigator: More likely related to ABT-494/placebo

- AbbVie: N/A

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] HERPES SIMPLEX TYPE 1 ANTIGEN:** POSITIVE

[redacted] **20[redacted] TZANCK TEST:** positive: giant viral cells detected

Subject [redacted] ([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
カポジ水痘様発疹				X
気胸	X			

Treatment Group	Age at Study Start	Sex	Race
P1:Placebo /P2:Upa 30 mg QD	3[redacted]	MALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
BLEPHARITIS	20[redacted]
LUNG OPACITY	20[redacted]
PLEURAL SCARRING	20[redacted]
PLEURAL THICKENING	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 CIGARETTE	19	20[redacted]
CIGARS	NEVER			
E-CIGARETTES	CURRENT	20 SESSIONS	0.5	
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	More than 4

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
P1:Placebo		ORAL	QD	[redacted]0[redacted] / 1	[redacted]20[redacted] / 109	109
P2:ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 110	[redacted]20[redacted] / 357	248

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
HEPARIN	5 mL	PRN	Y-M: 20[redacted]-[redacted]
LACTIC ACID	2 OTHER: TABLET	QD	Y: 20[redacted]

ALCLOMETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
EPINASTINE	20 mg	PRN	Y-M: 20[redacted]
TRAMADOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
VALISONE-G	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
BETNESOL-N	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
VALISONE-G	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
EPINASTINE	20 mg	PRN	Y-M: 20[redacted]
VALISONE-G	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
EPINASTINE	20 mg	PRN	Y-M: 20[redacted]
DIFLUPREDNATE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -28
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	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
HEPARIN	5 mL	PRN	Y-M: 20[redacted]	Y-M: 20[redacted] / 375
LACTIC ACID	2 OTHER: TABLET	QD	Y: 20[redacted]	NOT REPORTED
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -7	NOT REPORTED
MOMETASONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 110	NOT REPORTED
PREDNISOLONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 110	NOT REPORTED
CEFMETAZOLE	1 g	QD	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 184
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 184	Y-M: 20[redacted] / 188
FEBUXOSTAT	20 mg	QD	Y-M: 20[redacted] / 233	Y-M: 20[redacted] / 263
FLURBIPROFEN	50 mg	PRN	Y-M: 20[redacted] / 255	Y-M: 20[redacted] / 257
CEFMETAZOLE	1 g	BID	Y-M: 20[redacted] / 255	Y-M: 20[redacted] / 259
HYDROXYZINE	25 mg	PRN	Y-M: 20[redacted] / 256	Y-M: 20[redacted] / 257
VALACICLOVIR	500 mg	BID	Y-M: 20[redacted] / 278	Y-M: 20[redacted] / 282
TRAMADOL	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 278	Y-M: 20[redacted] / 348
BREO ELLIPTA	400 mg	QD	Y-M: 20[redacted] / 359	Y-M: 20[redacted] / 360
GARENOXACIN	200 mg	QD	Y-M: 20[redacted] / 359	Y-M: 20[redacted] / 360

MEPIVACAINE	5 mL	QD	Y-M: 20[redacted] / 360	Y-M: 20[redacted] / 360
LOXOPROFEN	60 mg	PRN	Y-M: 20[redacted] / 360	Y-M: 20[redacted] / 375
REBAMIPIDE	100 mg	PRN	Y-M: 20[redacted] / 360	Y-M: 20[redacted] / 375
MEPIVACAINE	5 mL	QD	Y-M: 20[redacted] / 366	Y-M: 20[redacted] / 366
CEFAZOLIN	5 mL	QD	Y-M: 20[redacted] / 367	Y-M: 20[redacted] / 375
BETAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 374	Y-M: 20[redacted] / 382
CLOBETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 374	Y-M: 20[redacted] / 382
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 374	Y-M: 20[redacted] / 382
OLOPATADINE	5 mg	BID	Y-M: 20[redacted] / 374	Y-M: 20[redacted] / 382
CEFALEXIN	500 mg	TID	Y-M: 20[redacted] / 376	Y-M: 20[redacted] / 380
GENTAMICIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / 376	Y-M: 20[redacted] / 380

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

Event Description	APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 183
Age at AE Onset	3[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 255): ABDOMINAL X-RAY: NOT CLINICAL SIGNIFICANT; LAPAROSCOPIC APPENDECTOMY: DONE
AE Stopped Rx Day	278
Duration of AE	96 DAYS
Severity	Severe
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

Event #2: Event of Interest - Opportunistic Infection excluding Tuberculosis and Herpes Zosters

Event Description	KPOSI'S VARICELLIFORM ERUPTION
Preferred term	カポジ水痘様発疹
AE Onset Date / Rx Day	[redacted]20[redacted] / 264
Age at AE Onset	4[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE

SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	349
Duration of AE	86 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	CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

Event #3: Serious Adverse Event

Event Description	PNEUMOTHORAX
Preferred term	気胸
AE Onset Date / Rx Day	[redacted]20[redacted] / 358
Age at AE Onset	4[redacted]
Laboratory Testing	NOT REPORTED
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 358): CHEST X-P: PNEUMOTHORAX,AND PLEURAL EFFUSION; [redacted]20[redacted] (RX DAY 360): CHEST CT: PNEUMOTHORAX,MULTIPLE CYSTS ON BOTH LUNG APICES,AND ADHESIONS IN THE RIGHT PLUMONARY APEX.; CHEST DRAINAGE INSERTION: BY THE NEXT MORNING,THERE WAS 780 ML BLOODY DRAINAGE, CLAMP TEST ON [redacted]20[redacted],AND DRAIN WAS REMOVED ON [redacted]20[redacted] BECAUSE NO PROBLEM.; [redacted]20[redacted] (RX DAY 366): CHEST X-P: NO LUNG COLLAPSE; [redacted]20[redacted] (RX DAY 368): CHEST DRAIN INSERTION: AIR LEAK DISAPPENDED ON [redacted]20[redacted],CLAMP TEST ON [redacted]20[redacted],AND DRAIN WAS REMOVED ON [redacted]20[redacted] BECAUSE NO PROBLEM.; CHEST X-P: RIGHT LUNG COLLAPSE; [redacted]20[redacted] (RX DAY 375): CHEST CT: MULTIPLE BULLAS ON PULMONARY APEX; CHEST X-P: NO LUNG COLLAPSE
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Severe
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 3[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬，モメタゾンフランカルボン酸エステル及びプレドニゾロンを投与され，虫垂炎を発現した。被験者は元喫煙者（紙巻タバコ 20 本／日，19 年間）かつ飲酒者（4 杯超／日）で，関連する病歴はアトピー性皮膚炎であり，虫垂炎の家族歴（母，兄弟）があった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は虫垂炎を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，虫垂炎は消失した。

入院前の 20[redacted] 年 [redacted] 月 [redacted] 日，被験者は重度の腹痛を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は近医を受診し，虫垂炎と診断された。近医では外科手術が後日必要と判断され，セフメタゾールナトリウム（1 g）が 1 回静脈内投与された後，Cravit 錠が投与された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は虫垂切除を目的に入院した。20[redacted] 年 [redacted] 月 [redacted] 日，腹腔鏡下虫垂切除術が施行された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

ATARAX，ROPION，セフメタゾールナトリウム及び CRAVIT が投与された。

Causality for UPADACITINIB (Blinded)

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1) Appendicitis (10003011) (Appendicitis (10003011)) [v.22.1] [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

Causality for MOMETASONE FUROATE (Open Label)

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1) Appendicitis (10003011) (Appendicitis (10003011)) [v.22.1] [10003011]

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

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

Dechallenge: Not Applicable

Causality for PREDNISOLONE (Open Label)

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1) Appendicitis (10003011) (Appendicitis (10003011)) [v.22.1] [10003011]

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 APPENDICITIS

- Investigator: Not applicable.

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males.

Alternative Etiology for MOMETASONE FUROATE (Open Label)

Event of APPENDICITIS

- Investigator: More likely related to Upadacitinib/Placebo.

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males.

Alternative Etiology for PREDNISOLONE (Open Label)

Event of APPENDICITIS

- Investigator: More likely related to Upadacitinib/Placebo.

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males.

Relevant Laboratory & Other Diagnostic Tests

[redacted] [redacted] 20[redacted] **ABDOMINAL X-RAY:** Not clinical significant.

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 4[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬，モメタゾンフランカルボン酸エステル及びプレドニゾロンを投与され，気胸を発現した。被験者は元喫煙者（紙巻タバコ 20 本／日，19 年間），電子タバコ使用者（20 セッション 0.5 年間）かつ飲酒者（4 杯超／日）で，関連する病歴はアトピー性皮膚炎，肺陰影，胸膜癒痕及び胸膜肥厚であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は気胸を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸痛及び胸部不快感を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は胸部不快感の増強を訴えており，呼吸器感染が疑われた。20[redacted] 年 [redacted] 月 [redacted] 日，医師は第 52 週の規定来院日に撮影された胸部 X 線像を評価し，気胸と診断した。被験者は入院し，胸腔ドレーンを留置された。ドレーンのクランプテストが行われ，血性排液 780 mL が確認された。20[redacted] 年 [redacted] 月 [redacted] 日，ドレーンチューブが抜去された。同日，被験者は胸膜炎及び胸腔ドレーン留置部位感染（いずれも非重篤）を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，右肺の虚脱状態が認められ，もう一度ドレーンが留置された。20[redacted] 年 [redacted] 月 [redacted] 日，右肺のエアリークは消失し，クランプテストは陰性で，ドレーンチューブ抜去による問題も生じなかった。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は退院した。

GENINAX 及び RELVAR が投与された。

The patient's past medications include:

ALESION for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ALMETA for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON-VG for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] [redacted] 20[redacted] - [redacted] 20[redacted])

RINDERON-A for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] [redacted] 20[redacted])

MYSER for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for UPADACITINIB (Blinded)

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1) Pneumothorax (10035759) (Pneumothorax (10035759)) [v.23.0] [10035759]

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

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

Dechallenge: No

Causality for MOMETASONE FUROATE (Open Label)

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1) Pneumothorax (10035759) (Pneumothorax (10035759)) [v.23.0] [10035759]

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

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

Dechallenge: Not Applicable

Causality for PREDNISOLONE (Open Label)

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1) Pneumothorax (10035759) (Pneumothorax (10035759)) [v.23.0] [10035759]

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 PNEUMOTHORAX

- Investigator: Not Applicable

- AbbVie: Risk factors include significant tobacco history of 19 pack years and a male with relatively tall stature.

Alternative Etiology for MOMETASONE FUROATE (Open Label)

Event of PNEUMOTHORAX

- Investigator: More likely related to Upadacitinib/Placebo

- AbbVie: Event not consistent with study drug's mechanism of action.

Alternative Etiology for PREDNISOLONE (Open Label)

Event of PNEUMOTHORAX

- Investigator: More likely related to Upadacitinib/Placebo

- AbbVie: Event not consistent with study drug's mechanism of action.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST CT:** Pneumothorax, multiple cysts on both lung apices, and adhesions in the right pulmonary apex.

[redacted] **20[redacted] CHEST CT:** Multiple bullas on pulmonary apex.

[redacted] **20[redacted] CHEST X-RAY:** AT SCREENING: Abnormal: Positive pleural scarring and pleural thickening, no calcified granulomas, no signs of active TB infection.

[redacted] **20[redacted] CHEST X-RAY:** Week 52: Abnormal - calcified granulomas and pleural scarring present. No signs of pleural thickening or active TB. Pneumothorax and pleural effusion.

[redacted] **20[redacted] CHEST X-RAY:** No lung collapse.

[redacted] **20[redacted] CHEST X-RAY:** Right lung collapse.

[redacted] **20[redacted] CHEST X-RAY:** No lung collapse.

非重篤な有害事象

被験者はカポジ水痘様発疹（罹患範囲不明）を発現し，抗ウイルス薬及び外用薬が投与された。丘疹小水疱性の発疹であった。カポジ水痘様発疹の推定罹患面積は 1.5%であった。原因は不明であった。細菌による重複感染の発現有無は不明であった。本事象による治験薬の投与変更はなかった。本事象は消失した。

Subject [redacted] ([redacted])

Reason for Narrative

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

Treatment Group	Age at Study Start	Sex	Race
P1:Upa 15 mg QD /P2:Upa 15 mg QD	1[redacted]	MALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	20[redacted]
ALLERGIC RHINITIS	20[redacted]
FOOD ALLERGY	20[redacted]
ECZEMA IMPETIGINOUS	20[redacted]
HERPES SIMPLEX	20[redacted]
ACNE	20[redacted]
ALLERGIC RHINITIS	NOT REPORTED
FOOD ALLERGY	NOT REPORTED

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
P1:ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 110	110
P2:ABT-494	15 MG	ORAL	QD	[redacted]20[redacted] / 111	[redacted]20[redacted] / 360	250

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
DEXAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]-[redacted]

RETINOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
DEXAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
RETINOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
DEXAMETHASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
PREDNISOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
RETINOL	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
ALCLOMETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
GUAIAZULENE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
CLOBETASONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
HYDROCORTISONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
GUAIAZULENE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
DIFLUCORTOLONE	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]
BEPOTASTINE	10 mg	BID	Y-M: 20[redacted] / -117
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	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
HEPARINOID	1 OTHER: APPLICATION	BID	Y-M: 20[redacted]	NOT REPORTED
BEPOTASTINE	10 mg	BID	Y-M: 20[redacted] / -117	NOT REPORTED
WHITE SOFT PARAFFIN	1 OTHER: APPLICATION	BID	Y-M: 20[redacted] / -7	NOT REPORTED
MOMETASONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 111	NOT REPORTED
PREDNISOLONE	1 OTHER: APPLICATION	QD	Y-M: 20[redacted] / 111	NOT REPORTED
PARACETAMOL	200 mg	PRN	Y-M: 20[redacted] / 302	Y-M: 20[redacted] / 303

SULPERAZON	1 g	BID	Y-M: 20[redacted] / 302	Y-M: 20[redacted] / 303
DICLOFENAC	25 mg	PRN	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 303
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 303
MEROPENEM	0.5 g	TID	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 308
STRONG NEO-MINOPHAGEN C	20 mL	QD	Y-M: 20[redacted] / 303	Y-M: 20[redacted] / 310
CEFTRIAXONE	1 g	BID	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 312
PARACETAMOL	400 mg	PRN	Y-M: 20[redacted] / 309	Y-M: 20[redacted] / 312
LEVOFLOXACIN	500 mg	QD	Y-M: 20[redacted] / 318	Y-M: 20[redacted] / 323

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

Event Description	APPENDICITIS
Preferred term	虫垂炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 301
Age at AE Onset	1[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 302): Leukocytes: 13 [3.9 - 9.8] 10^9/L
Microbiology	NOT REPORTED
SAE Supplemental Procedure	[redacted]20[redacted] (RX DAY 303): ABDOMINAL CT SCAN: GANGRENE APPENDICITIS; [redacted]20[redacted] (RX DAY 308): ABSCESSES DRAINAGE: DRAINED PUS
AE Stopped Rx Day	NOT REPORTED
Duration of AE	NOT REPORTED
Severity	Severe
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

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

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 1[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬，モメタゾンフランカルボン酸エステル及びプレドニゾロンを投与され，虫垂炎を発現した。被験者は非喫

煙者かつ非飲酒者であり，関連する病歴はアトピー性皮膚炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は虫垂炎を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は重度の腹痛を発現したため病院を受診したが，診断や薬剤治療は行われず帰宅した。その夜，被験者は発熱した（体温の報告なし）。20[redacted] 年 [redacted] 月 [redacted] 日，腹痛が持続したため，被験者は別の小児科病院を受診した。被験者は虫垂炎と診断され，同日に入院した。白血球数は 13000 U/L であった。sulperazon 及び calonal の投与が開始された。20[redacted] 年 [redacted] 月 [redacted] 日，腹部コンピュータ断層撮影で壊疽性虫垂炎と確認された。Neo-Minophagen C，voltaren 及び Acelio の投与が開始され，抗生物質は meropenem に変更された。20[redacted] 年 [redacted] 月 [redacted] 日，腹痛及び発熱は持続していた。ドレーンチューブを挿入して膿瘍ドレナージを行い，排膿させた。meropenem の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，ceftriaxone の投与が開始され，Neo-Minophagen C の投与は中止された。20[redacted] 年 [redacted] 月 [redacted] 日，ceftriaxone の投与が終了した。20[redacted] 年 [redacted] 月 [redacted] 日，ドレーンチューブが抜去された。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は levofloxacin を処方されて退院した。20[redacted] 年 [redacted] 月 [redacted] 日，被験者はクリニックを受診し，症状はないと確認された。

SULPERAZON，meropenem，NEO-MINOPHAGEN C，levofloxacin，CEFTRIAXONE NA，ACELIO，VOLTAREN 及び CALONAL が投与された。

The patient's past medications include:

MAINVATE OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

SAHNE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ABOCOAT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

SPIRAZON LOTION for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ALMETA for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

AZUNOL OINTMENT for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

KINDALONE for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

HEPARINOID OIL-BASED CREAM for ATOPIC DERMATITIS ([redacted] 20[redacted] - [redacted] 20[redacted])

ARUSONA UNIVERSAL CREAM for ATOPIC DERMATITIS ([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: No

Causality for MOMETASONE FUROATE (Open Label)

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1) Appendicitis (10003011) (Appendicitis (10003011)) [v.23.0] [10003011]

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

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

Dechallenge: Not Applicable

Causality for PREDNISOLONE (Open Label)

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1) Appendicitis (10003011) (Appendicitis (10003011)) [v.23.0] [10003011]

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 APPENDICITIS

- Investigator: Not applicable

- AbbVie: Event is common in the general population; lifetime incidence is 8.6percent in males.

Alternative Etiology for MOMETASONE FUROATE (Open Label)

Event of APPENDICITIS

- Investigator: More likely related to UPADACITINIB/Placebo

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males.

Alternative Etiology for PREDNISOLONE (Open Label)

Event of APPENDICITIS

- Investigator: More likely related to UPADACITINIB/Placebo

- AbbVie: Event is common in the general population; lifetime incidence is 8.6 percent in males.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT SCAN:** Gangrene appendicitis.

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

[redacted] **20[redacted] WHITE BLOOD CELLS:** 13000 U/L (normal 3900 to 9800)

Subject [redacted] ([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 Study Start	Sex	Race
P1:Upa 30 mg QD /P2:Upa 30 mg QD	4[redacted]	MALE	ASIAN

Medical History	Onset Year
ATOPIC DERMATITIS	19[redacted]
CHICKENPOX	20[redacted]
SHINGLES	20[redacted]
ATOPIC DERMATITIS	20[redacted]

Prior Procedures	Procedure Year
Not reported.	

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

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	Less than 2

Study Drug Administration

Study Drug	Dose/Units	Route	Frequency	First Dose Date/Day	Last Dose Date/Day	Duration (Days)
P1:ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 1	[redacted]20[redacted] / 110	110
P2:ABT-494	30 MG	ORAL	QD	[redacted]20[redacted] / 111	[redacted]20[redacted] / 362	252

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
BETAMETHASONE	0.05 %	BID	Y-M: 20[redacted]
HEPARINOID	0.3 %	QD	Y-M: 20[redacted]
PREDNISOLONE	0.3 %	BID	Y-M: 20[redacted]
DIFLUPREDNATE	0.05 %	QD	Y-M: 20[redacted]
TACROLIMUS	0.1 %	QD	Y-M: 20[redacted]

BILASTINE	20 mg	QD	Y-M: 20[redacted] / -331
CICLOSPORIN	50 mg	QD	Y-M: 20[redacted] / -296
BEPOTASTINE	20 mg	BID	Y-M: 20[redacted] / -212
WHITE SOFT PARAFFIN	500 mg	BID	Y-M: 20[redacted] / -9

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
HEPARINOID	0.3 %	QD	Y-M: 20[redacted]	NOT REPORTED
BILASTINE	20 mg	QD	Y-M: 20[redacted] / -331	NOT REPORTED
WHITE SOFT PARAFFIN	500 mg	BID	Y-M: 20[redacted] / -9	NOT REPORTED
ELECTROLYTES NOS	500 mL	QD	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 236
SODIUM CHLORIDE	500 mL	QD	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 236
FAMCICLOVIR	500 mg	TID	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 237
ACICLOVIR	250 mg	TID	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 243
GENTAMICIN	0.1 %	BID	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 279
PARACETAMOL	600 mg	TID	Y-M: 20[redacted] / 236	Y-M: 20[redacted] / 314
ACICLOVIR	3 %	TID	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 279
BROMFENAC	0.1 %	BID	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 279
LEVOFLOXACIN	0.5 %	TID	Y-M: 20[redacted] / 238	Y-M: 20[redacted] / 309
PARACETAMOL	600 mg	TID	Y-M: 20[redacted] / 315	Y-M: 20[redacted] / 363

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 / Rx Day	[redacted]20[redacted] / 231
Age at AE Onset	4[redacted]
Laboratory Testing	[redacted]20[redacted] (RX DAY 236): NPTST116-VARICELLA-ZOSTER VIRU-SPECIFIC: POSITIVE [NOT REPORTED - NOT REPORTED] RATIO; NPTST117-VARICELLA-ZOSTER VIRUS-SPECIFIC: POSITIVE [NOT REPORTED - NOT REPORTED] RATIO
Microbiology	[redacted]20[redacted] (RX DAY 236): OTHER VESICULAR FLUID NPTST044-DIRECT FIUORESCENT ANTIBODY: POSITIVE-POSITIVE
SAE Supplemental Procedure	NOT REPORTED
AE Stopped Rx Day	315
Duration of AE	85 DAYS
Severity	Severe
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
Investigator Alternative Etiology	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

Event #2: Event of Interest - Herpes Zoster

Event Description	POST HERPETIC NEURALGIA
Preferred term	ヘルペス後神経痛

AE Onset Date / Rx Day	[redacted]20[redacted] / 315
Age at AE Onset	4[redacted]
Laboratory Testing	NOT APPLICABLE
Microbiology	NOT APPLICABLE
SAE Supplemental Procedure	NOT APPLICABLE
AE Stopped Rx Day	363
Duration of AE	49 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	CONCOMITANT OR ADDITIONAL TRTMNT GIVEN

Generated: [redacted]
Program Source Code [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M17-377

本被験者は日本の 4[redacted] 歳男性であり，ウパダシチニブの治験で盲検化された治験薬を投与され，帯状疱疹を発現した。被験者は非喫煙者かつ飲酒者（2 杯未満／日）であり，関連する病歴は水痘，帯状疱疹及びアトピー性皮膚炎であった。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹を発現した。20[redacted] 年 [redacted] 月 [redacted] 日，帯状疱疹は消失した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は右顔面痛を自覚し始めた。20[redacted] 年 [redacted] 月 [redacted] 日，被験者は耳鼻咽喉科を受診した。20[redacted] 年 [redacted] 月 [redacted] 日，右顔面に水疱が認められた。被験者はその後，帯状疱疹と診断された。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹のため皮膚科を受診した。被験者は，入院にて acyclovir の点滴投与を受けるよう勧められたが，入院は拒否した。点滴治療の後にめまい感が始まり，念のため，被験者はストレッチャーで皮膚科の診療室に戻された。その後，被験者は意識を消失し，救急科に搬送された。被験者は血圧が降下しており，熱射病（非重篤）と判断され静脈内補液を受けた。被験者は血圧が正常に復したため，同日に帰宅した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は帯状疱疹による発熱（36.8℃）及び倦怠感のため睡眠障害を発現し，入院した。入院中，下痢及び歩き回り（いずれも非重篤）を発現した。この他，発汗，失神，腹痛，脱水，不眠症及び食欲不振も発現した。帯状疱疹によるびらんが口内及び口蓋右側に認められた。項部硬直は認められなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，右前額部，下顎及び口唇右側の水疱が増悪した。20[redacted] 年 [redacted] 月 [redacted] 日，両頬部などに膿疱が残存するが，両耳及び顎部では痂皮形成が進んでいた。ピリピリ感はあったが，問題となるほどの疼痛はなかった。被験者のリンパ球は改善し，20[redacted] 年 [redacted] 月 [redacted] 日に被験者は退院

した。

被験者には水痘及び帯状疱疹の病歴があった。

被験者は本事象の発現前に帯状疱疹の予防接種を受けていなかった。

COCARL，アシクロビル，YD SOLITA-T NO. 1，BRONUCK OPHTHALMIC SOLUTION，LEVOFLOXACIN OPHTHALMIC SOLUTION，静注用生理食塩液，ゲンタマイシン硫酸塩，FAMVIR 及び ZOVIRAX OPHTHALMIC OINTMENT が投与された。

The patient's past medications include:

BETAMETHASONE BUTYRATE PROPINATE for ATOPIC DERMATITIS ([redacted])

PREDNISOLONE VALERATE ACETATE for ATOPIC DERMATITIS ([redacted])

DIFLUPREDNATE for ATOPIC DERMATITIS ([redacted])

NEORAL for ATOPIC DERMATITIS ([redacted])

BEPOTASTINE BESILATE for ATOPIC DERMATITIS ([redacted])

PREDNISOLONE for ATOPIC DERMATITIS ([redacted])

TRIAMCINOLONE ACETONIDE for ATOPIC DERMATITIS ([redacted])

Causality for UPADACITINIB (Blinded)

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1) Herpes zoster (10019974) (Herpes zoster (10019974)) [v.22.1] [10019974]

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

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

Dechallenge: Not Applicable

Alternative Etiology for UPADACITINIB (Blinded)

Event of HERPES ZOSTER

- Investigator: Not applicable

- AbbVie: Not applicable

Relevant Laboratory & Other Diagnostic Tests

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

[redacted] 20[redacted] DIRECT FLUORESCENT ANTIBODY (WOUND): (Vesicular fluid) Positive

20[redacted] LYMPHOCYTES: After hospitalization: 1.33 (no units)

Unknown date LYMPHOCYTES: Before hospitalization: 1.47 (no units)

[redacted] 20[redacted] VARICELLA VIRUS TEST: (Blood) Positive

[redacted] 20[redacted] VARICELLA VIRUS TEST: (Vesicular fluid) Positive

非重篤な有害事象

被験者はヘルペス後神経痛を発現し，治療としてアセトアミノフェンが投与された。本事象による治験薬の投与変更はなかった。本事象は消失した。